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| FINAL REGISTRATION REPORT  Part B  Section 9  Ecotoxicology  Detailed summary of the risk assessment |
| Product code: SAP250F  Product name(s): **Dyllis** (prev. INDOFIL Prothio 250 EC)  Chemical active substance:  Prothioconazole, 250 g/L |
| Central Zone  Zonal Rapporteur Member State: Poland |
| CORE ASSESSMENT |
| Applicant: Indofil Industries (Netherlands) BV  Submission date: 30/04/2021  MS Finalisation date: 08/2022, 02/2023, 05/2024, 07/2024, 08/2024 |

Version history

|  |  |
| --- | --- |
| When | What |
| April 2021 | V0 - Original version from applicant Indofil Industries (Netherlands) B.V. for submission to z-RMS in the frame of the PPP Authorization according to Article 33 of Regulation (EC) No 1107/2009. |
| August 2022 | zRMS first evaluation |
| February 2023 | Final Version after commenting period process. |
| April 2024 | Applicant updates addresing evaluator’s comment about buffer zone |
| May, July 2024 | Assessmet of updated risk for aquatic. |
| August 2024 | Assessmet of updated risk for aquatic. |

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# Ecotoxicology (KCP 10)

This document reviews the eco-toxicological studies for the product SAP250F an emulsifiable concentrate formulation containing 250 g/L Prothioconazole for use on wheat, barley, oat, rye and triticale and oilseed rape.

Prothioconazole was first included in Annex I to Directive 91/414/EEC by Commission Directive 2008/44/EC of 4 April 2008.

A full risk assessment according to Uniform Principles is provided which demonstrates that the product is safe for the environment.

Where appropriate this document refers to the conclusions of the EU review of Prothioconazole. This will be where:

• the active substance data are relied upon in the risk assessment of the formulation; or when

• the EU review concluded that additional data/information should be considered at national re-registration.

Note: this Part B document only reviews data (Annex II or Annex III) and additional information that has not previously been considered within the EU review process, as part of the Annex I inclusion decision. New annex II data must only be included if they are considered essential for the evaluation and in this case a full study summary must be provided. In the case where the formulation has been previously evaluated, at European level, detailed summaries have not been provided.

This product was not the representative formulation and has not been previously evaluated according to the Uniform Principles.

The EFSA Scientific report for Prothioconazole (EFSA Scientific Report, 2007) is considered to provide the relevant review information or a reference to where such information can be found.

The Commission Implementing Regulation for Prothioconazole (540/2011) provides specific provisions under Part B which need to be considered by the applicant in the preparation of their submission and by the MS prior to granting an authorisation.

For the implementation of the uniform principles as referred to in Article 29(6) of Regulation (EC) No 1107/2009, the conclusions of the review report on prothioconazole, and in particular Appendices I and II thereof, as finalised in the Standing Committee on the Food Chain and Animal Health on 22 January 2008 shall be taken into account.

In this overall assessment Member States must pay particular attention to:

— the operator safety in spray applications. Conditions of use shall include adequate protective measures,

— the protection of aquatic organisms. Risk mitigation measures such as buffer zones shall be applied, where appropriate,

— the protection of birds and small mammals. Risk mitigation measures shall be applied, where appropriate.

Conditions of use shall include risk mitigation measures, where appropriate.

Information on the detailed composition of SAP250F can be found in the confidential dossier of this submission (Registration Report - Part C).

## Critical GAP and overall conclusions

Table 9.1‑1: Table of critical GAPs

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Use-No. \* | Member state(s) | Crop and/or situation  (crop destination / purpose of crop) | F, Fn, Fpn G, Gn, Gpn or  I \*\* | Pests or Group of pests controlled  (additionally: developmental stages of the pest or pest group) | Application | | | | Application rate | | | PHI  (days) | Remarks:  e.g. g saf­ener/ syner­gist per ha | Conclusion | | | | | | |
| Method / Kind | Timing / Growth stage of crop & season | Max. number  a) per use  b) per crop/ season | Min. interval between applications (days) | kg or L product/ha  a) max. rate per appl.  b) max. total rate per crop/season | g or kg as/ha  a) max. rate per appl.  b) max. total rate per crop/season | Water L/ha  min/max | Birds | Mammals | Aquatic organisms | Bees | Non-target arthropods | Soil organisms | Non-target plants |
| Zonal uses (field or outdoor uses, certain types of protected crops) | | | | | | | | | | | | | | | | | | | | |
| 1 | ~~SEU (ES, FR, IT, EL, PT, BG, HR)~~  DE, AT, UK, IE, NL, BE, CZ, SI,  PL  SK, HU, RO | Wheat (winter and spring; soft and durum) | F | Fusarium (FUSASP)*, Septoria* (SEPTTR)*, Puccinia* (PUCCSP),  *Oculimacula yallundae* (PSDCHE),*Blumeria graminis* (ERYSGR) | High vol spray | BBCH  26-69 | a) 3  b) 3 | 14 | a) 0.8 L/ha  b) ~~1.6~~ 2.4 L/ha | a) 0.2 kg as/ha  b) ~~0.4~~ 0.6 kg as/ha | 150-400 | 35 |  |  |  |  |  |  |  |  |
| 2 | ~~SEU (ES, FR, IT, EL, PT, BG, HR)~~  DE, AT, UK, IE, NL, BE, CZ, SI,  PL  SK, HU, RO | Barley (spring and winter) | F | Fusarium (FUSASP)*, Helminthosporium* (PYRNSP)*,Ramulariose* (RAMUCC)*,Rhynchosporium*  (RHYNSE)*,Puccinia* (PUCCSP),*Oculimacula yallundae* (PSDCHE)*,Blumeria graminis* (ERYSGR) | High vol spray | BBCH  26-69 | a) 3  b) 3 | 14 | a) 0.8 L/ha  b) ~~1.6~~ 2.4 L/ha | a) 0.2 kg as/ha  b) ~~0.4~~ 0.6 kg as/ha | 150-400 | 35 |  |  |  |  |  |  |  |  |
| 3 | ~~SEU (ES, FR, IT, EL, PT, BG, HR)~~  DE, AT, UK, IE, NL, BE, CZ, SI,  PL  SK, HU, RO | Oat | F | Fusarium (FUSASP)*, Puccinia* (PUCCSP),*Oculimacula yallundae* (PSDCHE)*,Blumeria graminis* (ERYSGR) | High vol spray | BBCH  26-69 | a) 3  b) 3 | 14 | a) 0,8 L/ha  b) ~~1,6~~ 2.4 L/ha | a) 0,2 kg as/ha  b) ~~0,4~~ 0.6 Kg as/ha | 150-400 | 35 |  |  |  |  |  |  |  |  |
| 4 | ~~SEU (ES, FR, IT, EL, PT, BG, HR)~~  DE, AT, UK, IE, NL, BE, CZ, SI,  PL  SK, HU, RO | Rye | F | Fusarium (FUSASP)*, Rhynchosporium* (RHYNSE)*,*  *Puccinia* (PUCCSP) | High vol spray | BBCH  26-69 | a) 3  b) 3 | 14 | a) 0,8 L/ha  b) ~~1,6~~ 2.4 L/ha | a) 0,2 kg as/ha  b~~) 0,4~~ 0.6 Kg as/ha | 150-400 | 35 |  |  |  |  |  |  |  |  |
| 5 | ~~SEU (ES, FR, IT, EL, PT, BG, HR)~~  DE, AT, UK, IE, NL, BE, CZ, SI,  PL  SK, HU, RO | Triticale | F | Fusarium (FUSASP)*, Septoria* (SEPTTR)*,*  *Blumeria graminis* (ERYSGR) | High vol spray | BBCH  26-69 | a) 3  b) 3 | 14 | a) 0,8 L/ha  b) ~~1,6~~ 2.4 L/ha | a) 0,2 kg as/ha  b) ~~0,4~~ 0.6 Kg as/ha | 150-400 | 35 |  |  |  |  |  |  |  |  |
| 6 | ~~FR, IT, BG, HR~~  DE, AT, UK, IE, NL, BE, CZ, SI,  PL  SK, HU, RO | OSR | F | *Sclerotinia* (SCLESC) *Cylindrosporiose* (PYRPBR)  *Alternaria* (ALTEBA), | High vol spray | BBCH  20-80 | a) 3  b) 3 | 14-21 | a) 0.7 L/ha  b) ~~1.4~~ 2.1 L/ha | a) 0.175 kg as/ha  b) 0.525 ~~0.35~~ kg as/ha | 200-400 | 56 |  |  |  |  |  |  |  |  |
| ~~FR, IT, ES, BG, HR~~  DE, AT, UK, IE, NL, BE, CZ, SI,  PL  SK, HU, RO | OSR | F | *Erysiphe cruciferarum* (ERYSCR) |
| **Minor uses according to Article 51 (field uses)** | | | | | | | | | | | | | | | | | | | | |
| 7 | ~~PT, ES, EL~~  DE, AT, UK, IE, NL, BE, CZ, SI,  PL  SK, HU, RO | OSR | F | *Sclerotinia* (SCLESC) *Cylindrosporiose* (PYRPBR)  *Alternaria* (ALTEBA), | High vol spray | BBCH  20-80 | a) 3  b) 3 | 14-21 | a) 0.7 L/ha  b) ~~1.4~~ 2.1 L/ha | a) 0.175 kg as/ha  b) ~~0.35~~ 0.525 kg as/ha | 200-400 | 56 |  |  |  |  |  |  |  |  |
| ~~PT, EL~~  DE, AT, UK, IE, NL, BE, CZ, SI,  PL  SK, HU, RO | OSR | F | *Erysiphe cruciferarum* (ERYSCR) |

\* 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

Explanation for column 15 – 21 “Conclusion”

|  |  |
| --- | --- |
| A | Acceptable, Safe use |
| R | Further refinement and/or risk mitigation measures required |
| C | To be confirmed by cMS |
| N | No safe use |

|  |  |  |  |
| --- | --- | --- | --- |
|  |  |  |  |
| **Remarks**  **table:** | (1) Numeration necessary to allow references  (2) Use official codes/nomenclatures of EU  (3) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)  (4) 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  (5) Scientific names and EPPO-Codes of target pests/diseases/ weeds or when relevant the common names of the pest groups (e.g. biting and sucking insects, soil born insects, foliar fungi, weeds) and the developmental stages of the pests and pest groups at the moment of application must be named  (6) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench  Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated |  | (7) Growth stage at first and last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3‑8263-3152-4), including where relevant, information on season at time of application  (8) The maximum number of application possible under practical conditions of use must be provided  (9) Minimum interval (in days) between applications of the same product.  (10) For specific uses other specifications might be possible, e.g.: g/m³ in case of fumigation of empty rooms. See also EPPO-Guideline PP 1/239 Dose expression for plant protection products  (11) The dimension (g, kg) must be clearly specified. (Maximum) dose of a.s. per treatment (usually g, kg or L product / ha).  (12) If water volume range depends on application equipments (e.g. ULVA or LVA) it should be mentioned under “application: method/kind”.  (13) PHI - minimum pre-harvest interval  (14) Remarks may include: Extent of use/economic importance/restrictions |

### Overall conclusions

**zRMS comment:**

Since report in dRR format is prepared by the applicant, all remarks, comments, additional calculations and assessment done by the ZRMS are included in the commenting boxes or indicated in blue.

#### Effects on birds (KCP 10.1.1), Effects on terrestrial vertebrates other than birds (KCP 10.1.2), Effects on other terrestrial vertebrate wildlife (reptiles and amphibians) (KCP 10.1.3)

For acute dietary exposure of birds to the active substance Prothioconazole, the TER for the required uses are above the trigger value at the Screening step whereas an acceptable acute risk was demonstrated for Prothioconazole-desthio at the first tier. For the chronic (reproductive) dietary exposure of birds to the active substance Prothioconazole and its metabolite JAU 6476-desthio, the TER for the required uses are above the trigger value at the screening step for the active substance (Prothioconazole) or at the first-tier step for the metabolite (JAU 6476-desthio). The risk to birds exposed to SAP250F via drinking water is acceptable for the intended use as the ratio between the effective application rate and the acute and long-term endpoints is below 3000 (Prothioconazole is more sorptive). Secondary poisoning assessments were triggered for ~~both P~~rothioconazole and its metabolites (JAU 6476-desthio) and M01. No unacceptable risks were found on the assessment of biomagnification in terrestrial food chains after application of SAP250F in the intended uses. Therefore, treatment with SAP250F in accordance with the proposed uses poses an acceptable risk to birds.

For acute dietary exposure of mammals to the active substance Prothioconazole and its metabolite JAU 6476-desthio, the TER for the required uses are above the trigger value at the Screening step. For the chronic (reproductive) dietary exposure of mammals to the active substance Prothioconazole, the TER for the required uses is ~~above~~ below the trigger value at the screening step, indicating a potential risk from the exposure of mammals to the metabolite. In the first risk assessment step, unacceptable risks were still found from herbivorous mammals exposure to the metabolite JAU 6476-desthio. After refinement of PT, fTWA, refined data from residue studies and/or focal species, no unacceptable risks were found for either small or large herbivorous mammals. The risk to mammals exposed to SAP250F via drinking water is acceptable for the intended use as the ratio between the effective application rate and the acute and long-term endpoints is below 3000 (Prothioconazole is more sorptive). Secondary poisoning assessments were triggered for ~~both~~ Prothioconazole and its metabolites (JAU 6476-desthio) and M01. No unacceptable risks were found on the assessment of biomagnification in terrestrial food chains after application of SAP250F in the intended uses. Therefore, treatment with SAP250F in accordance with the proposed uses poses an acceptable risk to mammals.

#### Effects on aquatic organisms (KCP 10.2)

~~The risk to aquatic non-target organisms following treatment with SAP250F according to all proposed use patterns is acceptable without any mitigation measures.~~

~~After re-evaluation of the metabolite JAU6467-desthio, from the risk assessment results presented above it can be conclude that a 10 meters of an unsprayed buffer zone, including vegetated filter guarantees that the exposure assessment presented is protective for aquatic systems when SAP250F is applied once per season, for all uses defended in the GAP.~~

~~For winter cereals, winter oilseed rape and spring oilseed rape, 20 meters of an unsprayed buffer zone, including vegetated filter guarantees is protective for aquatic systems when SAP250F is applied twice per season.~~

~~Also a mitigation measure concerning the artificial drained soils should be applied for winter cereals and winter oilseed rape.~~

~~Regarding the use of spring cereals, a restriction on BBCH is proposed. Therefore, for BBCH 41-69, the mitigation measure of 10 meters of a non-sprayed buffer zone, including a vegetated filter, is sufficiently protective for the aquatic system.~~

The risk assessment for a.s. prothioconazole and metabolites Prothioconazole-thiazocine and , 1,2,4-triazole is considered acceptable for aquatic organism as PEC/RAC ratio is below trigger value of 1 without risk mitigation measure. For metabolite of a.s. - JAU6476-desthio for the most sensitive organism O.mykiss the PEC/RAC is below trigger of 1 when the following risk mitigation measures for the multiple application as the worst case, are applied to surface water bodies:

*Winter Cereals (3 x 200 g/ha)*

For R1 and R3 stream scenarios: 20 m unsprayed buffer zone + 20 meter vegetative buffer strip

For R4 scenarios further refinement is required as the 20 m unsprayed buffer zone + 20 meter vegetative buffer strip is not sufficient to conclude acceptable risk for fish

*Spring Cereals (3 x 200 g/ha)*

For R4 scenarios further refinement is required as the 20 m unsprayed buffer zone + 20 meter vegetative buffer strip is not sufficient to conclude acceptable risk for fish

*Winter Oilseed rape – early (2 x 175 g/ha)*

For R1 and R3 stream scenarios: 20 m unsprayed buffer zone + 20 meter vegetative buffer strip

*Winter Oilseed rape – late (2 x 175 g/ha)*

For R1 and R3 stream scenarios: 10 m unsprayed buffer zone + 10 meter vegetative buffer strip

*Spring Oilseed Rape (2 x 175 g/ha)*

For R1 stream scenario 20 m unsprayed buffer zone + 20 meter vegetative buffer strip

**Further refinement for chronic risk for fish for R4 scenario is required for winter and spring cereals at MSs level.**

#### Effects on bees (KCP 10.3.1)

The risk assessment performed for both the active substance and the formulated product derived hazard quotients lower than 50, indicating that the active substance as well as the formulation SAP250F pose an acceptable risk to bees from oral and contact exposure according the proposed use. Besides, a chronic study is being performed to prove the lack of unacceptable risks from SAP250F application in the intended uses to Honey Bees.

#### Effects on arthropods other than bees (KCP 10.3.2)

The in-field HQ values for the highest application rate are below the trigger of 2.0 for the three-standard species *Typhlodromus pyri*, *Aphidius rhopalosiphi* and *Chrysoperla carnea*. The off-field HQ values for all tested species, are below the trigger ~~of 2.0,~~ indicating that SAP250F is unlikely to pose an unacceptable risk to non-target-arthropods in or off-field.

#### Effects on non-target soil meso- and macrofauna (KCP 10.4), Effects on soil microbial activity (KCP 10.5)

No unacceptable acute risks are expected in earthworms due to exposure to either Prothioconazole or its metabolites (JAU 6476-desthio and JAU 6476-S-methyl). From the derived long-term TER values, unacceptable risks to earthworms are expected from Prothioconazole and the metabolite JAU 6476-desthio. However, in a field study, the occurrence of Prothioconazole and the Desthio-metabolite was confirmed slightly under the PECsoil derived. As the depth of soil from which the sample cores were taken is highly unlikely to have been less than 5 cm and would more typically be expected to be 10 cm, the maximum PEC values are likely to be an overestimation, with the level of exposure in the field study being considered more realistic. Besides, from the 5 identified earthworm species, only the number of juveniles of 1 (*Aporrectodea caliginosa*) was affected. In fact, by the end of the study, an overall increase in the number and biomass of earthworms in the treated plots was observed (11 months of exposure with 3 applications of 200g a.s./ha). Also, no unacceptable effects are expected when using the endpoint obtained in the chronic study with the formulation in question (TER value of 12.6, well above 5). Therefore, no unacceptable effects are expected in earthworms and other soil meso and macrofauna due to the application of SAP250F in the intended uses.

The use of SAP250F according to the proposed use patterns will not have unacceptable effects on soil micro-organisms as more 1000-fold of the applied maximum concentration did not cause any significant effects on soil nitrogen transformation.

#### Effects on non-target terrestrial plants (KCP 10.6)

The worst-case TER values are well greater than the trigger value of 5 and therefore it is considered that risks to non-target plants after SAP250F applications are acceptable.

#### Effects on other terrestrial organisms (flora and fauna) (KCP 10.7)

No data available.

### Grouping of intended uses for risk assessment

The following table documents the grouping of the intended uses to support application of the risk envelope approach (according to SANCO/11244/2011).

Table 9.1‑2: Critical use pattern of SAP250F grouped according to the application time

| Grouping according to crop group and application pattern | | | |
| --- | --- | --- | --- |
| Group | Intended uses | relevant use parameters for grouping | Crop group and application pattern |
| Effects on birds and mammals (9.2 and 9.3) | | | |
| Bulbs and onion like crops, **cereals**, fruiting vegetables, leafy vegetables, legume forage, maize, oilseed rape, potatoes, pulses, root and stem vegetables, strawberries, sugar beet, and sunflower | Wheat  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Wheat  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| Barley  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Barley  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| Oat  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Oat  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| Rye  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Rye  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| Triticale  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Triticale  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| Bulbs and onion like crops, cereals, fruiting vegetables, leafy vegetables, legume forage, maize, **oilseed rape**, potatoes, pulses, root and stem vegetables, strawberries, sugar beet, and sunflower | OSR  BBCH 20-80 | Crop group according to EFSA/2009/1438 | OSR  Prothioconazole: 3 x 0.175 kg a.s./ha, interval 14 days |
| **Effects on non-target soil meso- and macrofauna (9.8)** | | | |
| Annual crops | Wheat  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Wheat  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| Barley  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Barley  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| Oat  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Oat  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| Rye  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Rye  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| Triticale  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Triticale  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| OSR  BBCH 20-80 | Crop group according to EFSA/2009/1438 | OSR  Prothioconazole: 3 x 0.175 kg a.s./ha, interval 14 days |
| **Effects on soil microbial activity (9.9)** | | | |
| Annual crops | Wheat  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Wheat  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| Barley  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Barley  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| Oat  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Oat  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| Rye  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Rye  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| Triticale  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Triticale  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| OSR  BBCH 20-80 | Crop group according to EFSA/2009/1438 | OSR  Prothioconazole: 3 x 0.175 kg a.s./ha, interval 14 days |
| **Effects on non-target terrestrial plants (9.10)** | | | |
| Field crops | Wheat  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Wheat  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| Barley  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Barley  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| Oat  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Oat  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| Rye  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Rye  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| Triticale  BBCH 26-69 | Crop group according to EFSA/2009/1438 | Triticale  Prothioconazole: 3 x 0.2 kg a.s./ha, interval 14 days |
| OSR  BBCH 20-80 | Crop group according to EFSA/2009/1438 | OSR  Prothioconazole: 3 x 0.175 kg a.s./ha, interval 14 days |

### Consideration of metabolites

A list of metabolites found in environmental compartments is provided below. The need for conducting a metabolite-specific risk assessment in the context of the evaluation of SAP250F is indicated in the table.

Table 9.1‑3 Metabolites of Prothioconazole

| Metabolite | Chemical structure | Molar mass | Maximum occurrence in compartments | Risk assessment required? |
| --- | --- | --- | --- | --- |
| M01:  JAU 6476-S methyl  Prothioconazole-S-methyl  CAS 178928-71-7 |  | 358.281 | Soil: 14.6% AR, day 7  Sediment: 77.0% AR, day 240 | Yes, soil and aquatic organisms |
| M04:  JAU 6476-desthio  Prothioconazole-desthio  CAS 120983-64-4 |  | 312.19 | Soil: 49.4% AR, day 7  Water: 55.7% AR, day 11  Sediment: 26.9% AR, day 14 | Yes, soil and aquatic organisms |
| M12:  Prothioconazole thiazocine |  | - | Water: max 14.1% after 5d (photolysis) | Yes, aquatic organisms |
| M13:  1,2,4-triazole  CAS 288-88-0 | https://www.sigmaaldrich.com/content/dam/sigma-aldrich/structure3/099/mfcd00005228.eps/_jcr_content/renditions/mfcd00005228-large.png | 69.07 | Soil: minor metabolite (<2% AR in aerobic soil degradation studies)  Water: max 11.9% after 18d | Yes, aquatic organisms |

## Effects on birds (KCP 10.1.1)

### Toxicity data

Avian toxicity studies have been carried out with Prothioconazole and its relevant metabolites. Full details of these studies are provided in the respective EU DAR and related documents.

Effects on birds of SAP250F were not evaluated as part of the EU assessment of Prothioconazole. However, the provision of further data on the SAP250F is not considered essential.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.2‑1: Endpoints and effect values relevant for the risk assessment for birds

| Species | Substance | Exposure  System | Results | Reference |
| --- | --- | --- | --- | --- |
| Bobwhite quail | Prothioconazole | Acute | LD50 > 2000 mg a.s./kg bw | EFSA Scientific Report (2007) |
| Bobwhite quail | Prothioconazole | 5d, dietary | LC50 > 5000 mg a.s./kg diet  **Calc. LD50 > 1413 mg a.s./kg bw/day** | EFSA Scientific Report (2007) |
| Mallard Duck | Prothioconazole | 5d, dietary | LC50 > 5000 mg a.s./kg diet  Calc. LD50 > 2457 mg a.s./kg bw/day | EFSA Scientific Report (2007) |
| Bobwhite quail | Prothioconazole | Reproduction  22w, dietary | NOEC ≥ 1000 mg a.s./kg diet  Calc. NOEL ≥ 86 mg a.s./kg bw/day | EFSA Scientific Report (2007) |
| Mallard Duck | Prothioconazole | Reproduction  21w, dietary | NOEC = 700 mg a.s./kg diet  **Calc. NOEL = 78 mg a.s./kg bw/day** | EFSA Scientific Report (2007) |
| Bobwhite quail | JAU 6476-desthio | Acute | LD50 > 2000 mg p.m./kg b.w. | EFSA Scientific Report (2007) |
| Bobwhite quail | JAU 6476-desthio | 5d, dietary | LC50 = 4090 mg p.m./kg diet  **Calc. LD501 > 297 mg p.m./kg bw/d** | EFSA Scientific Report (2007) |
| Bobwhite quail | JAU 6476-desthio | Reproduction  20w, dietary | NOEC = 173 mg p.m./kg diet  **Calc. NOEL = 14.8 mg p.m./kg bw/day** | EFSA Scientific Report (2007) |
| Mallard Duck | JAU 6476-desthio | Reproduction  20w, dietary | NOEC ≥ 500 mg p.m./kg diet  Calc. NOEL = 63 mg p.m./kg bw/day | EFSA Scientific Report (2007) |

**Bold** indicates endpoints used in risk assessment.

1 value represents the dose converted from the test group in which No Effect on mortality or food consumption was reported (1243 mg/kg diet/d multiplied by the mean daily food consumption (6.4 g/d for the 5 day exposure period) divided by the mean bodyweight (26.75 g for the 5 day exposure period). A more precise conversion of the LC50 value requires reanalysis of data using the converted daily dietary doses for each test group.

Prothioconazole-desthio (JAU 6476-desthio) was considered to be the only major metabolite in cereal foliage. A total conversion of prothioconazole to the desthio metabolite was assumed in the risk assessment.

#### Justification for new endpoints

In line with the EFSA Guidance Document on Risk Assessment for Birds and Mammals (2009) Section 2.2. where it is lower than the acute LD50, the dietary LD50 should be used in the acute risk assessment. Therefore, the dietary LD50 values for Prothioconazole and its metabolite Prothioconazole-desthio have been considered in the risk assessment instead the acute LD50 EU Agreed endpoints according to EFSA Scientific Report (2007).

### Risk assessment for spray applications

The risk assessment is based on the methods presented in the Guidance Document on Risk Assessment for Birds and Mammals on request from EFSA (EFSA Journal 2009; 7(12): 1438; hereafter referred to as EFSA/2009/1438).

#### First-tier assessment (screening/generic focal species)

For the screening step risk assessment, it has been assumed that 100% of the parent becomes the metabolite. The application rate calculation for the metabolite was calculated as the respective maximum occurrence transformation, multiplying by a conversion factor (metabolite molecular weight ÷ parent molecular weight) to correct the molecular weight. ~~This is a worst-case assumption and therefore appropriate as a screening/first-tier assessment.~~

In addition, zRMS added the calculations assuming total dose applied as a multiple application with no degradation between treatments and 100% conversion from parent prothioconazole.

The results of the acute and reproductive screening/first-tier risk assessments are summarised in the following tables.

Table 9.2‑2: Screening step of the acute and long-term/reproductive risk for birds due to the use of SAP250F in Cereals and OSR

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Intended use | | Cereals (wheat, barley, oat, rye and triticale) and OSR | | | | |
| Active substance/product | | Prothioconazole/SAP250F | | | | |
| Application rate (g/ha) | | 3 × 200 (cereals) / 175 (OSR) – Prothioconazole  3 x 181.4 (Cereals) / 158.7 (OSR) – JAU 6476-desthio, 3 x200 /175 ( Cereals, OSR)\* | | | | |
| Acute toxicity (mg/kg bw) | | 1413 (as) / 297 (metabolite) | | | | |
| TER criterion | | 10 | | | | |
| Crop scenario  Growth stage | Indicator/generic focal species | | SV90 | MAF90 | DDD90  (mg/kg bw/d) | TERa |
| Cereals  Prothioconazole | Small omnivorous bird | | 158.8 | 1.3 | 41.29 | 34.22 |
| Cereals  JAU 6476-desthio  (metabolite) | Small omnivorous bird | | 158.8 | 1.3 | 37.45  41.29 | **7.93**  **7.19** |
| OSR  Prothioconazole | Small omnivorous bird | | 158.8 | 1.3 | 36.13 | 39.11 |
| OSR  JAU 6476-desthio  (metabolite) | Small omnivorous bird | | 158.8 | 1.3 | 32.76  36.13 | **9.07**  **8.22** |
| Reprod. toxicity (mg/kg bw/d) | | 78 (as) / 14.8 (metabolite) | | | | |
| TER criterion | | 5 | | | | |
| Crop scenario  Growth stage | Indicator/generic focal species | | SVm | MAFm × TWA | DDDm  (mg/kg bw/d) | TERlt |
| Cereals  Prothioconazole | Small omnivorous bird | | 64.8 | 1.5 x 0.53 | 10.30 | 7.57 |
| Cereals  JAU 6476-desthio  (metabolite) | Small omnivorous bird | | 64.8 | 1.5 x 0.53 | 9.35  10.30 | **1.58**  **1.43** |
| OSR  Prothioconazole | Small omnivorous bird | | 64.8 | 1.5 x 0.53 | 9.02 | 8.65 |
| OSR  JAU 6476-desthio  (metabolite) | Small omnivorous bird | | 64.8 | 1.5 x 0.53 | 8.17  9.02 | **1.81**  **~~1.84~~**  **4.90** |

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

\* Assuming total dose applied as a multiple application with no degradation between treatments and 100% conversion from parent prothioconazole.

No unacceptable risks of birds exposure the active substance are expected after application of SAP250F in the intended uses. However, for the metabolite this is not the case. Therefore, a first-tier risk assessment for the metabolite is presented below.

Table 9.2‑3: First-tier assessment of the acute and long-term/reproductive risk for birds due to the use of SAP250F in Cereals (metabolite)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Intended use | | Cereals (wheat, barley, oat, rye and triticale) | | | | |
| Active substance/product | | JAU 6476-desthio | | | | |
| Application rate (g/ha) | | 3 x 181.4 (Cereals) – JAU 6476-desthio, 3 x200 (Cereals)\* | | | | |
| Acute toxicity (mg/kg bw) | | 297 | | | | |
| TER criterion | | 10 | | | | |
| Crop scenario  Growth stage | Indicator/generic focal species | | SV90 | MAF90 | DDD90  (mg/kg bw/d) | TERa |
| Cereals  BBCH ≥ 40 | Small omnivorous bird “lark” Combination (invertebrates with interception) 25% crop leaves 25% weed seeds 50% ground arthropods | | 7.2 | 1.3 | 1.70  1.872 | 175  185.65 |
| Cereals  BBCH 30-39 | Small omnivorous bird “lark” Combination (invertebrates with interception) 25% crop leaves 25% weed seeds 50% ground arthropods | | 12.0 | 1.3 | 2.83  3.12 | 105  95.20 |
| Cereals  BBCH 10-29 | Large herbivorous bird “goose” Grass + cereals 100% cereals shoots | | 30.5 | 1.3 | 7.19  7.93 | 41.3  37.45 |
| Cereals  BBCH 10-29 | Small omnivorous bird “lark” Combination (invertebrates with interception) 25% crop leaves 25% weed seeds 50% ground arthropods | | 24.0 | 1.3 | 5.66  6.24 | 52.5  47.6 |
| Cereals  Late season-Seed heads | Small granivorous/insectivorous bird “bunting” | | 27.0 | 1.3 | 6.35 | 46.75 |
| Reprod. toxicity (mg/kg bw/d) | | 14.8 | | | | |
| TER criterion | | 5 | | | | |
| Crop scenario  Growth stage | Indicator/generic focal species | | SVm | MAFm × TWA | DDDm  (mg/kg bw/d) | TERlt |
| Cereals  BBCH ≥ 40 | Small omnivorous bird “lark” Combination (invertebrates with interception) 25% crop leaves 25% weed seeds 50% ground arthropods | | 3.3 | 1.5 x 0.53 | 0.48  0.52 | 31.1  28.46 |
| Cereals  BBCH 30-39 | Small omnivorous bird “lark” Combination (invertebrates with interception) 25% crop leaves 25% weed seeds 50% ground arthropods | | 5.4 | 1.5 x 0.53 | 0.78  0.85 | 19.0  17.41 |
| Cereals  BBCH 10-29 | Large herbivorous bird “goose” Grass + cereals 100% cereals shoots | | 16.2 | 1.5 x 0.53 | 2.34  2.57 | 6.33  5.75 |
| Cereals  BBCH 10-29 | Small omnivorous bird “lark” Combination (invertebrates with interception) 25% crop leaves 25% weed seeds 50% ground arthropods | | 10.9 | 1.5 x 0.53 | 1.57  1.73 | 9.42  8.55 |
| Cereals  Late season-Seed heads | Small granivorous/insectivorous bird “bunting” | | 12.5 | 1.3 | 0.80 | 18.53 |

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

\* Assuming total dose applied as a multiple application with no degradation between treatments and 100% conversion from parent prothioconazole.

Table 9.2‑4: First-tier assessment of the acute and long-term/reproductive risk for birds due to the use of SAP250F in OSR (metabolite)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Intended use | | OSR | | | | |
| Active substance/product | | JAU 6476-desthio | | | | |
| Application rate (g/ha) | | 158.7 (OSR) – JAU 6476-desthio, 3 x 175 (OSR) | | | | |
| Acute toxicity (mg/kg bw) | | 297 | | | | |
| TER criterion | | 10 | | | | |
| Crop scenario  Growth stage | Indicator/generic focal species | | SV90 | MAF90 | DDD90  (mg/kg bw/d) | TERa |
| OSR  BBCH ≥ 40 | Small omnivorous bird “lark” Combination (invertebrates with interception) 25% crop leaves 25% weed seeds 50% ground arthropods | | 6.0 | 1.3 | 1.24  1.36 | 240  218.4 |
| OSR  BBCH ≥ 40 | Medium herbivorous/granivorous bird “pigeon” Comby to be calculated 50% crop leaves 50% weed seeds | | 2.0 | 1.3 | 0.41  0.45 | 720  660 |
| OSR  BBCH 10-29 | Small omnivorous bird “lark” Combination (invertebrates with interception) 25% crop leaves 25% weed seeds 50% ground arthropods | | 24.0 | 1.3 | 4.95  5.46 | 60  54.4 |
| OSR  BBCH 20-29 | Medium herbivorous/granivorous bird “pigeon” Comby to be calculated 50% crop leaves 50% weed seeds | | 4.0 | 1.3 | 0.83  0.91 | 360  326.4 |
| OSR  BBCH 20-29 | Small insectivorous bird “wagtail” ground invertebrates with interception 100% soil dwelling invertebrates | | 7.7 | 1.3 | 1.59  1.75 | 187 |
| OSR  BBCH 30-39 | Medium herbivorous/granivorous bird “pigeon” Comby to be calculated 50% crop leaves 50% weed seeds | | 2.4 | 1.3 | 0.50  0.546 | 600  543.95 |
| OSR  BBCH 30-39 | Small omnivorous bird “lark” Combination (invertebrates with interception) 25% crop leaves 25% weed seeds 50% ground arthropods | | 7.2 | 1.3 | 1.49  1.63 | 200  182.20 |
| OSR  BBCH 30-99 | Small insectivorous bord “dunnock” ground invertebrates with interception 100% soil dwelling invertebrates | | 7.4 | 1.3 | 1.53  1.68 | 195  176.80 |
| OSR  BBCH 80-99 | Small granivorous bird “Finch” Small seeds 100% weed seeds | | 24.7 | 1.3 | 5.10  5.62 | 58.3  52.84 |
| Reprod. toxicity (mg/kg bw/d) | | 14.8 | | | | |
| TER criterion | | 5 | | | | |
| Crop scenario  Growth stage | Indicator/generic focal species | | SVm | MAFm × TWA | DDDm  (mg/kg bw/d) | TERlt |
| OSR  BBCH ≥ 40 | Small omnivorous bird “lark” Combination (invertebrates with interception) 25% crop leaves 25% weed seeds 50% ground arthropods | | 2.7 | 1.5 x 0.53 | 0.34  0.37 | 43.5  40 |
| OSR  BBCH ≥ 40 | Medium herbivorous/granivorous bird “pigeon” Comby to be calculated 50% crop leaves 50% weed seeds | | 0.9 | 1.5 x 0.53 | 0.11  0.125 | 130.34  118.4 |
| OSR  BBCH 10-29 | Small omnivorous bird “lark” Combination (invertebrates with interception) 25% crop leaves 25% weed seeds 50% ground arthropods | | 10.9 | 1.5 x 0.53 | 1.38  1.51 | 10.76  9.8 |
| OSR  BBCH 20-29 | Medium herbivorous/granivorous bird “pigeon” Comby to be calculated 50% crop leaves 50% weed seeds | | 3.5 | 1.5 x 0.53 | 0.44  0.48 | 33.52  30.83 |
| OSR  BBCH 20-29 | Small insectivorous bird “wagtail” ground invertebrates with interception 100% soil dwelling invertebrates | | 2.8 | 1.5 x 0.53 | 0.35  0.39 | 41.89  37.94 |
| OSR  BBCH 30-39 | Medium herbivorous/granivorous bird “pigeon” Comby to be calculated 50% crop leaves 50% weed seeds | | 1.1 | 1.5 x 0.53 | 0.14  0.15 | 106.64  98.66 |
| OSR  BBCH 30-39 | Small omnivorous bird “lark” Combination (invertebrates with interception) 25% crop leaves 25% weed seeds 50% ground arthropods | | 3.3 | 1.5 x 0.53 | 0.42  0.46 | 35.55  32.17 |
| OSR  BBCH 30-99 | Small insectivorous bord “dunnock” ground invertebrates with interception 100% soil dwelling invertebrates | | 2.7 | 1.5 x 0.53 | 0.34  0.37 | 43.45  40 |
| OSR  BBCH 80-99 | Small granivorous bird “Finch” Small seeds 100% weed seeds | | 11.4 | 1.5 x 0.53 | 1.44  1.58 | 10.29  9.37 |

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

\* Assuming total dose applied as a multiple application with no degradation between treatments and 100% conversion from parent prothioconazole.

After first-tier risk assessment, the risk of birds exposure to the metabolite JAU6476-desthio is acceptable. Therefore, the risk of birds exposure to both the active substance and metabolite is considered sufficiently addressed.

|  |
| --- |
| **zRMS comment:**  The risk assessment is based on the methods presented in the Guidance Document on Risk Assessment for Birds and Mammals on request from EFSA (EFSA Journal 2009; 7(12): 1438; hereafter referred to as EFSA/2009/1438). Safe use of prothiconazole and prothioconazole-desthio (M04) for birds were confirmed based on TERA and TERLT above the trigger values of 10 and 5, respectively, indicating the acute and long-term risk is acceptable. |

#### Higher-tier risk assessment

Not relevant.

#### Drinking water exposure

When necessary, the assessment of the risk for birds due to uptake of contaminated drinking water is conducted for a small granivorous bird with a body weight of 15.3 g (*Carduelis cannabina*) and a drinking water uptake rate of 0.46 L/kg bw/d (*cf*. Appendix K of EFSA/2009/1438).

Leaf scenario

Since SAP250F is not intended to be applied on leafy vegetables forming heads or crop plants with comparable water collecting structures at principal growth stage 4 or later, the leaf scenario does not have to be considered.

Puddle scenario

Due to the characteristics of the exposure scenario in connection with the standard assumptions for water uptake by animals, no specific calculations of exposure and TER are necessary when the ratio of effective application rate (in g/ha) to relevant endpoint (in mg/kg bw/d) does not exceed 50 in the case of less sorptive substances (Koc < 500 L/kg) or 3000 in the case of more sorptive substances (Koc ≥ 500 L/kg).

AReff = AR x MAFm = AR x 

Where

k = ln(2)/DT50 (rate constant)

n = number of applications

i = application interval (days)

When multiple spray applications are considered, a MAF based on the DT50 in soil (single first order kinetics, geometric mean as used for PECgw and PECsw) is applied to achieve the effective application rate AReff.

With a K(f)oc of 1765 and 575.4 respectively for Prothioconazole and JAU 6476-desthio, both belong to the group of more sorptive substances.

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group cereals also covers the risk for birds from all other intended uses in group OSR (see 9.1.2).

Table 9.~~3~~2 -5 Effective application rate

| **Crop** | **Substance** | **DT50\*** | **Max application rate (AR) (g as/ha)** | **No. of applications** | **1-e-nki** | **1-e-ki** | **MAFmean** | **AReff** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Cereals | Prothioconazole | 2.8 | 200 | 3 | 0.9999 | 0.97 | 1.03 | 206.4 |

\*DT50 (field) in soil, EFSA Scientific Report (2007) 106, 1-98

**Table 9.3-6 Ratio of AReff to acute/long term toxicity endpoint**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **No concern if ratio** | | | | |
| Prothioconazole: Effective application rate (g/ha) = | 206.4, 3 x200\* | | | |
| Active substance (Prothioconazole) | | | | |
| Koc (l/kg) = | 1765 | | | |
| Acute toxicity (mg/kg bw) = | 1413 | quotient = | 0.15  0.42 | ≤ 3000 |
| Reprod. toxicity (mg/kg bw/d) = | 78 | quotient = | 2.65  7.7 | ≤ 3000 |
| Metabolite (JAU 6476-desthio) | | | | |
| Koc (l/kg) = | 575.4 | | | |
| Acute toxicity (mg/kg bw) = | 297 | quotient = | 0.70  2.02 | ≤ 3000 |
| Reprod. toxicity (mg/kg bw/d) = | 14.8 | quotient = | 13.9  40.54 | ≤ 3000 |

\*worst case

The acute and long-term risk to birds exposed to SAP250F via drinking water is therefore acceptable for the intended uses.

**zRMS comment:**

~~Since is not a for spray applications / not intended to be applied on leafy vegetables forming heads or crop plants with comparable water collecting structures at principal growth stage 4 or later.~~

As INDOFIL Prothio 250 EC is not intended for leafy crops forming heads, the leaf scenario does not have to be therefore considered ~~taking onto account~~ based on the proposed uses (cereals and oilseed rape). Evaluation of exposing for birds through the drinking water Puddle scenario for the active substance and metabolite M04, demonstrate that the acceptable risk for birds for proposed use pattern of **SAP250F/Indofil.**

#### Effects of secondary poisoning

The log Pow of Prothioconazole and JAU 6476-desthio amounts to 4.05 and 3.04 and for M01 to 4.19 , respectively and thus exceeds the trigger value of 3. A risk assessment for effects due to secondary poisoning is required.

Risk assessment for earthworm-eating birds via secondary poisoning

According to EFSA/2009/1438, the risk for vermivorous birds is assessed for a bird of 100 g body weight with a daily food consumption of 104.6 g. Bioaccumulation in earthworms is estimated based on measured/predicted concentrations in soil/porewater / is based on experimental data.

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group cereals also covers the risk for mammals from all other intended uses in group OSR (see 9.1.2).

Table 9.~~3~~ 2 ‑7: Assessment of the risk for earthworm-eating birds due to exposure to Prothioconazole via bioaccumulation in earthworms (secondary poisoning) for the intended use in cereals

| Parameter | Prothioconazole | comments |
| --- | --- | --- |
| PECsoil (twa = 21 d) (mg/kg soil) | 0.220 | Worst-case PECsoil calculated for multiple applications in all crops |
| Pow | 4.05 |  |
| Koc | 1765 | (aged leaching study, only one soil tested, value used for PELMOgw modelling; 1/n set to 0.90) |
| foc | 0.02 | Default |
| BCFworm | 3.84 | BCFworm/soil = (PECworm,ww/PECsoil,dw) = (0.84 + 0.012 × Pow) / foc × Koc |
| PECworm | 0.84 | PECworm = PECsoil × BCFworm/soil |
| Daily dietary dose (mg/kg bw/d) | 0.89 | DDD = PECworm × 1.05 |
| NOEL (mg/kg bw/d) | 78 |  |
| TERlt | 87.98 | >5, no further refinement |

TER values shown in bold fall below the relevant trigger.

Table 9.~~3~~ 2‑8: Assessment of the risk for earthworm-eating birds due to exposure to JAU 6476-desthio via bioaccumulation in earthworms (secondary poisoning) for the intended use in cereals

| Parameter | JAU 6476-desthio (M04) | comments |
| --- | --- | --- |
| PECsoil (twa = 21 d) (mg/kg soil) | 0.394 | Worst-case PECsoil calculated for multiple applications in all crops. |
| Pow | 3.04 |  |
| Koc | 574.4 | Mean (n=4) |
| foc | 0.02 | Default |
| BCFworm | 1.22 | BCFworm/soil = (PECworm,ww/PECsoil,dw) = (0.84 + 0.012 × Pow) / foc × Koc |
| PECworm | 0.481 | PECworm = PECsoil × BCFworm/soil |
| Daily dietary dose (mg/kg bw/d) | 0.505 | DDD = PECworm × 1.05 |
| NOEL (mg/kg bw/d) | 14.8 |  |
| TERlt | 29 | >5, no further refinement |

TER values shown in bold fall below the relevant trigger.

Table 9.2‑9: Assessment of the risk for earthworm-eating birds due to exposure to prothioconazole-S-methyl (M01) via bioaccumulation in earthworms (secondary poisoning) for the intended use in cereals

| Parameter | Prothioconazole-S-methyl (M01) | Comments |
| --- | --- | --- |
| PECsoil (mg/kg soil) | 0.267 | PECs multiple accumulation |
| log Pow / Pow | 4.19/15448.2 | EFSA Conclusion  (EFSA Scientific Report (2007) 106, 1-98) |
| Koc | 2256.3 |  |
| foc | 0.02 | Default |
| BCFworm |  | BCFworm/soil = (PECworm,ww/PECsoil,dw) = (0.84 + 0.012 × Pow) / foc × Koc |
| PECworm | 1.096 | PECworm = PECsoil × BCFworm/soil |
| Daily dietary dose (mg/kg bw/d) | 1.15 | DDD = PECworm × 1.05 |
| NOEL (mg/kg bw/d) | 7.8\* | Derived endpoint |
| TERlt | 6.78 |  |

TER values shown in bold fall below the relevant trigger.

\*Endpoint estimated as parent NOEL/10.

The TERlt for the assessment of the risk for earthworm-eating birds due to exposure to prothioconazole, prothioconazole-S-methyl (M01), and JAU 6476-desthio (M04) via bioaccumulation in earthworms does not fall below the relevant trigger TER value of 5, indicating low risk to birds following applications of Indofil.

Risk assessment for fish-eating birds via secondary poisoning

According to EFSA/2009/1438, the risk for piscivorous birds is assessed for a bird of 1000 g body weight with a daily food consumption of 159 g. Bioaccumulation in fish is estimated based on predicted concentrations in surface water / is based on the regulatory acceptable concentration for aquatic organisms as a limit value for admissible concentrations of Prothioconazole in water.

Table 9.2‑10: Assessment of the risk for fish-eating birds due to exposure to Prothioconazole via bioaccumulation in fish (secondary poisoning) for the intended use in cereals

|  |  |  |
| --- | --- | --- |
| Parameter | Prothioconazole | comments |
| PECsw (max) (mg/L) | 0.022 | Worst-case Step 1 PECsw calculated for multiple application in winter and spring cereals (Table 9.5-3) |
| BCFfish | 19.7 |  |
| BMF | - | biomagnification factor (relevant for BCF ≥ 2000) |
| PECfish | 0.428 | PECfish = PECwater × BCFfish |
| Daily dietary dose (mg/kg bw/d) | 0.068 | DDD = PECfish × 0.159 |
| NOEL (mg/kg bw/d) | 78 |  |
| TERlt | 1146.5 | >5, no further refinement |

TER values shown in bold fall below the relevant trigger.

Table 9.~~3~~ 2‑11: Assessment of the risk for fish-eating birds due to exposure to JAU 6476-desthio via bioaccumulation in fish (secondary poisoning) for the intended use in cereals

|  |  |  |
| --- | --- | --- |
| Parameter | JAU 6476-desthio( M04) | comments |
| PECsw (max) (mg/L) | 0.111 | Worst-case Step 1 PECsw calculated for multiple application in winter and spring cereals (Table 9.5-4) |
| BCFfish | 65 |  |
| BMF | - | biomagnification factor (relevant for BCF ≥ 2000) |
| PECfish | 7.202 | PECfish = PECwater × BCFfish |
| Daily dietary dose (mg/kg bw/d) | 1.145 | DDD = PECfish × 0.159 |
| NOEL (mg/kg bw/d) | 14.8 |  |
| TERlt | 12.92 | >5, no further refinement |

TER values shown in bold fall below the relevant trigger.

In addition, the assessment of the risk for fish-eating birds due to exposure to prothioconazole-S-methyl (M01) via bioaccumulation in fish was provided by zRMS with a conservative assessment as the long-term NOEL for the metabolite is assumed to be 10 x more toxic than the parent (7.8 mg /kg bw/d).

Risk has been assessed against both the best (319 L/kg) and worse-case (1995 L/kg) whole fish BCF values for prothioconazole-S-methyl (M01) in the Table below.

**Table 9.2‑12: Assessment of the risk for fish-eating birds due to exposure to prothioconazole-S- methyl (M01) via bioaccumulation in fish (secondary poisoning) for the intended use in cereals assuming the best-case whole fish BCF value of 319 L/kg.**

|  |  |  |
| --- | --- | --- |
| **Parameter** | **Prothioconazole-S-methyl (M01)** | **Comments** |
| PECsw (mg/L) | 0.002898 | FOCUS Step 2 (Section 8) |
| BCFfish | 319 | EFSA Conclusion  (EFSA Scientific Report (2007) 106, 1-98) |
| BMF | N/A | biomagnification factor (relevant for BCF ≥ 2000) |
| PECfish | 0.89 | PECfish = PECwater × BCFfish |
| Daily dietary dose (mg/kg bw/d) | 0.142 | DDD = PECfish × 0.159 |
| NOEL (mg/kg bw/d) | 7.8\* | Derived endpoint |
| TERlt | 54.92 |  |

TER values shown in bold fall below the relevant trigger.

\*Endpoint estimated as parent NOEL/10.

**Table 9.2‑13: Assessment of the risk for fish-eating birds due to exposure to prothioconazole-S- methyl (M01) via bioaccumulation in fish (secondary poisoning) for the intended use in cereals assuming the worse-case whole fish BCF value of 1995 L/kg.**

|  |  |  |
| --- | --- | --- |
| **Parameter** | **Prothioconazole-S-methyl (M01)** | **Comments** |
| PECsw (mg/L) | 0.002898 | FOCUS Step 2 (Section 8) |
| BCFfish | 1995 | EFSA Conclusion  (EFSA Scientific Report (2007) 106, 1-98) |
| BMF | N/A | biomagnification factor (relevant for BCF ≥ 2000) |
| PECfish | 5.59 | PECfish = PECwater × BCFfish |
| Daily dietary dose (mg/kg bw/d) | 0.89 | DDD = PECfish × 0.159 |
| NOEL (mg/kg bw/d) | 7.8\* | Derived endpoint |
| TERlt | 8.76 |  |

TER values shown in bold fall below the relevant trigger.

\*Endpoint estimated as parent NOEL/10.

The TERlt for the assessment of the risk for fish-eating birds due to exposure to prothioconazole, prothioconazole-S-methyl (M01) and JAU 6476-desthio (M04) via bioaccumulation in fish is above the relevant trigger TER value of 5, indicating low risk to birds following applications of Indofil .

|  |
| --- |
| **zRMS comment:**  The risk for fish-eating birds and earthworms-eating birds due to exposure to prothioconalzole and its metabolites (M04) and (M01) is considered as acceptable for the worst case scenario-cereals, covering remained use in OSR. |

#### Biomagnification in terrestrial food chains

Not relevant.

### Risk assessment for baits, pellets, granules, prills or treated seed

Not relevant.

### Overall conclusions

For acute dietary exposure of birds to the active substance Prothioconazole, the TER for the required uses are above the trigger value at the Screening step whereas an acceptable acute risk was demonstrated for Prothioconazole-desthio at the first tier. For the chronic (reproductive) dietary exposure of birds to the active substance Prothioconazole and its metabolite JAU 6476-desthio, the TER for the required uses are above the trigger value at the screening step for the active substance (Prothioconazole) or at the first-tier step for the metabolite (JAU 6476-desthio). The risk to birds exposed to SAP250F via drinking water is acceptable for the intended use as the ratio between the effective application rate and the acute and long-term endpoints is below 3000 (Prothioconazole is more sorptive). Secondary poisoning assessments were triggered for both Prothioconazole and its metabolite (JAU 6476-desthio, M04) and prothioconazole-S-methyl (M01). No unacceptable risks were found on the assessment of biomagnification in terrestrial food chains after application of SAP250F in the intended uses. Therefore, treatment with SAP250F in accordance with the proposed uses poses an acceptable risk to birds.

## Effects on terrestrial vertebrates other than birds (KCP 10.1.2)

### Toxicity data

Mammalian toxicity studies have been carried out with Prothioconazole and its relevant metabolites. Full details of these studies are provided in the respective EU DAR and related documents.

Effects on mammals of SAP250F were not evaluated as part of the EU assessment of Prothioconazole. However, the provision of further data on the formulation SAP250F is not considered essential.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.3‑1: Endpoints and effect values relevant for the risk assessment for mammals

| Species | Substance | Exposure  System | Results | Reference |
| --- | --- | --- | --- | --- |
| Rat | Prothioconazole | Oral Acute | **LD50(male, female) > 6200 mg a.s./kg bw/d** | EFSA Scientific Report (2007) |
| Rat | EC 250 | Oral Acute | LD50(male, female) > 2500 mg a.s./kg bw/d | EFSA Scientific Report (2007) |
| Rat | FS 100 | Oral Acute | LD50(male, female) > 2500 mg a.s./kg bw/d | EFSA Scientific Report (2007) |
| Rat | Prothioconazole | Long-term  (2-generation), gavage | NOELparental = 9.7 mg a.s./kg bw/d  **NOELreproduction = 95.6 mg a.s./kg bw/d** | EFSA Scientific Report (2007) |
| Rat | JAU 6476-desthio | Oral Acute | LD50(female) = 2506 mg p.m./kg bw/d  LD50(male) = 2806 mg p.m./kg bw/d | EFSA Scientific Report (2007) |
| Mouse | JAU 6476-desthio | Oral Acute | LD50(female) = 3459 mg p.m./kg bw/d  **LD50(male) = 2235 mg a.s./kg bw/d** | EFSA Scientific Report (2007) |
| Rat | JAU 6476-desthio | Long-term  (2-generation), oral | NOELparental = 2.5 mg p.m./kg bw/d  **NOELreproduction = 10 mg p.m./kg bw/d** | EFSA Scientific Report (2007) |

**Bold** indicates endpoints used in risk assessment.

Prothioconazole-desthio (JAU 6476-desthio) was considered to be the only major metabolite in cereal foliage. A total conversion of prothioconazole to the desthio metabolite was assumed in the risk assessment.

#### Justification for new endpoints

Not relevant.

### Risk assessment for spray applications

The risk assessment is based on the methods presented in the Guidance Document on Risk Assessment for Mammals and Mammals on request from EFSA (EFSA Journal 2009; 7(12): 1438; hereafter referred to as EFSA/2009/1438).

#### First-tier assessment (screening/generic focal species)

For the screening step risk assessment, it has been assumed that 100% of the parent becomes the me-tabolite. The application rate calculation for the metabolite was calculated as the respective maximum occurrence transformation, multiplying by a conversion factor (metabolite molecular weight ÷ parent molecular weight) to correct the molecular weight. ~~This is a worst-case assumption and therefore ap-propriate as a screening/first-tier assessment.~~ In addition, zRMS added the calculations assuming total dose applied as a multiple application with no degradation between treatments and 100% conversion from parent prothioconazole.

The results of the acute and reproductive screening/first-tier risk assessments are summarised in the following tables.

Table 9.3‑2: Screening step of the acute and long-term/reproductive risk for mammals due to the use of SAP250F in Cereals and OSR

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Intended use | | **Cereals (wheat, barley, oat, rye and triticale) and OSR** | | | | |
| Active substance/product | | Prothioconazole/SAP250F | | | | |
| Application rate (g/ha) | | 3 × 200 (Cereals) / 175 (OSR) - Prothioconazole  3 × 181.4 (Cereals) / 158.7 (OSR) – JAU 6476-desthio, 3 x200 ( cereals), x 175 (OSR) | | | | |
| Acute toxicity (mg/kg bw) | | 6200 (a.s.) / 2235 (metabolite) | | | | |
| TER criterion | | 10 | | | | |
| Crop scenario  Growth stage | Indicator/generic focal species | | SV90 | MAF90 | DDD90  (mg/kg bw/d) | TERa |
| Cereals  Prothioconazole | Small herbivorous mammal | | 118.4 | 1.3 | 30.78 | 201.4 |
| Cereals  JAU 6476-desthio  (metabolite) | Small herbivorous mammal | | 118.4 | 1.3 | 27.92  30.78 | 80.05  72.61 |
| OSR  Prothioconazole | Small herbivorous mammal | | 118.4 | 1.3 | 26.94 | 230.18 |
| OSR  JAU 6476-desthio  (metabolite) | Small herbivorous mammal | | 118.4 | 1.3 | 24.43  26.94 | 91.50  82.96 |
| Reprod. toxicity (mg/kg bw/d) | | 95.6 (a.s.) / 10 (metabolite) | | | | |
| TER criterion | | 5 | | | | |
| Crop scenario  Growth stage | Indicator/generic focal species | | SVm | MAFm × TWA | DDDm  (mg/kg bw/d) | TERlt |
| Cereals  Prothioconazole | Small herbivorous mammal | | 48.3 | 1.5 x 0.53 | 7.68 | 12.45 |
| Cereals  JAU 6476-desthio  (metabolite) | Small herbivorous mammal | | 48.3 | 1.5 x 0.53 | 6.97  7.68 | **1.44**  **1.3** |
| OSR  Prothioconazole | Small herbivorous mammal | | 48.3 | 1.5 x 0.53 | 6.72 | 14.23 |
| OSR  JAU 6476-desthio  (metabolite) | Small herbivorous mammal | | 48.3 | 1.5 x 0.53 | 6.09  6.72 | **1.64**  **1.48** |

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

\* Assuming total dose applied as a multiple application with no degradation between treatments and 100% conversion from parent prothioconazole.

adrienNo unacceptable risks of mammals exposure to the active substance are expected after application of SAP250F in the intended uses. However, for the metabolite and in long-term scenario this is not the case. Therefore, a first-tier long-term risk assessment for the metabolite is presented below.

Table 9.3‑3: First-tier assessment of the ~~acute and~~ long-term/reproductive risk for mammals due to the use of SAP250F in Cereals (metabolite)

| Intended use | | **Cereals (wheat, barley, oat, rye and triticale)** | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| Active substance/product | | JAU 6476-desthio (M04) | | | | |
| Application rate (g/ha) | | 3 × 181.4 (Cereals) – JAU 6476-desthio, 3 x200 \* | | | | |
| Reprod. toxicity (mg/kg bw/d) | | 10 | | | | |
| TER criterion | | 5 | | | | |
| Crop scenario  Growth stage | Indicator/generic focal species | | SVm | MAFm × TWA | DDDm  (mg/kg bw/d) | TERlt |
| Cereals  BBCH ≥ 20 | Small insectivorous mammal “shrew” ground dwelling invertebrates with interception 100% ground arthropods | | 1.9 | 1.5 x 0.53 | 0.28  0.30 | 36.5  33.3 |
| Cereals  BBCH ≥ 40 | Small herbivorous mammal “Vole grass + cereals 100% grass | | 21.7 | 1.5 x 0.53 | 3.13  3.45 | **3.20**  **2.9** |
| Cereals  BBCH ≥ 40 | Small omnivorous mammal “mouse” Combination (invertebrates with interception) 25% weeds 50% weed seeds 25% ground arthropods | | 2.3 | 1.5 x 0.53 | 0.33  0.36 | 30.15  27.77 |
| Cereals  BBCH 10-29 | Small omnivorous mammal “mouse” Combination (invertebrates with interception) 25% weeds 50% weed seeds 25% ground arthropods | | 7.8 | 1.5 x 0.53 | 1.12  1.24 | 8.89  8.06 |
| Cereals  BBCH 30-39 | Small omnivorous mammal “mouse” Combination (invertebrates with interception) 25% weeds 50% weed seeds 25% ground arthropods | | 3.9 | 1.5 x 0.53 | 0.56  0.62 | 17.78  16.13 |
| Cereals  Early (shoots) | Large herbivorous mammal “lagomorph” Grass + cereals 100% cereal shoots | | 22.3 | 1.5 x 0.53 | 3.22  3.54 | **3.11**  **2.82** |

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

\* Assuming total dose applied as a multiple application with no degradation between treatments and 100% conversion from parent prothioconazole.

Table 9.3‑4: First-tier assessment of the ~~acute and~~ long-term/reproductive risk for mammals due to the use of SAP250F in OSR (metabolite)

| Intended use | | **OSR** | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| Active substance/product | | JAU 6476-desthio (M04) | | | | |
| Application rate (g/ha) | | 158.7 (OSR) – JAU 6476-desthio, 3 x 175 \* | | | | |
| Reprod. toxicity (mg/kg bw/d) | | 10 | | | | |
| TER criterion | | 5 | | | | |
| Crop scenario  Growth stage | Indicator/generic focal species | | SVm | MAFm × TWA | DDDm  (mg/kg bw/d) | TERlt |
| OSR  All season | Large herbivorous mammal “lagomorph” Non-grass herbs 100% crop leaves | | 14.3 | 1.5 x 0.53 | 1.80  1.98 | 5.54  5.05 |
| OSR  BBCH ≥ 20 | Small insectivorous mammal “shrew” ground dwelling invertebrates with interception 100% ground arthropods | | 1.9 | 1.5 x 0.53 | 0.24  0.26 | 41.72  38.46 |
| OSR  BBCH ≥ 40 | Small herbivorous mammal “Vole grass + cereals 100% grass | | 18.1 | 1.5 x 0.53 | 2.28  2.51 | **4.38**  **3.98** |
| OSR  BBCH ≥ 40 | Small omnivorous mammal “mouse” Combination (invertebrates with interception) 25% weeds 50% weed seeds 25% ground arthropods | | 1.9 | 1.5 x 0.53 | 0.24  0.26 | 41.72  38.46 |
| OSR  BBCH 10-29 | Small omnivorous mammal “mouse” Combination (invertebrates with interception) 25% weeds 50% weed seeds 25% ground arthropods | | 7.8 | 1.5 x 0.53 | 0.98  1.08 | 10.16  9.25 |
| OSR  BBCH 30-39 | Small omnivorous mammal “mouse” Combination (invertebrates with interception) 25% weeds 50% weed seeds 25% ground arthropods | | 2.3 | 1.5 x 0.53 | 0.29  0.32 | 34.46  31.25 |

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

\* Assuming total dose applied as a multiple application with no degradation between treatments and 100% conversion from parent prothioconazole.

After first-tier risk assessment, the risk of mammals exposure to the metabolite JAU6476-desthio is still unacceptable. Therefore, a higher-tier for the long-term risk assessment of the risk of mammals exposure to the metabolite is presented below.

#### Higher-tier risk assessment

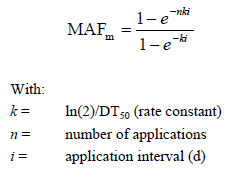
The first-Tier risk assessment after the application of SAP250F indicates a long-term risk of the metabolite JAU 6476-desthio (M04) for Small herbivorous mammal (Common vole) and Large herbivorous mammal (Lagomorph). Thus, a refined risk assessment for long-term exposure of mammals must be performed for two kinds of mammals following. Independent approaches are presented below (please be aware that each refinement proposal is independent, thus not connected between them).

**Tier 2a – Refinement of foliar DT50**

The following information was considered for a more realistic estimation of the residue decline in and on plant material as the measured residue decline of JAU 6476-desthio on plant material can be considered to calculate a refined MAF and/or fTWA. A total of 8 trials were conducted to determine the residue of Prothioconazole-desthio in wheat and the DT50 after a spray application of 200 g as/ha. The overall mean DT50 in wheat considering foliar residues is considered to be 3.2 days, with a measured maximum residue of 3.7 mg/kg (EFSA, 2007). This DT50 was proposed to be used as refinement in the EFSA Scientific Report (2007) 106, 1-98.

It can be therefore considered consistent/robust the use of a DT50 of 3.2 days in foliage.

Assuming first-order kinetics, the MAF can be calculated according to the following formula (EFSA bird and mammal guidance 2009, Appendix H):



And the time-weighted-average factor (fTWA) according to the following formula:

fTWA = (1-e-kt)/kt

where:

k velocity constant (ln2/DT50)

t average time (21 days)

The refined **MAF is 1.05**

The refined **time-weighted-average factor (fTWA) is 0.22**

Table 9.3-6: Refinement of the long-term/reproductive risk for mammals due to the use of SAP250F in Cereals ~~and OSR (metabolite)~~ - fTWA

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Intended use | | **Cereals (wheat, barley, oat, rye and triticale) ~~and OSR~~** | | | | | |
| Active substance/product | | JAU 6476-desthio | | | | | |
| Application rate (g/ha) | | 3 × 181.4 (Cereals) / 158.7 (OSR) - JAU 6476-desthio, 3 x200 ( cereals)\*, 3 x 175 (OSR)\* | | | | | |
| Reprod. toxicity (mg/kg bw/d) | | 10 | | | | | |
| TER criterion | | 5 | | | | | |
| Crop scenario  Growth stage | Indicator/generic focal species | | SVm | MAFm × fTWA (\*) | PT | DDDm  (mg/kg bw/d) | TERlt |
| Cereals  BBCH ≥ 40 | Small herbivorous mammal “Vole grass + cereals 100% grass | | 21.7 | 1.05 x 0.22 (\*) | 1.0 | 0.909  1 | 11.0  10 |
| Cereals  Early (shoots) | Large herbivorous mammal “lagomorph” Grass + cereals 100% cereal shoots | | 22.3 | 1.05 x 0.22 (\*) | 1.0 | 0.934  1.03 | 10.7  9.7 |
| OSR  BBCH ≥ 40 | Small herbivorous mammal “Vole grass + cereals 100% grass | | 18.1 | 1.05 x 0.22 (\*) | 1.0 | 0.664  0.83 | 15.1  12.04 |

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

\*refined parameter

\* Assuming total dose applied as a multiple application with no degradation between treatments and 100% conversion from parent prothioconazole.

After refinement of fTWA values, no unacceptable risks were found for mammals after application of SAP250F in the intended uses.

|  |
| --- |
| **zRMS comment:**  zRMS agrees with the refinement based on DT50 value for cereals and refined parameter of ftwa 0.22 according to EFSA Conclusion 2007. Safe use of prothiconazole and prothioconazole-desthio (M04) for mammals were confirmed based on TERA and TERLT above the trigger values of 10 and 5, respectively, indicating the acute and long-term risk is acceptable for cereals and oilseed rape. |

**Tier 2b – Refinement of parent-metabolite transformation portion**

The risk assessment for the metabolite JAU 6476-desthio in the previous steps was performed assuming a total transformation of Prothioconazole into such metabolite.

Haas and Bornatsch (2000), Haas (2001b) and Haas (2001c), referred in DAR (2004; sections B7.1.1 and B.7.1.5), studied the residue formation after spray application of Prothioconazole in wheat, peanut or confined rotational crops (wheat, chard and turnip seedlings were planted at 28, 146 and 269 days after Prothioconazole application, simulating three rotations), respectively.

Various crop matrices were collected for residue measurement in all studies. For the metabolite JAU 6476-desthio, the maximum residue content measured was 35.49% in wheat fodder. Therefore, and as a worst-case approach, the following refinement was made assuming a 40% transformation rate from the parent to the metabolite in foliar matrices. From these results, the total amount of Prothioconazole to be applied, 200g as described in the GAP, would correspond to 181.4g for cereals and 158.7g for OSR of JAU 6476-desthio which would be transformed into 72.6g for cereals and 63.5g for OSR of JAU 4676-desthio (40%). The refinement with these more realistic values was considered and is presented in Table 9.3-7.

Table 9.3‑7: Transformation amount of JAU 6476-desthio measured in plant matrices after Prothioconazole foliar application (results taken from DAR, 2004)

|  |  |  |
| --- | --- | --- |
| **Reference** | **Crop** | **Matrices** |
| Haas, Bornatsch, 2000 | Wheat | Fodder 35.4 %  Hay 18.5 %  Straw 22.3 %  Grain 15.9 % |
| Haas, 2001b | Peanut | Peanut hay 28.2 %  Nutmeat n.d. |
| Haas, 2001c | Wheat | Wheat hay (rotation 3) 19.9%  Wheat straw (rotation 1) 15.1 % |

n.d. – not determined

Table 9.3‑8a: Refinement of the long-term/reproductive risk for mammals due to the use of SAP250F in Cereals and OSR (metabolite)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Intended use | | **Cereals (wheat, barley, oat, rye and triticale) and OSR** | | | | | |
| Active substance/product | | JAU 6476-desthio | | | | | |
| Application rate (g/ha) | | 3 × 72.6 (cereals) / 63.5 (OSR) - JAU 6476-desthio | | | | | |
| Reprod. toxicity (mg/kg bw/d) | | 10 | | | | | |
| TER criterion | | 5 | | | | | |
| Crop scenario  Growth stage | Indicator/generic focal species | | SVm | MAFm × fTWA | PT | DDDm  (mg/kg bw/d) | TERlt |
| Cereals  BBCH ≥ 40 | Small herbivorous mammal “Vole grass + cereals 100% grass | | 21.7 | 1.5 x 0.53 | 1.0 | 1.25 | 7.98 |
| Cereals  Early (shoots) | Large herbivorous mammal “lagomorph” Grass + cereals 100% cereal shoots | | 22.3 | 1.5 x 0.53 | 1.0 | 1.29 | 7.77 |
| OSR  BBCH ≥ 40 | Small herbivorous mammal “Vole grass + cereals 100% grass | | 18.1 | 1.5 x 0.53 | 1.0 | 0.73 | 13.68 |

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

After refinement of parent-metabolite transformation portion in foliar matrices, no unacceptable risks were found for mammals after application of SAP250F in the intended uses.

|  |
| --- |
| **zRMS comment:**  According to EFSA Conclusion 2007 a total conversion of prothioconazole to the desthio - metabolite was assumed in the assessment.  Therefore, the refinement based on parent-metabolite transformation portion in foliar matrices is considered ( Tier 2b) as additionally information and can be considered at MSs level. |

Table 9.3-9b: Refinement of the long-term/reproductive risk for mammals due to the use of SAP250F in OSR (metabolite) – Deposition factor

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Intended use | | **OSR** | | | | | | | |
| Active substance/product | | JAU 6476-desthio  3 x 175 (OSR) | | | | | | | |
| Application rate (g/ha) | |
| Reprod. toxicity (mg/kg bw/d) | | 10  5 | | | | | | | |
| TER criterion | |
| Crop scenario  Growth stage | Indicator/generic focal species | | RUD | MAFm | ftwa | DF | PT | DDDm  (mg/kg bw/d) | TERlt |
| OSR  BBCH ≥ 40 | Small herbivorous mammal “Vole grass + cereals 100% grass | | 18.1 | 1.3 | 0.53 | 0.25 | 1.0 | 1.65 | 34.58 |

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger. DF: Deposition factor

**Overall conclusion**

For voles, risk assessment is considered to be covered through the assessment of other small mammalian species for the following reasons:

• High fecundity and population recuperation

• Primary source of food outside crops fields

• Necessity of population control measures since the vole is considered a crop pest when high population levels are reached

• Other agricultural techniques being also means of population control

This may not apply in many Member States were the “vole” scenario is considered as relevant. In such cases considering the **refinement options described above (PT or refined data from residue studies), the risk assessment for herbivorous mammals is considered sufficiently addressed.**

|  |
| --- |
| **zRMS comment:**  The acute and chronic risks of Indofil to mammals were assessed from toxicity exposure ratios between toxicity endpoints, estimated from study with active substance, its metabolites, and maximum residues occurring on food items.  For active substance all TER values exceed the relevant triggers indicating that Indofil does not pose an unacceptable risk to mammals following applications according to recommended use pattern. Nevertheless, for prothioconazole-desthio the safe uses were confirmed based on refined risk assessment for small herbivorous mammal (vole) for all proposed uses of Indofil.  **The relevance of voles as a focal species for those crops should be consider at national level.**  Evaluation of exposing to mammals through the drinking water demonstrated the acceptable risk.  The risk to earthworm- and fish-eating animals from secondary poisoning is low. |

When necessary, the assessment of the risk for mammals due to uptake of contaminated drinking water is conducted for a small omnivorous mammal with a body weight of 21.7 g (*Apodemus sylvaticus*) and a drinking water uptake rate of 0.24 L/kg bw/d (*cf*. Appendix K of EFSA/2009/1438).

Puddle scenario

Due to the characteristics of the exposure scenario in connection with the standard assumptions for water uptake by animals, no specific calculations of exposure and TER are necessary when the ratio of effective application rate (in g/ha) to relevant endpoint (in mg/kg bw/d) does not exceed 50 in the case of less sorptive substances (Koc < 500 L/kg) or 3000 in the case of more sorptive substances (Koc ≥ 500 L/kg).

AReff = AR x MAFm = AR x 

Where

k = ln(2)/DT50 (rate constant)

n = number of applications

i = application interval (days)

When multiple spray applications are considered, a MAF based on the DT50 in soil (single first order kinetics, geometric mean as used for PECgw and PECsw) is applied to achieve the effective application rate AReff.

With a K(f)oc of 1765 (mean value ) and 575.4 (mean value ) respectively for Prothioconazole and JAU 6476-desthio, both belong to the group of more sorptive substances.

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group cereals also covers the risk for birds from all other intended uses in group OSR (see 9.1.2).

Table 9.3-9 Effective application rate

| **Crop** | **Substance** | **DT50** | **Max application rate (AR) (g as/ha)** | **No. of applications** | **1-e-nki** | **1-e-ki** | **MAFmean** | **AReff** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Cereals | Prothioconazole | 2.8 | 200 | 3 | 0.9999 | 0.9688 | 1.03 | 206.4 |

**Table 9.3-10 Ratio of AReff to acute/long term toxicity endpoint**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **No concern if ratio** | | | | |
| Prothioconazole: Effective application rate (g/ha) = | 206.4, 3 x 200\* | | | |
| Active substance (Prothioconazole) | | | | |
| Koc (l/kg) = | 1765 | | | |
| Acute toxicity (mg/kg bw) = | 6200 | quotient = | 0.03  0.096 | ≤ 3000 |
| Reprod. toxicity (mg/kg bw/d) = | 95.6 | quotient = | 2.16  6.27 | ≤ 3000 |
| Metabolite (JAU 6476-desthio) | | | | |
| Koc (l/kg) = | 575.4 | | | |
| Acute toxicity (mg/kg bw) = | 2235 | quotient = | 0.09  0.26 | ≤ 3000 |
| Reprod. toxicity (mg/kg bw/d) = | 10 | quotient = | 20.6  29.12 | ≤ 3000 |

\*the worst case scenario

The acute and long-term risk to mammals exposed to SAP250F via drinking water is therefore acceptable for the intended uses.

**zRMS comment:**

~~Since is not a for spray applications / not intended to be applied on leafy vegetables forming heads or crop plants with comparable water collecting structures at principal growth stage 4 or later.~~

As INDOFIL Prothio 250 EC is not intended for leafy crops forming heads, the leaf scenario does not have to be therefore considered ~~taking onto account~~ based on the proposed uses (cereals and oilseed rape). Evaluation of exposing for birds through the drinking water Puddle scenario for the active substance and metabolite M04, demonstrate that the acceptable risk for mammals for proposed use pattern of SAP250F/Indofil.

#### Effects of secondary poisoning

The log Pow of Prothioconazole and Prothioconazole-desthio amounts to 4.05 and 3.04 and for M01 to 4.19, respectively and thus exceeds the trigger value of 3. A risk assessment for effects due to secondary poisoning is required.

Risk assessment for earthworm-eating mammals via secondary poisoning

According to EFSA/2009/1438, the risk for vermivorous mammals is assessed for a small mammal of 10 g body weight with a daily food consumption of 12.8 g. Bioaccumulation in earthworms is estimated based on measured/predicted concentrations in soil/porewater / is based on experimental data.

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group cereals also covers the risk for mammals from all other intended uses in group OSR (see 9.1.2).

Parameters used by zRMS in the assessment of the risk for earthworm-eating birds due to exposure to Prothioconazole and prothioconazole metabolites via bioaccumulation in earthworms and fish (secondary poisoning)

| Parameter | Prothioconazole | Prothioconazole-desthio  (M04) | Prothioconazole -S-methyl (M01) | comments |
| --- | --- | --- | --- | --- |
| log Pow / Pow | 3.4 / 2511.9 | 3.04 / 1096.5 | 4.19 / 15448.2 | EFSA Scientific Report (2007) 106, 1-98 |
| Koc | 1765 | 575.4 | 2556.3 | Geomean (M04 and M01) EFSA Scientific Report (2007) 106, 1-98 |
| foc | 0.02 | 0.02 | 0.02 | Default |

Table 9.3‑11: Assessment of the risk for earthworm-eating mammals due to exposure to Prothioconazole via bioaccumulation in earthworms (secondary poisoning) for the intended use in cereals

| Parameter | Prothioconazole | comments |
| --- | --- | --- |
| PECsoil (twa = 21 d) (mg/kg soil) | 0.220 | Worst-case PECsoil calculated for multiple applications in all crops |
| log Pow / Pow | ~~4.05 / 11220~~  3.4 / 2511.9 | EFSA 2007 |
| Koc | 1765 | (aged leaching study, only one soil tested, value used for PELMOgw modelling; 1/n set to 0.90) |
| foc | 0.02 | Default |
| BCFworm | ~~3.84~~  0.87 | BCFworm/soil = (PECworm,ww/PECsoil,dw) = (0.84 + 0.012 × Pow) / foc × Koc |
| PECworm | ~~0.845~~  0.19 | PECworm = PECsoil × BCFworm/soil |
| Daily dietary dose (mg/kg bw/d) | ~~1.08~~  0.25 | DDD = PECworm × 1.28 |
| NOEL (mg/kg bw/d) | 95.6 |  |
| TERlt | ~~89~~  382.4 | >5, no further refinement |

TER values shown in bold fall below the relevant trigger.

Table 9.3‑12: Assessment of the risk for earthworm-eating mammals due to exposure to JAU 6476-desthio via bioaccumulation in earthworms (secondary poisoning) for the intended use in cereals

| Parameter | JAU 6476-desthio (M04) | comments |
| --- | --- | --- |
| PECsoil (twa = 21 d) (mg/kg soil) | 0.394 | Worst-case PECsoil calculated for multiple applications in all crops. |
| log Pow / Pow | 3.04 / 1096.5 |  |
| Koc | 575.4 | Mean (n=4), EFSA 2007 |
| foc | 0.02 | Default |
| BCFworm | 1.22 | BCFworm/soil = (PECworm,ww/PECsoil,dw) = (0.84 + 0.012 × Pow) / foc × Koc |
| PECworm | 0.48 | PECworm = PECsoil × BCFworm/soil |
| Daily dietary dose (mg/kg bw/d) | 0.6144 | DDD = PECworm × 1.28 |
| NOEL (mg/kg bw/d) | 10 |  |
| TERlt | 16.27 | >5, no further refinement |

TER values shown in bold fall below the relevant trigger.

Table 9.3‑13. Assessment of the risk for earthworm-eating mammals due to exposure to prothioconazole-S-methyl (M01) via bioaccumulation in earthworms (secondary poisoning) for cereals covering oilseed rape.

| Parameter | Prothioconazole-S-methyl (M01) | Comments |
| --- | --- | --- |
| PECsoil (mg/kg soil) | 0.261 |  |
| log Pow / Pow | 4.19/15448.2 | EFSA Conclusion  (EFSA Scientific Report (2007) 106, 1-98) |
| Koc | 2256.3 |  |
| foc | 0.02 | Default |
| BCFworm | 4.12 | BCFworm/soil = (PECworm,ww/PECsoil,dw) = (0.84 + 0.012 × Pow) / foc × Koc |
| PECworm | 1.07 | PECworm = PECsoil × BCFworm/soil |
| Daily dietary dose (mg/kg bw/d) | 1.37 | DDD = PECworm × 1.28 |
| NOEL (mg/kg bw/d) | 9.56\* |  |
| TERlt | 6.97 |  |

TER values shown in bold fall below the relevant trigger.

\*Endpoint estimated as parent NOEL/10.

The TERlt for the assessment of the risk for earthworm-eating mammals due to exposure to prothioconazole, prothioconazole-S-methyl (M01), M04 via bioaccumulation in earthworms does not fall below the relevant trigger TER value of 5, indicating low risk to birds following applications of Indofil.

Risk assessment for fish-eating mammals via secondary poisoning

According to EFSA/2009/1438, the risk for piscivorous mammals is assessed for a mammal of 3000 g body weight with a daily food consumption of 425 g. Bioaccumulation in fish is estimated based on predicted concentrations in surface water / is based on the regulatory acceptable concentration for aquatic organisms as a limit value for admissible concentrations of Prothioconazole in water.

Table 9.3‑14: Assessment of the risk for fish-eating mammals due to exposure to Prothioconazole via bioaccumulation in fish (secondary poisoning) for the intended use in cereals

|  |  |  |
| --- | --- | --- |
| Parameter | Prothioconazole | comments |
| PECsw (max) (mg/L) | 0.021 | Worst-case Step 1 PECsw calculated for multiple application in winter and spring cereals (Table 9.5-3) |
| BCFfish | 19.7 |  |
| BMF | - | biomagnification factor (relevant for BCF ≥ 2000) |
| PECfish | 0.419 | PECfish = PECwater × BCFfish |
| Daily dietary dose (mg/kg bw/d) | 0.060 | DDD = PECfish × 0.142 |
| NOEL (mg/kg bw/d) | 95.6 |  |
| TERlt | 1606.7 | >5, no further refinement |

TER values shown in bold fall below the relevant trigger.

Table 9.3‑15: Assessment of the risk for fish-eating mammals due to exposure to JAU 6476-desthio via bioaccumulation in fish (secondary poisoning) for the intended use in cereals

|  |  |  |
| --- | --- | --- |
| Parameter | JAU 6476-desthio ( M04) | comments |
| PECsw (max) (mg/L) | 0.1108 | Worst-case Step 1 PECsw calculated for multiple application in winter and spring cereals. (Table 9.5-4) |
| BCFfish | 65 |  |
| BMF | - | biomagnification factor (relevant for BCF ≥ 2000) |
| PECfish | 7.202 | PECfish = PECwater × BCFfish |
| Daily dietary dose (mg/kg bw/d) | 1.023 | DDD = PECfish × 0.142 |
| NOEL (mg/kg bw/d) | 10 |  |
| TERlt | 9.78 | >5, no further refinement |

TER values shown in bold fall below the relevant trigger.

Table 9.3‑16 : Assessment of the risk for fish-eating mammals due to exposure to prothioconazole-S-methyl (M01) via bioaccumulation in fish (secondary poisoning) for the intended , assuming the best-case whole fish BCF value of 319 L/kg in cereals

|  |  |  |
| --- | --- | --- |
| **Parameter** | **Prothioconazole-S -methyl (M01)** | **Comments** |
| PECsw (mg/L) | 0.002898 | FOCUS Step 2 (Section 8) |
| BCFfish | 319 | EFSA Conclusion  (EFSA Scientific Report (2007) 106, 1-98) |
| BMF | N/A | biomagnification factor (relevant for BCF ≥ 2000) |
| PECfish | 0.9244 | PECfish = PECwater × BCFfish |
| Daily dietary dose (mg/kg bw/d) | 0.131 | DDD = PECfish × 0.142 |
| NOEL (mg/kg bw/d) | 9.56\* | Derived endpoint |
| TERlt | 72.98 |  |

TER values shown in bold fall below the relevant trigger.

\*Endpoint estimated as parent NOEL/10.

Table 9.3‑17: Assessment of the risk for fish-eating mammals due to exposure to prothioconazole-S-methyl (M01) via bioaccumulation in fish (secondary poisoning) for the intended use assuming the worst-case whole fish BCF value of 1995 L/kg in cereals

|  |  |  |
| --- | --- | --- |
| **Parameter** | **Prothioconazole-S -methyl (M01)** | **Comments** |
| PECsw (mg/L) | 0.002898 | FOCUS Step 2 (Section 8) |
| BCFfish | 1995 | EFSA Conclusion  (EFSA Scientific Report (2007) 106, 1-98) |
| BMF | N/A | biomagnification factor (relevant for BCF ≥ 2000) |
| PECfish | 5.78 | PECfish = PECwater × BCFfish |
| Daily dietary dose (mg/kg bw/d) | 0.82 | DDD = PECfish × 0.142 |
| NOEL (mg/kg bw/d) | 9.56\* | Derived endpoint |
| TERlt | 11.65 |  |

TER values shown in bold fall below the relevant trigger.

\*Endpoint estimated as parent NOEL/10.

The TERlt for the assessment of the risk for fish-eating mammals due to exposure to prothioconazole, prothioconazole-S-methyl (M01), JAU 6476-desthio (M04) via bioaccumulation in fish does not fall below the relevant trigger TER value of 5.

#### Biomagnification in terrestrial food chains

Not relevant.

### Risk assessment for baits, pellets, granules, prills or treated seed

Not relevant.

### Overall conclusions

For acute dietary exposure of mammals to the active substance Prothioconazole and its metabolite JAU 6476-desthio, the TER for the required uses are above the trigger value at the Screening step. For the chronic (reproductive) dietary exposure of mammals to the active substance Prothioconazole, the TER for the required uses is ~~above~~ below the trigger value at the screening step, indicating a potential risk from the exposure of mammals to the metabolite. In the first risk assessment step, unacceptable risks were still found from herbivorous mammals exposure to the metabolite JAU 6476-desthio. After refinement ~~of PT~~ or fTWA or refined data from residue studies and/or focal species, no unacceptable risks were found for either small or large herbivorous mammals. The risk to mammals exposed to SAP250F via drinking water is acceptable for the intended use as the ratio between the effective application rate and the acute and long-term endpoints is below 3000 (Prothioconazole is more sorptive). Secondary poisoning assessments were triggered for both Prothioconazole and its metabolites (JAU 6476-desthio) and M01. No unacceptable risks were found on the assessment of biomagnification in terrestrial food chains after application of SAP250F in the intended uses. Therefore, treatment with SAP250F in accordance with the proposed uses poses an acceptable risk to mammals.

## Effects on other terrestrial vertebrate wildlife (reptiles and amphibians) (KCP 10.1.3)

No available information.

## Effects on aquatic organisms (KCP 10.2)

### Toxicity data

Studies on the toxicity to aquatic organisms have been carried out with Prothioconazole and its relevant metabolites. Full details of these studies are provided in the respective EU DAR and related documents, as well as in Appendix 2 of this document (new studies).

Effects on aquatic organisms of SAP250F were not evaluated as part of the EU assessment of Prothioconazole. New data submitted with this application are listed in Appendix 1 and summarised in Appendix 2.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.5‑1: Endpoints and effect values relevant for the risk assessment for aquatic organisms – Prothioconazole and relevant metabolites

| Species | Substance | Exposure  System | Results | Reference |
| --- | --- | --- | --- | --- |
| Fish | | | | |
| *Oncorhynchus mykiss* | Prothioconazole | Acute | **LC50 = 1.83 mg a.s./L** | EFSA Scientific Report (2007) |
| *Oncorhynchus mykiss* | Prothioconazole  (EC 250) | Acute | LC50 = 1.00 mg a.s./L | EFSA Scientific Report (2007) |
| *Lepomis macrochirus* | Prothioconazole | Acute | LC50 = 4.59 mg a.s./L | EFSA Scientific Report (2007) |
| *Cyprinus carpio* | Prothioconazole | Acute | LC50 = 6.91 mg a.s./L | EFSA Scientific Report (2007) |
| *Cyprinus carpio* | Prothioconazole  (EC250) | Acute | LC50 = 3.72 mg a.s./L | EFSA Scientific Report (2007) |
| *Oncorhynchus mykiss* | Prothioconazole | Chronic, ELS | **NOEC = 0.308 mg a.s./L** | EFSA Scientific Report (2007) |
| *Oncorhynchus mykiss* | JAU 6476-desthio | Acute | LC50 = 6.63 mg p.m./L | EFSA Scientific Report (2007) |
| *Leuciscus idus melanotus* | JAU 6476-desthio | Acute | LC50 = 13.2 mg p.m./L | EFSA Scientific Report (2007) |
| *Oncorhynchus mykiss* | JAU 6476-desthio | Chronic, ELS | NOEC = 3.34 mg p.m./L | EFSA Scientific Report (2007) |
| *Oncorhynchus mykiss* | JAU 6476-S-methyl | Acute | LC50 = 1.8 mg p.m./L | EFSA Scientific Report (2007) |
| *Oncorhynchus mykiss* | 1,2,4-Triazole | Acute | LC50 = 498 mg p.m./L | EFSA Scientific Report (2007) |
| *Oncorhynchus mykiss* | 1,2,4-Triazole | Chronic | NOErC = 3.2 mg a.s./L | EFSA Scientific Report (2007) |
| *Daphnia* | | | | |
| *Daphnia magna* | Prothioconazole | Acute | **EC50 = 1.3 mg a.s./L** | EFSA Scientific Report (2007) |
| *Daphnia magna* | Prothioconazole  (EC250) | Acute | EC50 = 0.71 mg a.s./L | EFSA Scientific Report (2007) |
| *Daphnia magna* | Prothioconazole | Chronic | **NOEC = 0.56 mg a.s./L** | EFSA Scientific Report (2007) |
| *Daphnia magna* | JAU 6476-desthio | Acute | EC50 > 10 mg p.m./L | EFSA Scientific Report (2007) |
| *Daphnia magna* | JAU 6476-desthio | Chronic | NOEC = 0.10 mg p.m./L | EFSA Scientific Report (2007) |
| *Daphnia magna* | JAU 6476-S-methyl | Acute | EC50 = 2.8 mg p.m./L | EFSA Scientific Report (2007) |
| *Daphnia magna* | 1,2,4-Triazole | Acute | EC50 = 900 mg p.m./L | EFSA Scientific Report (2007) |
| Freshwater Algae | | | | |
| *Pseudokirchneriella subcapitata* | Prothioconazole | Sub-chronic | EbC50 = 1.10 mg a.s./L  **ErC50 = 2.18mg a.s./L** | EFSA Scientific Report (2007) |
| *Pseudokirchneriella subcapitata* | Prothioconazole  (EC250) | Sub-chronic | EbC50 = 2.92 mg a.s./L  ErC50 = 1.11 mg a.s./L | EFSA Scientific Report (2007) |
| *Scenedesmus subspicatus* | JAU 6476-desthio | Sub-chronic | EbC50 = 0.073 mg p.m./L  ErC50 = 0.55 mg p.m./L | EFSA Scientific Report (2007) |
| *Pseudokirchneriella subcapitata* | JAU 6476-S-methyl | Sub-chronic | EbC50 = 3.77 mg p.m./L  ErC50 = 47.4 mg p.m./L | EFSA Scientific Report (2007) |
| *Pseudokirchneriella subcapitata* | 1,2,4-Triazole | Sub-chronic | EbC50 = 8.2 mg p.m./L\*  ErC50 = 22.5 mg p.m./L\* | EFSA Scientific Report (2007) |
| Sediment organisms | | | | |
| *Chironomus riparius* | Prothioconazole | Chronic | **NOEC = 9.14 mg a.s./L** | EFSA Scientific Report (2007) |
| *Chironomus riparius* | JAU 6476-desthio | Chronic | NOEC = 2.0 mg p.m../L | EFSA Scientific Report (2007) |
| Fish, Bioconcentration | | | | |
| *Lepomis macrochirus* | Prothioconazole | BCFparent = 19.7  Clearance time (CT50 days): 0.8  Level of residue (%) after 14 day depuration phase: 9% | | EFSA Scientific Report (2007) |
| *Lepomis macrochirus* | JAU 6476-desthio | BCFparent = 65  Clearance time (CT50 days): 0.4-05  Level of residue (%) after 14 day depuration phase: 4% | | EFSA Scientific Report (2007) |
| Higher-tier studies (micro- or mesocosm studies) | | | | |
| - | | | | |

s: static; ss: semi-static; f: flow-through; nom: based on nominal concentrations; mm: based on mean measured concentrations; im: based on initial measured concentrations

\* Endpoint value according to agreement in PRAPeR expert meeting on triazole metabolites (PRAPeP 13, January 2007).

Table 9.5‑2: Endpoints and effect values relevant for the risk assessment for aquatic organisms – SAP250F

| Species | Substance | Exposure  System | Results | Reference |
| --- | --- | --- | --- | --- |
| *Daphnia magna* | SAP250F | 48 h, ss | EC50 = 2.93 mg/L ~~nom~~ geomean  EC20 = 2.11 mg/L ~~nom~~ geomean  EC10 = 1.69 mg/L ~~nom~~ geomean  NOEC = 1.12 mg/L geomean | KCP 10.2.1/01, Siche, O., Wydra, V. (2019) |
| *Pseudokirchneriella subcapitata* | SAP250F | 72 h, s | EyC50 = 4.68 mg/L ~~mm~~ geomean  **ErC50 = 15.8 mg/L ~~m~~m** geomean  ErC20 = 6.69 mg/L ~~mm~~geomean  ErC10 = 4.26 mg/L ~~mm~~geomean  NOECr = 0.49 mg/L geomean | KCP 10.2.1/02, Siche, O., Wydra, V. (2019) |
| *Lemna gibba* | SAP250F | 7 d, ss | EyC50 = 2.50 mg/L ~~mm~~~~g~~eomean  **ErC50 = 11.6 mg/L mm**  ErC20 = 5.54 mg/L ~~mm~~ geomean  ErC10 = 3.77 mg/L ~~mm~~ geomean  NOECr < 0.274 mg/L geomean | KCP 10.2.1/03, Siche, O., Wydra, V. (2019) |

s: static; ss: semi-static; f: flow-through; nom: based on nominal concentrations; mm: based on mean measured concentrations

geomean=geomean concentration

**Model Deviation Ratio:**

Following the scheme presented in the Aquatic Guidance (EFSA Journal, 2013; 11(7):3290):

1. There are sufficient data for two aquatic organisms (Daphnia magna and Pseudokirchneriella subcapitata) from the active substance (ECxa.s.) and the formulated product (ECxppp)
2. MDR = ECxmix—CA/ECxppp

To demonstrate that risk assessments can be conducted with data from the active substance, the comparison of the lowest formulation end point (biomass/yield or growth; nominal or measured) to the calculated toxicity, according to the formula provided in the Guidance on aquatic organisms[[1]](#footnote-1) was performed: the comparison between the formulation toxicity and the calculated toxicity can be done by the formula (MRD = ECx-ca/ECxppp). If MDR is lower than 0.2 the formulation in less toxic than the expected, if MDR is > 5 the formulation is more toxic than the concentration addition, if MDR = 0.2 to 5 the concentration addition approximately holds for the formulation.

In order to address the expected toxicity with the formulation driven by the individual a.s., it is considered the following equation:

1/expected Tox = (% a.i. 1/measured Tox a.i.)

Where,

Expected Tox: expected theoretical EC50 value for the preparation SAP250F.

% a.i.. Fraction (weight/weight) of active ingredient (25% in this case)

Measured Tox a.i.: lowest LC50 value for active ingredient

*Daphnia magna*

*Pseudokirchneriella subcapitata*

The expected EC50 values of SAP250F were **5.20 mg/L** for *Daphnia magna*, and **8.72** **mg/L** for algae.

*Daphnia magna* = 5.20 / 2.93 = 1.77

*Pseudokirchneriella subcapitata* = 8.72 / 15.8 = 0.55

The model deviation ratios (MDR) for *Daphnia magna* and the algae *Pseudokirchneriella subcapitata* is considered in agreement as the MDR (Model Deviation Ratio) is between 0.2 and 5.0.

1. The formulated product here assessed only contains one active substance (Prothioconazole), therefore the further steps on the assessment of the combination of a.s. in formulations (toxic unit approaches) do not apply. As the results from the toxicity tests using the formulation indicate that the toxicity of the formulation reflects the toxicity of the constituent a.s., the risk assessment conducted with the a.s. endpoint is considered adequate and conservative.

**Fish acute test**

Following the scheme presented in the Aquatic Guidance (EFSA Journal, 2013; 11(7):3290), an acute toxicity test using fish is a requirement unless enough data on the active substance is available proving that from the three groups of aquatic organisms (fish, invertebrates and algae; the aquatic plant is not a requirement as SAP250F is a fungicide), one other than fish is clearly more sensitive by a factor of 10.

Data on the active substance is available for the three above-mentioned aquatic organisms:

Fish (*Oncorhynchus mykiss*) LC50 = 1.83 mg/L

Invertebrates (*Daphnia magna*) EC50 = 1.3 mg/L

Algae (*Pseudokirchneriella subcapitata*) ErC50 = 2.18 mg/L

From this data, invertebrates are the most sensitive group (lowest endpoint). This lower sensitivity does not fulfill the factor of 10 criteria for exclusion of the fish acute test (1.83/1.3 = 1.4). However, according to Article 62 of Regulation (EC) No 1107/2009 tests and studies on vertebrates should be avoided.

From the endpoints presented in EFSA Scientific Report (2007) for the active substance and the endpoints obtained in the studies performed with SAP250F, it is clear that the formulated product is less toxic than the active substance for the algae *Pseudokirchneriella subcapitata*.

|  |  |  |  |
| --- | --- | --- | --- |
| *Pseudokirchneriella subcapitata* | Prothioconazole | ErC50 = 2.18mg a.s./L | EFSA Scientific Report (2007) |
| SAP250F | ErC50 = 15.8 mg test item/L mm  ErC50 = 3.95 mg a.s./L mm | KCP 10.2.1/02, Siche, O., Wydra, V. (2019) |

When looking at the endpoints of the invertebrate *Daphnia magna*, the formulated product SAP250F seems to be slightly more toxic than the active substance, but with comparable toxicity to the formulated product presented in the EFSA Scientific Report (2007).

|  |  |  |  |
| --- | --- | --- | --- |
| *Daphnia magna* | Prothioconazole | EC50 = 1.3 mg a.s./L | EFSA Scientific Report (2007) |
| Prothioconazole  (EC250) | EC50 = 0.71 mg a.s./L | EFSA Scientific Report (2007) |
| SAP250F | EC50 = 2.93 mg test item/L nom  EC50 = 0.73 mg a.s./L nom | KCP 10.2.1/01, Siche, O., Wydra, V. (2019) |

In EFSA Scientific Report (2007) there are acute fish results from two commercial formulations presented. The acute endpoints presented for the active substance vary between 1.83 and 6.91 mg a.s./L depending on the fish species used. For both commercial formulations, the endpoints presented are 1.00 and 3.72 mg a.s./L. Both formulations have 250 g/L Prothioconazole, being constituted by only one active substance. This is similar to the formulated product here assessed. It is therefore expected that the toxicity of the formulated product here assessed, and the ones presented in EFSA Scientific Report (2007) should be similar.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Fish | | | | |
| *Oncorhynchus mykiss* | Prothioconazole | Acute | **LC50 = 1.83 mg a.s./L** | EFSA Scientific Report (2007) |
| *Oncorhynchus mykiss* | Prothioconazole  (EC 250) | Acute | LC50 = 1.00 mg a.s./L | EFSA Scientific Report (2007) |
| *Lepomis macrochirus* | Prothioconazole | Acute | LC50 = 4.59 mg a.s./L | EFSA Scientific Report (2007) |
| *Cyprinus carpio* | Prothioconazole | Acute | LC50 = 6.91 mg a.s./L | EFSA Scientific Report (2007) |
| *Cyprinus carpio* | Prothioconazole  (EC250) | Acute | LC50 = 3.72 mg a.s./L | EFSA Scientific Report (2007) |

As a conservative approach, in the table below please find the risk assessment for the lowest fish acute endpoint considering the formulated products in EFSA Scientific Report (2007): 1.00 mg a.s./L. In accordance with Article 62 of Regulation (EC) No 1107/2009, the acute risk assessment for fish is considered covered by this.

| Group |  | Fish acute |
| --- | --- | --- |
| Test species |  | *Oncorhynchus mykiss* |
| Endpoint |  | LC50 |
| (µg/L) |  | 1000 |
| AF |  | 100 |
| RAC (µg/L) |  | 10 |
| ***Winter Cereals*** | | |
| FOCUS Scenario | PEC gl-max (µg/L) | PEC/RAC |
| Step 1 |  |  |
|  | 21.72 | **2.2** |
| Step 2 |  |  |
| N-Europe | 1.84 | 0.2 |
| S-Europe | 1.84 | 0.2 |
| ***Spring Cereals*** | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |
| Step 1 |  |  |
|  | 21.72 | **2.2** |
| Step 2 |  |  |
| N-Europe | 1.84 | 0.2 |
| S-Europe | 1.84 | 0.2 |
| ***Winter Oilseed rape*** | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |
| Step 1 |  |  |
|  | 19.01 | **1.9** |
| Step 2 |  |  |
| N-Europe | 1.61 | 0.2 |
| S-Europe | 1.61 | 0.2 |
| ***Spring Oilseed rape*** | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |
| Step 1 |  |  |
|  | 19.01 | **1.9** |
| Step 2 |  |  |
| N-Europe | 1.61 | 0.2 |
| S-Europe | 1.61 | 0.2 |

An acceptable risk when using the lowest fish acute endpoint presented in EFSA Scientific Report (2007) for a formulated product. Therefore, it is considered that SAP250F will not pose any unacceptable risks in the intended uses.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **zRMS comment:**  The MDR ratio is not required for solo formulation according to EFSA GD 2013.  Based on the argumentation provided by the applicant we agree that the study for formulation SAP250F with one active substance - prothioconzole for fish is not required in this case.  The lowest fish acute endpoint for representative formulation 250 EC (with the same amount of the a.s./L as Indoifil) in LoEP EFSA Scientific Report (2007), indicated only slight difference in the toxicity in comparison to a.s. endpoints for fish.  In addition, when using the lowest fish acute endpoint presented in EFSA Scientific Report (2007) for a formulated product (expressed in a.s. units) an acceptable acute risk is concluded without risk mitigation measures.   |  |  |  |  |  | | --- | --- | --- | --- | --- | | *Oncorhynchus mykiss* | Prothioconazole | Acute | **LC50 = 1.83 mg a.s./L** | EFSA Scientific Report (2007) | | *Oncorhynchus mykiss* | Prothioconazole  (EC 250) | Acute | LC50 = 1.00 mg a.s./L | EFSA Scientific Report (2007) | | *Fish* | SAP250F | The study is not required for fish | | | |

#### Justification for new endpoints

Not relevant.

### Risk assessment

The evaluation of the risk for aquatic and sediment-dwelling organisms was performed in accordance with the recommendations of the “Guidance document on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters in the context of Regulation (EC) No 1107/2009”, as provided by the Commission Services (SANTE-2015-00080, 15 January 2015).

The relevant global maximum FOCUS Step 1, 2 and 3 PECSW for risk assessments covering the proposed use pattern and the resulting PEC/RAC ratios are presented in the table below.

In the following table, the ratios between predicted environmental concentrations in surface water bodies (PECSW, PECSED) and regulatory acceptable concentrations (RAC) for aquatic organisms are given per intended use for each FOCUS scenario and each organism group.

Table 9.5‑3: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Prothioconazole for each organism group based on FOCUS Steps 1, 2 calculations for the use of SAP250F

| Group |  | Fish acute | Fish prolonged | Inverteb. acute | Inverteb. prolonged | Algae | Sed. dwell. prolonged |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Test species |  | *Oncorhynchus mykiss* | *Oncorhynchus mykiss* | *Daphnia magna* | *Daphnia magna* | *Pseudokirchn. subcapitata* | *Chironomus riparius* |
| Endpoint |  | LC50 | NOEC | EC50 | NOEC | ErC50 | NOEC |
| (µg/L) |  | 1830 | 308 | 1300 | 560 | 2180 | 9140 |
| AF |  | 100 | 10 | 100 | 10 | 10 | 10 |
| RAC (µg/L) |  | 18.3 | 30.8 | 13 | 56 | 218 | 914 |
| ***Winter Cereals*** | | | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  | **PEC/RAC** |  |  |  |
| Step 1 |  |  |  |  |  |  |  |
|  | 21.72 | **1.187** | 0.702 | **1.671** | 0.388 | 0.100 | 0.024 |
| Step 2 |  |  |  |  |  |  |  |
| N-Europe | 1.839 | 0.100 | 0.060 | 0.141 | 0.033 | 0.008 | 0.002 |
| ***Spring Cereals*** | | | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  | **PEC/RAC** |  |  |  |
| Step 1 |  |  |  |  |  |  |  |
|  | 21.72 | **1.187** | 0.705 | **1.671** | 0.388 | 0.100 | 0.024 |
| Step 2 |  |  |  |  |  |  |  |
| N-Europe | 1.839 | 0.100 | 0.060 | 0.141 | 0.033 | 0.008 | 0.002 |
| ***Winter Oilseed rape*** | | | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  |  |  |  |  |
| Step 1 |  |  |  |  |  |  |  |
|  | 19.01 | **1.039** | 0.617 | **1.462** | 0.339 | 0.087 | 0.021 |
| Step 2 |  |  |  |  |  |  |  |
| N-Europe | 1.609 | 0.088 | 0.052 | 0.124 | 0.029 | 0.007 | 0.002 |
| ***Spring Oilseed rape*** | | | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  | **PEC/RAC** |  |  |  |
| Step 1 |  |  |  |  |  |  |  |
|  | 19.01 | **1.039** | 0.617 | **1.462** | 0.339 | 0.087 | 0.021 |
| Step 2 |  |  |  |  |  |  |  |
| N-Europe | 1.609 | 0.088 | 0.052 | 0.124 | 0.029 | 0.007 | 0.002 |

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

|  |
| --- |
| **zRMS comment:**  The risk assessment for the a.s. – prothiconazole is considered acceptable. Further calculations are not required. |

The step 3 PECsw values presented are worst-case between single and multiple applications.

Table 9.5‑4: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for JAU6476-desthio for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of SAP250F

| Group |  | Fish acute | Fish prolonged | Inverteb. acute | Inverteb. prolonged | Algae | Sed. dwell. prolonged |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Test species |  | *Oncorhynchus mykiss* | *Oncorhynchus mykiss* | *Daphnia magna* | *Daphnia magna* | *Scenedesmus subspicatus* | *Chironomus riparius* |
| Endpoint |  | LC50 | NOEC | EC50 | NOEC | ErC50 | NOEC |
| (µg/L) |  | 6630 | 3.34 | 10000 | 100 | 550 | 2000 |
| AF |  | 100 | 10 | 100 | 10 | 10 | 10 |
| RAC (µg/L) |  | 66.3 | 0.334 | 100 | 10 | 55 | 200 |
| ***Winter Cereals (3 x 200 g/ha)*** | | | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  |  |  |  |  |
| Step 1 |  |  |  |  |  |  |  |
|  | 110.8 | **1.671** | **5.004**  **331.73** | **1.108** | **11.080** | **2.015** | 0.554 |
| Step 2 |  |  |  |  |  |  |  |
| N-Europe (Oct – Feb) | 14.54 | 0.219 | **~~0.657~~**  **43.43** | 0.145 | **1.454** | 0.264 | 0.073 |
| N-Europe (Mar – May) | 6.619 | 0.100 | **~~0.299~~**  **19.81** | 0.066 | **0.662** | 0.120 | 0.033 |
| Step 3 |  |  |  |  |  |  |  |
| D3/ditch | 0.090 | 0.001 | ~~0.004~~  0.269 | 0.001 | 0.009 | 0.001 | 0.000 |
| D4/pond | 0.048 | 0.001 | ~~0.002~~  0.1437 | 0.000 | 0.005 | 0.001 | 0.000 |
| D4/stream | 0.058 | 0.001 | ~~0.003~~  0.1736 | 0.001 | 0.006 | 0.001 | 0.000 |
| D5/pond | 0.057 | 0.001 | ~~0.003~~  0.1706 | 0.001 | 0.006 | 0.001 | 0.000 |
| D5/stream | 0.115 | 0.002 | ~~0.005~~  0.344 | 0.001 | 0.012 | 0.002 | 0.001 |
| R1/pond | 0.207 | 0.003 | ~~0.009~~  0.619 | 0.002 | 0.021 | 0.004 | 0.001 |
| R1/stream | 1.073 | 0.016 | **~~0.048~~**  **3.21** | 0.011 | 0.107 | 0.020 | 0.005 |
| R3/stream | 1.161 | 0.018 | **~~0.052~~**  **3.47** | 0.012 | 0.116 | 0.021 | 0.006 |
| R4/stream | 2.412 | 0.036 | **~~0.109~~**  **7.22** | 0.024 | 0.241 | 0.044 | 0.012 |
| ***Winter Cereals (2 x 200 g/ha)*** | | | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  |  |  |  |  |
| Step 1 | | | | | | | |
|  | 73.87 | **1.11** | **221.17** | 0.74 | **7.39** | **1.34** | 0.37 |
| Step 2 | | | | | | | |
| N. Europe. Oct-Feb | 11.74 | 0.18 | **35.15** | 0.12 | **1.17** | 0.21 | 0.06 |
| N. Europe. Mar – May | 5.34 | 0.08 | **15.99** | 0.05 | 0.53 | 0.10 | 0.03 |
| Step 3 | | | | | | | |
| D3 Ditch | 1.107 | 0.017 | **3.31** | 0.011 | 0.11 | 0.020 | 0.0055 |
| D4 Pond | 0.039 | 0.00059 | 0.12 | 0.00039 | 0.0039 | 0.00071 | 0.00020 |
| D4 Stream | 0.837 | 0.013 | **2.51** | 0.0084 | 0.084 | 0.015 | 0.0042 |
| D5 Pond | 0.042 | 0.00063 | 0.13 | 0.00042 | 0.0042 | 0.0008 | 0.00021 |
| D5 Stream | 0.0965 | 0.0015 | 0.29 | 0.0010 | 0.0097 | 0.0018 | 0.00048 |
| R1 Pond | 0.041 | 0.00062 | 0.12 | 0.00041 | 0.0041 | 0.00075 | 0.00021 |
| R1 Stream | 0.721 | 0.011 | **2.16** | 0.0072 | 0.072 | 0.013 | 0.0036 |
| R3 Stream | 1.019 | 0.015 | **3.051** | 0.010 | 0.10 | 0.019 | 0.0051 |
| R4 Stream | 0.724 | 0.011 | **2.17** | 0.0072 | 0.072 | 0.013 | 0.0036 |
| ***Winter Cereals (1 x 200 g/ha)*** | | | | | | | |
| Step 1 | | | | | | | |
|  | 73.87 | **1.11** | **221.17** | 0.74 | **7.39** | **1.34** | 0.37 |
| Step 2 | | | | | | | |
| N. Europe. Oct-Feb | 7.362 | 0.11 | **22.04** | 0.07 | 0.74 | 0.13 | 0.04 |
| N. Europe. Mar – May | 3.313 | 0.05 | **9.92** | 0.03 | 0.33 | 0.06 | 0.02 |
| Step 3 | | | | | | | |
| D3 Ditch | 0.058 | 0.001 | 0.17 | 0.001 | 0.01 | 0.001 | 0.0003 |
| D4 Pond | 0.21 | 0.00317 | 0.63 | 0.00210 | 0.0210 | 0.00382 | 0.00105 |
| D4 Stream | 0.074 | 0.001 | 0.22 | 0.0007 | 0.007 | 0.001 | 0.0004 |
| D5 Pond | 0.026 | 0.00039 | 0.08 | 0.00026 | 0.0026 | 0.0005 | 0.00013 |
| D5 Stream | 0.114 | 0.0017 | 0.34 | 0.0011 | 0.0114 | 0.0021 | 0.00057 |
| R1 Pond | 0.056 | 0.00084 | 0.17 | 0.00056 | 0.0056 | 0.00102 | 0.00028 |
| R1 Stream | 0.363 | 0.005 | **1.09** | 0.0036 | 0.036 | 0.007 | 0.0018 |
| R3 Stream | 0.472 | 0.007 | **1.413** | 0.005 | 0.05 | 0.009 | 0.0024 |
| R4 Stream | 0.448 | 0.007 | **1.34** | 0.0045 | 0.045 | 0.008 | 0.0022 |
| ***Spring Cereals (3 x 200 g/ha)*** | | | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  |  |  |  |  |
| Step 1 |  |  |  |  |  |  |  |
|  | 110.8 | **1.671** | **~~5.004~~**  **331.73** | **1.108** | **11.080** | **2.015** | 0.554 |
| Step 2 |  |  |  |  |  |  |  |
| N-Europe (Oct-Feb) | 14.54 | 0.219 | **~~0.657~~**  **43.53** | 0.145 | **1.454** | 0.264 | 0.073 |
| N-Europe (Mar-May) | 6.619 | 0.100 | **~~0.299~~**  **19.81** | 0.066 | 0.662 | 0.120 | 0.033 |
| Step 3 |  |  |  |  |  |  |  |
| D3/ditch | 0.091 | 0.001 | ~~0.004~~  0.272 | 0.001 | 0.009 | 0.002 | 0.000 |
| D4/pond | 0.057 | 0.001 | ~~0.003~~  0.17 | 0.001 | 0.006 | 0.001 | 0.000 |
| D4/stream | 0.082 | 0.001 | ~~0.004~~  0.245 | 0.001 | 0.008 | 0.001 | 0.000 |
| D5/pond | 0.055 | 0.001 | ~~0.002~~  0.16 | 0.001 | 0.006 | 0.001 | 0.000 |
| D5/stream | 0.091 | 0.001 | ~~0.004~~  0.272 | 0.001 | 0.009 | 0.002 | 0.000 |
| R4/stream | 1.941 | 0.029 | ~~0.088~~  **5.81** | 0.019 | 0.194 | 0.035 | 0.010 |
| ***Winter Oilseed rape – early ( 2 x 175 g/ha)*** | | | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  |  |  |  |  |
| Step 1 |  |  |  |  |  |  |  |
|  | 64.63 | 0.975 | **~~2.919~~**  **193.50** | 0.646 | **6.463** | **1.175** | 0.323 |
| Step 2 |  |  |  |  |  |  |  |
| N-Europe (Jun-Sep) | 2.343 | 0.035 | **~~0.106~~**  **7.01** | 0.023 | 0.234 | 0.043 | 0.012 |
| N. Europe (Oct-Feb) | 4.441 | 0.067 | **~~0.201~~**  **13.30** | 0.044 | 0.444 | 0.081 | 0.022 |
| N. Europe (Mar-May) | 2.343 | 0.035 | **~~0.106~~**  **7.01** | 0.023 | 0.234 | 0.043 | 0.012 |
| Step 3 |  |  |  |  |  |  |  |
| D3/ditch | 0.129 | 0.002 | ~~0.006~~  0.39 | 0.001 | 0.013 | 0.001 | 0.002 |
| D4/pond | 0.058 | 0.001 | ~~0.003~~  0.17 | 0.001 | 0.006 | 0.000 | 0.001 |
| D4/stream | 0.21 | 0.003 | ~~0.009~~  0.63 | 0.002 | 0.021 | 0.001 | 0.004 |
| D5/pond | 0.038 | 0.001 | ~~0.002~~  0.11 | 0.000 | 0.004 | 0.000 | 0.001 |
| D5/stream | 0.118 | 0.002 | ~~0.005~~  0.35 | 0.001 | 0.012 | 0.001 | 0.002 |
| R1/pond | 0.09 | 0.001 | ~~0.004~~  0.27 | 0.001 | 0.009 | 0.000 | 0.002 |
| R1/stream | 0.861 | 0.013 | ~~0.039~~  **2.58** | 0.009 | 0.086 | 0.004 | 0.016 |
| R3/stream | 1.269 | 0.019 | ~~0.057~~  **3.80** | 0.013 | 0.127 | 0.006 | 0.023 |
| ***Winter Oilseed rape – late ( 2 x 175 g/ha)*** | | | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  |  |  |  |  |
| Step 1 |  |  |  |  |  |  |  |
|  | 64.63 | 0.975 | ~~2.919~~  **193.50** | 0.646 | **6.463** | 0.323 | **1.175** |
| Step 2 |  |  |  |  |  |  |  |
| N-Europe (Jun-Sep) | 2.343 | 0.035 | **~~0.106~~**  **7.01** | 0.023 | 0.234 | 0.043 | 0.012 |
| N. Europe (Oct-Feb) | 4.441 | 0.067 | **~~0.201~~**  **13.30** | 0.044 | 0.444 | 0.081 | 0.022 |
| N. Europe (Mar-May) | 2.343 | 0.035 | **~~0.106~~**  **7.01** | 0.023 | 0.234 | 0.043 | 0.012 |
| Step 3 |  |  |  |  |  |  |  |
| D3/ditch | 0.036 | 0.001 | ~~0.002~~  0.11 | 0.000 | 0.004 | 0.001 | 0.000 |
| D4/pond | 0.029 | 0.000 | ~~0.001~~  0.09 | 0.000 | 0.003 | 0.001 | 0.000 |
| D4/stream | 0.059 | 0.001 | ~~0.003~~  0.18 | 0.001 | 0.006 | 0.001 | 0.000 |
| D5/pond | 0.034 | 0.001 | ~~0.002~~  0.10 | 0.000 | 0.003 | 0.001 | 0.000 |
| D5/stream | 0.086 | 0.001 | ~~0.004~~  0.26 | 0.001 | 0.009 | 0.002 | 0.000 |
| R1/pond | 0.087 | 0.001 | ~~0.004~~  0.26 | 0.001 | 0.009 | 0.002 | 0.000 |
| R1/stream | 0.610 | 0.009 | ~~0.028~~  **1.83** | 0.006 | 0.061 | 0.011 | 0.003 |
| R3/stream | 0.494 | 0.007 | ~~0.022~~  **1.48** | 0.005 | 0.049 | 0.009 | 0.002 |
| ***Spring Oilseed rape*** | | | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  |  |  |  |  |
| Step 1 |  |  |  |  |  |  |  |
|  | 64.64 | 0.6 | **~~194~~**  **193.59** | 0.6 | **6.5** | **1.2** | 0.3 |
| Step 2 |  |  |  |  |  |  |  |
| N-Europe (Jun-Sep) | 2.343 | 0.035 | **~~0.106~~**  **7.01** | 0.023 | 0.234 | 0.043 | 0.012 |
| N. Europe (Oct-Feb) | 4.441 | 0.067 | **~~0.201~~**  **13.30** | 0.044 | 0.444 | 0.081 | 0.022 |
| N. Europe (Mar-May) | 2.343 | 0.035 | **~~0.106~~**  **7.01** | 0.023 | 0.234 | 0.043 | 0.012 |
| Step 3 |  |  |  |  |  |  |  |
| D3/ditch | 0.1 | 0.002 | ~~0.005~~  0.30 | 0.001 | 0.010 | 0.001 | 0.002 |
| D4/pond | 0.039 | 0.001 | ~~0.002~~  0.12 | 0.000 | 0.004 | 0.000 | 0.001 |
| D4/stream | 0.071 | 0.001 | ~~0.003~~  0.21 | 0.001 | 0.007 | 0.000 | 0.001 |
| D5/pond | 0.038 | 0.001 | ~~0.002~~  0.11 | 0.000 | 0.004 | 0.000 | 0.001 |
| D5/stream | 0.094 | 0.001 | ~~0.004~~  0.28 | 0.001 | 0.009 | 0.000 | 0.002 |
| R1/pond | 0.126 | 0.002 | ~~0.006~~  0.38 | 0.001 | 0.013 | 0.001 | 0.002 |
| R1/stream | 1.093 | 0.016 | ~~0.049~~  **3.27** | 0.011 | 0.109 | 0.005 | 0.020 |

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

An unacceptable risk is concluded at Step 3 calculations for fish long-term exposure. Therefore, mitigation measures (Step 4) are needed. The calculations are presented below.

|  |
| --- |
| **zRMS comment:**  The risk assessment for metabolite JAU6476-desthio needs further refinement as PECsw/RAC ratio for chronic risk for fish for stream scenarios such as: R1, R3 and R4 for Winter Cereals, for Spring Cereals at rate 3 x 200 g/ha for R4 scenario, for Winter Oilseed Rape at rate 2 x 175 g /ha (early and late applications) for R1 and R3 scenarios and for Spring Oilseed Rape for R1 stream scenario.  The calculations with PECsw FOCUS STEP 4 values were required for chronic risk for fish (please see in the Table below). |

Table 9.5‑4a: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for JAU6476-desthio for each organism group based on FOCUS Step ~~1, 2~~ 4 calculations for the use of SAP250F

| Group | Fish prolonged | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| Test species | *Oncorhynchus mykiss* | | | | | |
| Endpoint | NOEC | | | | | |
| (µg/L) | 3.34 | | | | | |
| AF | 10 | | | | | |
| RAC (µg/L) | 0.334 | | | | | |
| ***Winter Cereals (3 x 200 g/ha)*** | | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) | | **PEC/RAC** | | **PEC gl-max (µg/L)** | **PEC/RAC** |
| Step 4 | Multiple application, 10 m VFS | | | | Multiple applications, 20 m VFS | |
| D3/ditch | 0.012 | | ~~0.001~~  0.04 | | 0.006 | ~~0.000~~  0.02 |
| D4/pond | 0.029 | | ~~0.001~~  0.09 | | 0.019 | ~~0.001~~  0.06 |
| D4/stream | 0.014 | | ~~0.001~~  0.04 | | 0.014 | ~~0.001~~  0.04 |
| D5/pond | 0.035 | | ~~0.002~~  0.10 | | 0.023 | ~~0.001~~  0.07 |
| D5/stream | 0.022 | | ~~0.001~~  0.07 | | 0.011 | ~~0.000~~  0.03 |
| R1/pond | 0.094 | | ~~0.004~~  0.28 | | 0.051 | ~~0.002~~  0.15 |
| R1/stream | 0.487 | | ~~0.022~~  **1.46** | | 0.255 | ~~0.012~~  0.76 |
| R3/stream | 0.530 | | ~~0.024~~  **1.59** | | 0.278 | ~~0.013~~  0.83 |
| R4/stream | 1.097 | | ~~0.050~~  **3.28** | | 0.575 | ~~0.026~~  **1.72** |
| ***Winter Cereals (2 x 200 g/ha)*** | | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) | | PEC/RAC | | PEC gl-max (µg/L) | PEC/RAC |
| Step 4 | Multiple application, 10 m VFS | | | | Multiple applications, 20 m VFS | |
| D3/ditch | 0.0075 | | 0.022 | | 0.0038 | 0.011 |
| D4/pond | 0.021 | | 0.063 | | 0.014 | 0.042 |
| D4/stream | 0.012 | | 0.036 | | 0.0086 | 0.026 |
| D5/pond | 0.027 | | 0.081 | | 0.017 | 0.051 |
| D5/stream | 0.020 | | 0.060 | | 0.010 | 0.030 |
| R1/pond | 0.066 | | 0.20 | | 0.037 | 0.111 |
| R1/stream | 0.487 | | **1.46** | | 0.255 | 0.763 |
| R3/stream | 0.530 | | **1.59** | | 0.278 | 0.832 |
| R4/stream | 0.610 | | **1.83** | | 0.32 | 0.958 |
|  |  | |  | |  |  |
| ***Winter Cereals (1 x 200 g/ha)*** | | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) | PEC/RAC | | PEC gl-max (µg/L) | | PEC/RAC |
| Step 4 | Multiple application, 10 m VFS | | | Multiple applications, 20 m VFS | | |
| D3/ditch | 0.0084 | 0.025 | | 0.0043 | | 0.013 |
| D4/pond | 0.013 | 0.039 | | 0.0084 | | 0.025 |
| D4/stream | 0.014 | 0.042 | | 0.0075 | | 0.022 |
| D5/pond | 0.016 | 0.048 | | 0.011 | | 0.033 |
| D5/stream | 0.022 | 0.066 | | 0.011 | | 0.033 |
| R1/pond | 0.028 | 0.08 | | 0.014 | | 0.042 |
| R1/stream | **0.165** | **0.49** | | 0.065 | | 0.195 |
| R3/stream | **0.215** | **0.64** | | 0.086 | | 0.257 |
| R4/stream | **0.204** | **0.61** | | 0.081 | | 0.243 |
| ***Spring Cereals (3 x 200 g/ha)*** | | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) | |  | | **PEC gl-max (µg/L)** |  |
| Step 4 | Multiple application, 10 m VFS | | | | Multiple applications, 20 m VFS | |
| D3/ditch | 0.013 | | ~~0.001~~  0.04 | | 0.006 | ~~0.000~~  0.02 |
| D4/pond | 0.035 | | ~~0.002~~  0.10 | | 0.023 | ~~0.001~~  0.07 |
| D4/stream | 0.032 | | ~~0.001~~  0.10 | | 0.032 | ~~0.001~~  0.10 |
| D5/pond | 0.033 | | ~~0.001~~  0.10 | | 0.022 | ~~0.001~~  0.07 |
| D5/stream | 0.017 | | ~~0.001~~  0.05 | | 0.009 | ~~0.000~~  0.03 |
| R4/stream | 0.883 | | ~~0.040~~  **2.64** | | 0.463 | ~~0.021~~  **1.39** |
| ***Winter Oilseed rape – early (2 x 175 g/ha)*** | | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) | |  | | **PEC gl-max (µg/L)** |  |
| Step 4 | Multiple application, 10 m VFS | | | | Multiple applications, 20 m VFS | |
| D3/ditch | 0.017 | | ~~0.001~~  0.05 | | 0.009 | ~~0.000~~  0.03 |
| D4/pond | 0.048 | | ~~0.002~~  0.14 | | 0.042 | ~~0.002~~  0.13 |
| D4/stream | 0.21 | | ~~0.009~~  0.63 | | 0.21 | ~~0.009~~  0.63 |
| D5/pond | 0.023 | | ~~0.001~~  0.07 | | 0.02 | ~~0.001~~  0.06 |
| D5/stream | 0.099 | | 0~~.004~~  0.30 | | 0.099 | ~~0.004~~  0.30 |
| R1/pond | 0.04 | | ~~0.002~~  0.12 | | 0.022 | ~~0.001~~  0.07 |
| R1/stream | 0.378 | | ~~0.017~~  **1.13** | | 0.195 | ~~0.009~~  0.58 |
| R3/stream | 0.576 | | ~~0.026~~  **1.72** | | 0.302 | ~~0.014~~  0.90 |
| ***WinterOilseed rape – late (2 x 175 g/ha)*** | | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) | |  | | **PEC gl-max (µg/L)** |  |
| Step 4 | Multiple application, 10 m VFS | | | | Multiple applications, 20 m VFS | |
| D3/ditch | 0.005 | | ~~0.000~~  0.01 | | N/A | **-** |
| D4/pond | 0.017 | | ~~0.001~~  0.05 | | N/A | - |
| D4/stream | 0.011 | | ~~0.000~~  0.03 | | N/A | **-** |
| D5/pond | 0.021 | | ~~0.001~~  0.06 | | N/A | - |
| D5/stream | 0.016 | | ~~0.001~~  0.05 | | N/A | **-** |
| R1/pond | 0.041 | | ~~0.002~~  0.12 | | N/A | - |
| R1/stream | 0.277 | | ~~0.013~~  0.83 | | N/A | - |
| R3/stream | 0.218 | | ~~0.010~~  0.65 | | N/A | - |
| ***Spring Oilseed Rape (2 x 175 g/ha)*** | | | | | | |
| **FOCUS Scenario** | **PEC gl-max (µg/L)** | |  | | **PEC gl-max (µg/L)** |  |
| **Step 4** | Multiple application, 10 m VFS | | | | Multiple applications, 20 m VFS | |
| D3/ditch | 0.013 | | ~~0.001~~  0.04 | | 0.007 | ~~0.000~~  0.02 |
| D4/pond | 0.024 | | ~~0.001~~  0.07 | | 0.015 | ~~0.001~~  0.04 |
| D4/stream | 0.013 | | ~~0.001~~  0.04 | | 0.008 | ~~0.000~~  0.02 |
| D5/pond | 0.023 | | ~~0.001~~  0.07 | | 0.015 | ~~0.001~~  0.04 |
| D5/stream | 0.017 | | ~~0.001~~  0.05 | | 0.009 | ~~0.000~~  0.03 |
| R1/pond | 0.058 | | ~~0.003~~  0.17 | | 0.032 | ~~0.001~~  0.10 |
| R1/stream | 0.496 | | ~~0.022~~  **1.49** | | 0.26 | ~~0.012~~  0.78 |

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

~~No acceptable risk can be concluded for Spring Cereals at scenario R4 with the largest mitigation measure allowed. Therefore, in countries requiring scenario R4, a refinement of BBCH from 26-69 to 41-69 is proposed below.~~

~~Table 9.5‑4b: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for JAU6476-desthio for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of SAP250F~~

| ~~Group~~ |  | ~~Fish acute~~ | ~~Fish prolonged~~ | ~~Inverteb. acute~~ | ~~Inverteb. prolonged~~ | ~~Algae~~ | ~~Sed. dwell. prolonged~~ |
| --- | --- | --- | --- | --- | --- | --- | --- |
| ~~Test species~~ |  | *~~Oncorhynchus mykiss~~* | *~~Oncorhynchus mykiss~~* | *~~Daphnia magna~~* | *~~Daphnia magna~~* | *~~Scenedesmus subspicatus~~* | *~~Chironomus riparius~~* |
| ~~Endpoint~~ |  | ~~LC~~~~50~~ | ~~NOEC~~ | ~~EC~~~~50~~ | ~~NOEC~~ | ~~E~~~~r~~~~C~~~~50~~ | ~~NOEC~~ |
| ~~(µg/L)~~ |  | ~~6630~~ | ~~3.34~~ | ~~10000~~ | ~~100~~ | ~~550~~ | ~~2000~~ |
| ~~AF~~ |  | ~~100~~ | ~~10~~ | ~~100~~ | ~~10~~ | ~~10~~ | ~~10~~ |
| ~~RAC (µg/L)~~ |  | ~~66.3~~ | ~~0.334~~ | ~~100~~ | ~~10~~ | ~~55~~ | ~~200~~ |
| ***~~Spring Cereals~~*** | | | | | | | |
| ~~FOCUS Scenario~~ | ~~PEC~~ ~~gl-max~~ ~~(µg/L)~~ |  |  |  |  |  |  |
| ~~Step 3, Multiple applications~~ |  |  |  |  |  |  |  |
| ~~D3/ditch~~ | ~~0.07403~~ | ~~N. A.~~ | ~~0.2~~ | ~~N. A.~~ | ~~0.0~~ | ~~N. A.~~ | ~~N. A.~~ |
| ~~D4/pond~~ | ~~0.01467~~ | ~~N. A.~~ | ~~0.0~~ | ~~N. A.~~ | ~~0.0~~ | ~~N. A.~~ | ~~N. A.~~ |
| ~~D4/stream~~ | ~~0.05095~~ | ~~N. A.~~ | ~~0.2~~ | ~~N. A.~~ | ~~0.0~~ | ~~N. A.~~ | ~~N. A.~~ |
| ~~D5/pond~~ | ~~0.01532~~ | ~~N. A.~~ | ~~0.0~~ | ~~N. A.~~ | ~~0.0~~ | ~~N. A.~~ | ~~N. A.~~ |
| ~~D5/stream~~ | ~~0.04575~~ | ~~N. A.~~ | ~~0.1~~ | ~~N. A.~~ | ~~0.0~~ | ~~N. A.~~ | ~~N. A.~~ |
| ~~R4/stream~~ | ~~0.5875~~ | ~~N. A.~~ | **~~1.8~~** | ~~N. A.~~ | ~~0.1~~ | ~~N. A.~~ | ~~N. A.~~ |
| ~~Step 3, Single applications~~ |  |  |  |  |  |  |  |
| ~~D3/ditch~~ | ~~0.07840~~ | ~~N. A.~~ | ~~0.2~~ | ~~N. A.~~ | ~~0.0~~ | ~~N. A.~~ | ~~N. A.~~ |
| ~~D4/pond~~ | ~~0.01005~~ | ~~N. A.~~ | ~~0.0~~ | ~~N. A.~~ | ~~0.0~~ | ~~N. A.~~ | ~~N. A.~~ |
| ~~D4/stream~~ | ~~0.04222~~ | ~~N. A.~~ | ~~0.1~~ | ~~N. A.~~ | ~~0.0~~ | ~~N. A.~~ | ~~N. A.~~ |
| ~~D5/pond~~ | ~~0.009657~~ | ~~N. A.~~ | ~~0.0~~ | ~~N. A.~~ | ~~0.0~~ | ~~N. A.~~ | ~~N. A.~~ |
| ~~D5/stream~~ | ~~0.05056~~ | ~~N. A.~~ | ~~0.2~~ | ~~N. A.~~ | ~~0.0~~ | ~~N. A.~~ | ~~N. A.~~ |
| ~~R4/stream~~ | ~~0.5874~~ | ~~N. A.~~ | **~~1.8~~** | ~~N. A.~~ | ~~0.1~~ | ~~N. A.~~ | ~~N. A.~~ |
| ~~Step 4, Multiple applications, 10 m VFS~~ |  |  |  |  |  |  |  |
| ~~R4/stream~~ | ~~0.2672~~ | ~~N. A.~~ | ~~0.8~~ | ~~N. A.~~ | ~~0.1~~ | ~~N. A.~~ | ~~N. A.~~ |
| ~~Step 3, Single applications, 10 m VFS~~ |  |  |  |  |  |  |  |
| ~~R4/stream~~ | ~~0.2672~~ | ~~N. A.~~ | ~~0.8~~ | ~~N. A.~~ | ~~0.1~~ | ~~N. A.~~ | ~~N. A.~~ |

~~From these PEC~~~~sw~~ ~~results we can conclude that a 10 meters of an unsprayed buffer zone, including vegetated filter guarantees that the exposure assessment presented is protective for aquatic systems when SAP250F is applied once per season, for all uses defended in the GAP.~~

~~For winter cereals, winter oilseed rape and spring oilseed rape, 20 meters of an unsprayed buffer zone, including vegetated filter guarantees is protective for aquatic systems when SAP250F is applied twice per season.~~

~~Regarding the use of spring cereals, a restriction on BBCH is proposed. Therefore, for BBCH 41-69, the mitigation measure of 10 meters of a non-sprayed buffer zone, including a vegetated filter, is sufficiently protective for the aquatic system.~~

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| **zRMS comment:**  The risk assessment for a.s. prothioconazole is considered acceptable for aquatic organism as PEC/RAC ratio is below trigger value of 1.  For metabolite of a.s. - JAU6476-desthio for the most sensitive organism O.mykiss the PEC/RAC for the multiple applications is below 1 when the following risk mitigation measures are applied to surface water bodies:  ***Winter Cereals (3 x 200 g/ha)***  For R1 and R3 stream scenarios: 20 m unsprayed buffer zone + 20 meter vegetative buffer strip  **For R4 scenarios further refinement is required as the 20 m unsprayed buffer zone + 20 meter vegetative buffer strip is not sufficient to conclude acceptable risk for fish.**  ***Spring Cereals (3 x 200 g/ha)***  **For R4 scenarios further refinement is required as the 20 m unsprayed buffer zone + 20 meter vegetative buffer strip is not sufficient to conclude acceptable risk for fish.**  ***Winter Oilseed rape – early (2 x 175 g/ha)***  For R1 and R3 stream scenarios: 20 m unsprayed buffer zone + 20 meter vegetative buffer strip  ***Winter Oilseed rape – late (2 x 175 g/ha)***  For R1 and R3 stream scenarios: 10 m unsprayed buffer zone + 10 meter vegetative buffer strip  ***Spring Oilseed Rape (2 x 175 g/ha)***  For R1 stream scenario 20 m unsprayed buffer zone + 20 meter vegetative buffer strip  **Further refinement for R4 scenario is required for winter and spring cereals at MSs level for applications on winter cereals (3 x 200 g/ha) and early application on spring cereals (3 x 200 g/ha).** |

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Mitigations up to 20 m for both drift and run-off were presented in the dossier so that the risk assessment could pass in all scenarios. However, run-off exposure for R4 was not mitigated by this for the these application use. This specific scenario, located in the maritime zone of France, does not represent the reality of farmers who use the product in the central zone. In all countries in the central zone where we want to place the product on the market, the product application date is at the end of March, beginning of April, which corresponds to BBCH 25. For the R4 scenario, the application window considered for this stage growth period is January 6th to March 5th for winter cereals, which is unrealistic. Furthermore, the R4 scenario is not considered relevant for MS other than Hungary, so we would like to discuss mitigations for this country directly with the MS. In this way, we would like the evaluator to consider decreasing the size of the buffer zone , only considering the relevant scenarios for the cMSs, as shown in the table below:   |  |  |  | | --- | --- | --- | | Crop | Application rate  (g as/ha) | Mitigation | | Winter Cereal | 2 x 200 | 10 m unsprayed buffer zone  + 10 m VBS | | Spring cereal | 3 x 200 | no buffer zone, passes at  step 3 |   For Hungary, we might consider changing the application rate for spring cereals (1 x 200 g as/ha), which would result in a lower Step 4 PECsw value for a 20m no-spray zone with an inclusive 20m VFS, which would pose no risk to the most sensitive of aquatic organisms.  Met. M04         **Step 3 PECsw     Step 4 PECsw\***  1 x 200 g as/ha      713 ug/L           0.168 ug/L |

Table 9.5‑6: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Prothioconazole-S-methyl for each organism group based on FOCUS Steps 1, 2 calculations for the use of SAP250F

| Group |  | Fish acute | Inverteb. acute | Algae |
| --- | --- | --- | --- | --- |
| Test species |  | *Oncorhynchus mykiss* | *Daphnia magna* | *Pseudokirchn. subcapitata* |
| Endpoint |  | LC50 | EC50 | ErC50 |
| (µg/L) |  | 1800 | 2800 | 47400 |
| AF |  | 100 | 100 | 10 |
| RAC (µg/L) |  | 18 | 28 | 4740 |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  |  |
| ***Winter Cereals*** | | | | |
| Step 1 |  |  |  |  |
|  | 48.07 | **2.671** | **1.717** | 0.010 |
| Step 2 |  |  |  |  |
| N-Europe (Oct-Feb) | 2.898 | 0.161 | 0.104 | 0.001 |
| N-Europe (Mar-May) | 1.754 | 0.097 | 0.063 | 0.000 |
| ***Spring Cereals*** | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  |  |
| Step 1 |  |  |  |  |
|  | 48.07 | **2.671** | **1.717** | 0.010 |
| Step 2 |  |  |  |  |
| N-Europe | 2.898 | 0.161 | 0.104 | 0.001 |
| ***Winter Oilseed rape*** | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  |  |
| Step 1 |  |  |  |  |
|  | 28.04 | **1.558** | **1.001** | 0.006 |
| Step 2 |  |  |  |  |
| N-Europe | 1.487 | 0.083 | 0.053 | 0.000 |
| ***Spring Oilseed rape*** | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  |  |
| Step 1 |  |  |  |  |
|  | 28.04 | **1.558** | **1.001** | 0.006 |
| Step 2 |  |  |  |  |
| N-Europe | 1.487 | 0.083 | 0.053 | 0.000 |

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

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| **zRMS comment:**  The risk assessment for metabolite Prothioconazole-S-methyl is considered acceptable. The PECsw/RAC ratio is below trigger value of 1. |

Table 9.5‑7: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for 1,2,4-triazole for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of SAP250F in cereals and OSR

| Group |  | Fish acute | Fish prolonged | Inverteb. acute | Algae |
| --- | --- | --- | --- | --- | --- |
| Test species |  | *Oncorhynchus mykiss* | *Oncorhynchus mykiss* | *Daphnia magna* | *Pseudokirchn. subcapitata* |
| Endpoint |  | LC50 | NOEC | EC50 | ErC50 |
| (µg/L) |  | 498000 | 3200 | 900000 | 22500 |
| AF |  | 100 | 10 | 100 | 10 |
| RAC (µg/L) |  | 4980 | 320 | 9000 | 2250 |
| ***Winter Cereals*** | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  |  |  |
| Step 1 |  |  |  |  |  |
|  | 5.66 | 0.001 | 0.018 | 0.001 | 0.003 |
| ***Spring Cereals*** | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  |  |  |
| Step 1 |  |  |  |  |  |
|  | 5.66 | 0.001 | 0.018 | 0.001 | 0.003 |
| ***Winter Oilseed rape*** | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  |  |  |
| Step 1 |  |  |  |  |  |
|  | 3.3 | 0.001 | 0.010 | 0.000 | 0.001 |
| ***Spring Oilseed rape*** | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  |  |  |
| Step 1 |  |  |  |  |  |
|  | 3.3 | 0.001 | 0.010 | 0.000 | 0.001 |

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

|  |
| --- |
| **zRMS comment:**  The risk assessment for metabolite 1,2,4-triazole is considered acceptable. The PECsw/RAC ratio is below trigger value of 1. |

Table 9.5‑8: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Prothioconazole-thiazocine for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of SAP250F in cereals

| Group |  | Fish acute | Fish prolonged | Inverteb. acute | Inverteb. prolonged | Algae | Sed. dwell. prolonged |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Test species |  | *Oncorhynchus mykiss* | *Oncorhynchus mykiss* | *Daphnia magna* | *Daphnia magna* | *Pseudokirchn. subcapitata* | *Chironomus riparius* |
| Endpoint |  | LC50 | NOEC | EC50 | NOEC | ErC50 | NOEC |
| (µg/L) |  | 183 | 30.8 | 130 | 56 | 218 | 914 |
| AF |  | 100 | 10 | 100 | 10 | 10 | 10 |
| RAC (µg/L) |  | 1.83\* | 3.08\* | 1.3\* | 5.6\* | 21.8\* | 91.4\* |
| ***Cereals*** | | | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  |  |  |  |  |
| Step 1 |  |  |  |  |  |  |  |
|  | 2.738 | 0.041 | 0.124 | 0.027 | 0.274 | 0.014 | 0.050 |
| Step 2 |  |  |  |  |  |  |  |
| N-Europe | 0.182 | 0.003 | 0.008 | 0.002 | 0.018 | 0.001 | 0.003 |
| ***Oilseed rape*** | | | | | | | |
| FOCUS Scenario | PEC gl-max (µg/L) |  |  |  |  |  |  |
| Step 1 |  |  |  |  |  |  |  |
|  | 2.396 | 0.036 | 0.108 | 0.024 | 0.240 | 0.012 | 0.044 |
| Step 2 |  |  |  |  |  |  |  |
| N-Europe | 0.19 | 0.003 | 0.009 | 0.002 | 0.019 | 0.001 | 0.003 |

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

\* No endpoint was established for the metabolite. Therefore, the endpoint to be used in the risk assessment will be derived by assuming the toxicity of the metabolite to be 10 times larger than the active substance

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| **zRMS comment:**  The risk assessment for metabolite Prothioconazole-thiazocine is considered acceptable. The PECsw/RAC ratio is below trigger value of 1. |

### Overall conclusions

~~The risk to aquatic non-target organisms following treatment with SAP250F according to the proposed use patterns is acceptable for all uses, with a buffer zone of 20m required for the desthio metabolite. The spring applications to winter oilseed rape are acceptable with a 10m unsprayed buffer.~~

~~After re-evaluation of the metabolite JAU6467-desthio, from the risk assessment results presented above it can be concluded that a 20-metre unsprayed buffer zone, including vegetated filter, guarantees that the exposure assessment presented is protective for aquatic systems when SAP250F is applied three times per season for winter cereals and spring oilseed rape. For spring cereals, applications of SAP250F are acceptable with a buffer zone of 10m. However, in countries where scenario R4 is not required, a buffer zone is not required for spring cereal applications.~~

~~For winter cereals, winter oilseed rape and spring oilseed rape, a 20 metre unsprayed buffer zone, including vegetated filter, guarantees protection for aquatic systems when SAP250F is applied three times per season, except for the R4 scenario for the desthio metabolite. Further mitigation is required for the desthio metabolite in the R4 scenario, required only for Ireland and Hungary.~~

The risk assessment for a.s. prothioconazole and metabolites Prothioconazole-thiazocine and , 1,2,4-triazole is considered acceptable for aquatic organism as PEC/RAC ratio is below trigger value of 1 without risk mitigation measure. For metabolite of a.s. - JAU6476-desthio for the most sensitive organism O.mykiss the PEC/RAC is below trigger of 1 when the following risk mitigation measures are applied to surface water bodies:

*Winter Cereals (3 x 200 g/ha)*

For R1 and R3 stream scenarios: 20 m unsprayed buffer zone + 20 meter vegetative buffer strip

For R4 scenarios further refinement is required as the 20m unsprayed buffer zone + 20 meter vegetative buffer strip is not sufficient to conclude acceptable risk for fish

*Spring Cereals (3 x 200 g/ha)*

For R4 scenarios further refinement is required as the 20 m unsprayed buffer zone + 20 meter vegetative buffer strip is not sufficient to conclude acceptable risk for fish

*Winter Oilseed rape – early (2 x 175 g/ha)*

For R1 and R3 stream scenarios: 20 m unsprayed buffer zone + 20 meter vegetative buffer strip

*Winter Oilseed rape – late (2 x 175 g/ha)*

For R1 and R3 stream scenarios: 10 m unsprayed buffer zone + 10 meter vegetative buffer strip

*Spring Oilseed Rape (2 x 175 g/ha)*

For R1 stream scenario 20 m unsprayed buffer zone + 20 meter vegetative buffer strip

Further refinement for R4 scenario for chronic risk for fish is required for winter and spring cereals at MSs level.

**zRMS comments:-**

The applicant provided new data on the PECsw/sed calculation together with a risk assessment for aquatic organisms, the result of which indicates:

- for scenarios important in PL (D3, D4, R1) following risk mitigation measures should be used for application to spring and winter cereal applied as 2 x 200 g as/ha would have a 20 m unsprayed buffer zone + 20 m VBS

- for scenarios important in PL (D3, D4, R1) following risk mitigation measures should be used for application to winter cereal applied as 1 x 200 g as/ha would have a 10 m unsprayed buffer zone + 10 m VBS.

**~~zRMS comments:-~~**

~~The applicant provided new data on the PECsw/sed calculation together with a risk assessment for aquatic organisms, the result of which indicates:~~

~~- for scenarios important in PL (D3, D4, R1) following risk mitigation measures should be used for application to winter cereal applied as 2 x 200 g as/ha would have a 10 m unsprayed buffer zone + 10 m VBS~~

~~For spring cereal applied as 3 x 200 g as/ha would have no buffer zone as it passes Step 3.~~

## Effects on bees (KCP 10.3.1)

### Toxicity data

Studies on the toxicity to bees have been carried out with Prothioconazole and its relevant metabolites. Full details of these studies are provided in the respective EU DAR and related documents as well as in Appendix 2 of this document (new studies).

Effects on bees of SAP250F were not evaluated as part of the EU assessment of Prothioconazole. New data submitted with this application are listed in Appendix 1 and summarised in Appendix 2.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.6‑1: Endpoints and effect values relevant for the risk assessment for bees

| Species | Substance | Exposure  System | Results | Reference |
| --- | --- | --- | --- | --- |
| *Apis mellifera* | Prothioconazole | Acute  Oral | **LD50 > 71 µg a.s./bee** | EFSA Scientific Report (2007) |
| *Apis mellifera* | Prothioconazole | Acute  Contact | LD50 > 200 µg a.s./bee | EFSA Scientific Report (2007) |
| *Apis mellifera* | Prothioconazole  (EC250) | Acute  Oral | LD50 >48.7 µg a.s./bee | EFSA Scientific Report (2007) |
| *Apis mellifera* | Prothioconazole  (EC250) | Acute  Contact | LD50 > 200 µg a.s./bee | EFSA Scientific Report (2007) |
| Higher-tier studies (tunnel test, field studies) | | | | |
| - | | | | |
| **SAP250F** | | | | |
| *Apis mellifera* | SAP250F | Acute | Oral LD50 = 158 µg a.s./bee (72h)  Contact LD50 > **84.2 µg a.s./bee** | KCP 10.3.1.1/01, Schabio, S. (2018) |
| *Apis mellifera* | SAP250F | Chronic | NOEDD = **6.18 µg a.i./bee/day** | KCP 10.3.1.2/01, Sekine, T., Kowalczyk, F. (2019) |
| *Apis mellifera* | SAP250F | Larvae | NOED = **3.12 µg a.i./larva** | KCP 10.3.1.3/01, Marin, M. (2019) |

#### Justification for new endpoints

Not relevant.

Besides the acute oral and contact risk assessment, data on the chronic effects of the formulation SAP250F to Honey Bees have been derived.

### Risk assessment

The evaluation of the risk for bees was performed in accordance with the recommendations of the “Guidance Document on Terrestrial Ecotoxicology”, as provided by the Commission Services (SANCO/10329/2002 rev.2 (final), October 17, 2002).

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group cereals also covers the risk for bees from all other intended uses in group OSR (see 9.1.2).

#### Hazard quotients for bees

A Hazard Quotient (HQ) approach has been defined by the EPPO risk assessment scheme to identify use patterns which pose a negligible acute risk to honey bees. The HQ is determined by calculating the ratio between the application rate (expressed in g a.s./ha) and the lowest laboratory contact and oral LD50 (expressed in μg a.s./bee). HQ values higher than 50 indicate the need of higher tiered activities to clarify the actual risk to honey bees.

Applications of pesticides can potentially result in exposure of bees either through direct over-spray, or by contact with residues on plants whilst bees are foraging for food.

Table 9.6‑2: First-tier assessment of the risk for bees due to the use of SAP250F in cereals

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Intended use | | Cereals | | |
| Active substance | | Prothioconazole | | |
| Application rate (g/ha) | | 3 × 200 | | |
| Test design | LD50 (lab.)  (µg/bee) | | Single application rate  (g/ha) | QHO, QHC  criterion: QH ≤ 50 |
| Oral toxicity | 48.7 | | 200 | 4.1 |
| Contact toxicity | 200 | | 1.0 |
| Product | | SAP250F | | |
| Application rate (g/ha) | | 3 × 200 | | |
| Test design | LD50 (lab.)  (µg/bee) | | Single application rate  (g/ha) | QHO, QHC  criterion: QH ≤ 50 |
| Oral toxicity | 158 | | 200 | 1.3 |
| Contact toxicity | 84.2 | | 2.4 |

QHO, QHC: Hazard quotients for oral and contact exposure. QH values shown in bold breach the relevant trigger.

All the hazard quotients for the active substances and formulation are less than 50, indicating that the risk to bees is acceptable following use of SAP250F according to the proposed use patterns.

**Chronic risk assessment**

The chronic risk to bees has been assessed following the **EPPO 2010 scheme**[[2]](#footnote-2), as proposed in the list of guidance documents relevant to the implementation of Regulation 1107/2009, published in the official EU Journal 2013/C 95/01 and 95/02.

*Larval assessment according to EPPO 2010*

Following the EPPO scheme for assessing potential risks to larvae (point 4 on the scheme), the scheme suggests that effects on growth or development can be excluded when considering SAP250F, since it is not an IGR, and shows no effects on juvenile stages in other organisms as demonstrated by the risk assessments for non-target arthropods. Thus, SAP250F can be categorized as posing a low risk to bees.

Additionally, honeybee larvae in a hive are never actually exposed to the formulated product. Therefore, studies on the toxicity of the formulated product to honeybee larvae are not considered required. Nevertheless, the larvae study with SAP250F was conducted and the endpoint is presented above in the table.

A worst-case of potential exposure via residues in pollen and nectar can be estimated based on the default worst-case residue of 1 mg a.s./kg proposed in the EPPO 2010 scheme (see Note 6), based on a database of measured values from aerial plant parts, as a surrogate for nectar and pollen.

Data for consumption of nectar and pollen by honey bee larvae are given in the EFSA Panel on Plant Protection Products and their Residues (PPR, 2012).

Worst case: 59.4 mg sugar/larva

The sugar content of nectar which may be foraged by the bees was gathered from the scientific literature (Maccagnani et al., 2003; Monzon et al., 2004; Nicolson, 2009). The worst-case value of sugar content (nectar with the lowest sugar content from the ranges which may be foraged by the bees), namely 15 % for honey bees, is used in calculating the total amount of nectar, honeybee larva consumes per day.

Worst-case consumption of nectar for a honey bee larvae: 396 mg nectar during its whole development

Therefore, the maximum amount of prothioconazole residues honeybee larva could ingest by consumption of nectar is 0.396 μg a.s./larva.

The maximum amount of pollen worker honeybee larva consumes during its development of 5 days amounts 2 mg (PPR, 2012).

Thus, considering residues of 1 mg a.s./kg sugar x consumption of 398 mg sugar/larva

Total exposure ETE = 0.398 µg a.s./larva

This value can be compared to the larval NOED of 3.12 µg a.s./larva at day 22 of exposure.

TER = NOED (µg a.s;/larva/day)/ ETE (µg /bee/day) = 3.12/0.398 = 7.8

The TER based on the residues of worst-case generic residue assumptions for the whole developmental period is higher than the respective trigger of 1. Thus, the risk to honeybee larva from consumption of sugar is considered acceptable when prothioconazole and SAP250F are applied in the intended uses.

*Adult assessment according to EPPO 2010*

The EPPO 2010 risk assessment scheme does not include a chronic risk assessment for adult bees. Besides, SAP250F is expected to pose a low risk to bees. Nevertheless, a chronic 10-day feeding assay was performed to demonstrate SAP250F low risk potential to bees.

The study was carried out with the representative formulation on the chronic toxicity to bees in accordance with the current testing guidelines to fulfil the data requirement in Commission Regulation (EU) No 284/2013 and a study summary is therefore presented and will be used for the risk assessment.

The chronic risk to bees has been assessed following the ***EPPO 2010 scheme***[[3]](#footnote-3), as proposed in the list of guidance documents relevant to the implementation of Regulation 1107/2009, published in the official EU Journal 2013/C 95/01 and 95/02.

A worst-case of potential exposure via residues in pollen / nectar can be estimated as before based on the default worst-case value of 1 mg a.s./kg proposed in the EPPO 2010 scheme (see Note 6), based on a database of measured values from aerial plant parts as a surrogate for nectar and pollen.

The default residues can then be combined with a measure of consumption in order to estimate the exposure. Worst case data from ***Rortais et al***., ***2005***[[4]](#footnote-4) as proposed in the EPPO 2010 scheme have been used to estimate the consumption by bee foragers:

Sugar consumption forager: 128 mg nectar/day (worst case).

The sugar content of nectar which may be foraged by the bees was gathered from the scientific literature (Maccagnani et al., 2003; Monzon et al., 2004; Nicolson, 2009). The worst-case value of sugar content (nectar with the lowest sugar content from the ranges which may be foraged by the bees), namely 15 % for honey bees, is used in calculating the total amount of nectar, honeybee larva consumes per day.

Thus, considering residues of 1 mg a.s./kg sugar x consumption of 853 mg nectar/bee/day

Total exposure ETE = 0.853 μg a.s./bee/day

This can be compared to the SAP250F NOEDD of 6.18 μg a.i./bee/day obtained in the study performed with the formulated product.

TER = NOEDD (μg a.s./bee/day)/ ETE (μg a.s./bee/day) = (6.18/0.853) = 7.2

The EPPO 2010 scheme proposes a trigger of 1 for assessment of the risk to honey bees. With a TER value of 7.2 there is a wide safety margin, indicating that the proposed uses of SAP250F pose an acceptable chronic risk to adult bees.

|  |
| --- |
| **zRMS comment:**  Based on the acute risk assessment with the consideration SANCO/10329/2002 rev.2 (final), October 17, 2002), HQ values for adult bees from exposure of Indofil are < 50, indicating un acceptable risk to adult bees.  Based on the chronic risk assessment with the consideration SANCO/10329/2002 rev.2 (final), October 17, 2002), HQ values from exposure of Indofil are >1 , indicating an acceptable chronic risk to bees.  The evaluation of the risk for bees was performed in accordance with the recommendations of the “Guidance Document on Terrestrial Ecotoxicology”, as provided by the Commission Services  (SANCO/10329/2002 rev.2 (final), October 17, 2002) as according to conclusions of the Central Zone Steering Committee (CZSC), recommendations of EFSA (2013) should not be considered for the zonal evaluations until the guidance is noted at the EU level. Therefore, risk assessment based on indications of EFSA (2013) must be performed at the national level by cMS that do require such evaluation. |

**Bee risk assessment in line with EFSA guidance on bees (EFSA Journal 2013;11(7):3295)**

The endpoints in bold reported in Table 9.6‑1 were used for the risk assessment for different exposure scenarios.

The rate application on cereals (i.e. 200 g a.s/L) were used for the risk assessment since it covers the application of INDOFIL Prothio 250 EC on oilseed rape (i.e. 175 g a.s/L).

Results of the risk assessment for the required exposure scenarios are provided below:

Table 9.6‑3: Acute risk assessment for contact exposure

| **scenario** | **BBCH** | **Honeybee** | |
| --- | --- | --- | --- |
| **HQ** | **trigger** |
| treated crop | < 30 | 0.0 | 42 |
| treated crop | 30 - 39 | 0.0 | 42 |
| treated crop | ≥ 40 | 0.0 | 42 |
| weeds | < 30 | 2.4 | 42 |
| weeds | 30 - 39 | 1.2 | 42 |
| weeds | ≥ 40 | 0.7 | 42 |
| field margin | < 30 | 0.1 | 42 |
| field margin | 30 - 39 | 0.1 | 42 |
| field margin | ≥ 40 | 0.1 | 42 |
| treated crop | 10 - 29 | 0.0 | 14 |
| treated crop | 30 - 39 | 0.0 | 14 |
| treated crop | ≥ 40 | 0.0 | 14 |
| weeds | 10 - 29 | 0.2 | 14 |
| weeds | 30 - 39 | 0.1 | 14 |
| weeds | ≥ 40 | 0.1 | 14 |
| field margin | 10 - 29 | 0.2 | 14 |
| field margin | 30 - 39 | 0.2 | 14 |
| field margin | ≥ 40 | 0.2 | 14 |

The risk to bees from an acute contact exposure is demonstrated to be acceptable as the calculated HQs are below their respective trigger values. Therefore, no further consideration is required.

Table 9.6‑4: Acute risk assessment for oral exposure

| **category** | **scenario** | **BBCH** | **Honeybee** | |
| --- | --- | --- | --- | --- |
| **ETR** | **trigger** |
| acute | treated crop | 10 - 29 | 0.00 | 0.2 |
| acute | treated crop | 30 - 39 | 0.00 | 0.2 |
| acute | treated crop | 40 - 69 | 0.00 | 0.2 |
| acute | weeds | 10 - 29 | 0.01 | 0.2 |
| acute | weeds | 30 - 39 | 0.01 | 0.2 |
| acute | weeds | 40 - 69 | 0.00 | 0.2 |
| acute | field margin | 10 - 29 | 0.00 | 0.2 |
| acute | field margin | 30 - 39 | 0.00 | 0.2 |
| acute | field margin | 40 - 69 | 0.00 | 0.2 |
| acute | adjacent crop | 10 - 29 | 0.00 | 0.2 |
| acute | adjacent crop | 30 - 39 | 0.00 | 0.2 |
| acute | adjacent crop | 40 - 69 | 0.00 | 0.2 |
| acute | next crop | 10 - 29 | 0.00 | 0.2 |
| acute | next crop | 30 - 39 | 0.00 | 0.2 |
| acute | next crop | 40 - 69 | 0.00 | 0.2 |

The risk to bees from an acute oral exposure is demonstrated to be acceptable as the calculated HQs are below the trigger value of 0.2. Therefore, no further consideration is required.

Table 9.6‑5: Chronic risk assessment for oral exposure (adult bees)

| **category** | **scenario** | **BBCH** | **Honeybee** | |
| --- | --- | --- | --- | --- |
| **ETR** | **trigger** |
| chronic | treated crop | 10 - 29 | 0.02 | 0.03 |
| chronic | treated crop | 30 - 39 | 0.02 | 0.03 |
| chronic | treated crop | 40 - 69 | 0.02 | 0.03 |
| chronic | weeds | 10 - 29 | **0.07** | 0.03 |
| chronic | weeds | 30 - 39 | **0.03** | 0.03 |
| chronic | weeds | 40 - 69 | 0.02 | 0.03 |
| chronic | field margin | 10 - 29 | 0.00 | 0.03 |
| chronic | field margin | 30 - 39 | 0.00 | 0.03 |
| chronic | field margin | 40 - 69 | 0.00 | 0.03 |
| chronic | adjacent crop | 10 - 29 | 0.00 | 0.03 |
| chronic | adjacent crop | 30 - 39 | 0.00 | 0.03 |
| chronic | adjacent crop | 40 - 69 | 0.00 | 0.03 |
| chronic | next crop | 10 - 29 | 0.01 | 0.03 |
| chronic | next crop | 30 - 39 | 0.01 | 0.03 |
| chronic | next crop | 40 - 69 | 0.01 | 0.03 |

The chronic risk to adult bees from an oral exposure is acceptable for most of the exposure scenarios expect for weed scenarios BBCH 10-29 and BBCH 30-39, where the calculated HQs were above the trigger value of 0.03. Cereals are not attractive crops to bees (EFSA Journal 2013;11(7):3295). Therefore, it is not expected that bees will actively forage flowering weeds located near cereal crops. Therefore, chronic risk to adult bees can be considered acceptable.

Table 9.6‑6: Risk assessment for oral exposure for larva

| **category** | **scenario** | **BBCH** | **Honeybee** | |
| --- | --- | --- | --- | --- |
| **ETR** | **trigger** |
| larva | treated crop | 10 - 29 | 0.01 | 0.2 |
| larva | treated crop | 30 - 39 | 0.01 | 0.2 |
| larva | treated crop | 40 - 69 | 0.01 | 0.2 |
| larva | weeds | 10 - 29 | 0.12 | 0.2 |
| larva | weeds | 30 - 39 | 0.06 | 0.2 |
| larva | weeds | 40 - 69 | 0.04 | 0.2 |
| larva | field margin | 10 - 29 | 0.00 | 0.2 |
| larva | field margin | 30 - 39 | 0.00 | 0.2 |
| larva | field margin | 40 - 69 | 0.00 | 0.2 |
| larva | adjacent crop | 10 - 29 | 0.00 | 0.2 |
| larva | adjacent crop | 30 - 39 | 0.00 | 0.2 |
| larva | adjacent crop | 40 - 69 | 0.00 | 0.2 |
| larva | next crop | 10 - 29 | 0.02 | 0.2 |
| larva | next crop | 30 - 39 | 0.02 | 0.2 |
| larva | next crop | 40 - 69 | 0.02 | 0.2 |

The risk to larva from an oral exposure scenario is demonstrated to be acceptable as the calculated HQs are below the trigger value of 0.2. Therefore, no further consideration is required.

#### Higher-tier risk assessment for bees (tunnel test, field studies)

Not relevant.

### Effects on bumble bees

No available information.

### Effects on solitary bees

No available information.

### Overall conclusions

The risk assessment performed for both the active substance and the formulated product derived hazard quotients lower than 50, indicating that the active substance as well as the formulation SAP250F pose an acceptable risk to bees from oral and contact exposure according the proposed use. Besides, a chronic study is being performed to prove the lack of unacceptable risks from SAP250F application in the intended uses to Honey Bees.

## Effects on arthropods other than bees (KCP 10.3.2)

### Toxicity data

Studies on the toxicity to non-target arthropods have been carried out with Prothioconazole. Full details of these studies are provided in the respective EU DAR and related documents as well as in Appendix 2 of this document (new studies).

Effects on non-target arthropods of SAP250F were not evaluated as part of the EU assessment of Prothioconazole. New data submitted with this application are listed in Appendix 1 and summarised in Appendix 2.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.7‑1: Endpoints and effect values relevant for the risk assessment for non-target arthropods

| Species | Substance | Exposure  System | Results | | Reference |
| --- | --- | --- | --- | --- | --- |
| Predatory mites | | | | | |
| *Typhlodromus pyri*  (larvae/adults) | Prothioconazole  EC250 | Lab., coffin cells, 14d | LR50 = 18.7 g a.s./ha | | EFSA Scientific Report (2007) |
| Corrected mortality [%]  11.2  18.5  4.0  27.5\*  52.9\* | Effect on reprod. [%]  4  -14  -6  19  n.a.a) |
| *Typhlodromus pyri*  (larvae/adults) | Prothioconazole  EC250 | Extended laboratory test bean leaves, 14 d | LR50 = 445.5 g a.s./ha | | EFSA Scientific Report (2007) |
| Corrected mortality [%]  -2.3  1.5  9.1  45.1\*  67.8\* | Effect on reprod. [%]  14  9  47\*  40\*  n.a.a) |
| *Typhlodromus pyri*  (larvae/adults) | Prothioconazole  EC250 | Extended laboratory test, aged residues bean leaves,  Exposure 14 d  Test started 1d after appl.  Test started 15d after appl. | Corrected mortality [%]  14.5  6.4 | Effect on reprod. [%]  7.5  -28.8 | EFSA Scientific Report (2007) |
| Parasitoids | | | | | |
| *Aphidius rhopalosiphi*  (adults) | Prothioconazole  EC250 | Laboratory test glass plates, 14 d  Control: 0.0%  63 g a.s./ha,  84 g a.s./ha,  112 g a.s./ha,  150 g a.s./ha,  200 g a.s./ha | LR50 = 139.9 g a.s./ha | | EFSA Scientific Report (2007) |
| Corrected mortality [%]  1st run:  3.5  6.9  3.5  3.5  100.0  2nd run:  13.3  13.3  33.3\*  33.3\*  96.7\* | Effect on reprod. [%]  21  10  39  34  n.a.a)  17  36  44\*  53\*  n.a.a) |
| *Aphidius rhopalosiphi*  (adults) | Prothioconazole  EC250 | Extended laboratory test wheat plants, 14 d | 48 h mortality <5% in any of test concentrations.  No significant effect on reproduction in any treatment | | EFSA Scientific Report (2007) |
| Foliage dwelling predators | | | | | |
| *Coccinella septempunctata*  (larvae) | Prothioconazole  EC250 | Laboratory test glass plates, 46 d  Control: 24%  25 g a.s./ha,  50 g a.s./ha,  97 g a.s./ha,  180 g a.s./ha,  375 g a.s./ha | LR50 = 229.8 g a.s./ha | | EFSA Scientific Report (2007) |
| Corrected mortality [%]  -  -9.6  -5.3  25.4  30.7  73.7\* | Larvae per eff laying female  147  54  0  84  549  n.a.a) |
| effects on reproduction are not considered to be treatment related (no adverse effects on reproduction at the highest tested treatment rate). | |
| *Chrysoperla carnea*  (larvae) | Prothioconazole  EC250 | Laboratory test glass plates, 23 d  Control: 8%  200 g a.s./ha  400 g a.s./ha  600 g a.s./ha | Corrected Mortality [%]  15.2\*  28.3\*  41.3\*  No adverse efects on reproduction | | EFSA Scientific Report (2007) |
| Ground dwelling predators | | | | | |
| *Poecilus cupreus*  (adults) | Prothioconazole  EC250 | Quartz sand, 14 d,  400 g a.s./ha  600 g a.s./ha | Corrected mortality [%]  0.0  3.3  No adverse effect on feeding rate | | EFSA Scientific Report (2007) |
| *Aleochara bilineata*  (adults/larvae) | Prothioconazole  EC250 | Quartz sand, 87 d,  42 g a.s./ha  200 g a.s./ha  400 g a.s./ha | Effect on reproduction [%]  2.5  9.9  24.6\* | | EFSA Scientific Report (2007) |
| *Poecilus cupreus*  (adults) | Prothioconazole  FS100 | FS 100, ext. lab.,  14 d, soil (Lufa 2.1),  dressed seeds,  22.47 g a.s./ha | Corrected mortality [%]  0  Effect on feeding rate [%]  5.6-9.6 | | EFSA Scientific Report (2007) |
| *Aleochara bilineata*  (adults/larvae) | Prothioconazole  FS100 | FS 100, ext. lab.,  82 d, soil (Lufa 2.1),  dressed seeds,  19.34 g a.s./ha | Effect on reproduction [%]  11.2 | | EFSA Scientific Report (2007) |
| *Pardosa spp.* | Prothioconazole  FS100 | FS 100, ext. Lab.,  14 d, soil (Lufa 2.1),  dressed seeds,  22.3 g a.s./ha | Corrected mortality [%]  -3.1  Effect on feeding rate [%]  -18 | | EFSA Scientific Report (2007) |
| Field or semi-field tests | | | | | |
| - | | | | | |
| **SAP250F** | | | | | |
| *T. pyri* | SAP250F | Extended laboratory test bean leaves (2-D) | LR50 and ER50 > 1360 mL test item/ha  Or 1468.8 g test item/ha\*\* | | KCP 10.4/01, Moll, M. (2019) |
| *A. rhopalosiphi* | SAP250F | Extended laboratory test barley leaves (3-D) | LR50 and ER50 > 1360 mL test item/ha  Or 1468.8 g test item/ha\*\* | | KCP 10.4/02, Moll, M. (2019) |
| *C. carnea* | SAP250F | Extended laboratory test bean leaves (2-D) | LR50 and ER50 > 1360 mL test item/ha  Or 1468.8 g test item/ha\*\* | | KCP 10.4/03, Moll, M. (2019) |

a) not assessed due to mortality > 50 % at this concentration

\* significantly different from control (t-test p <0.05)

\*\* Assuming a formulation density of 1.080 g/mL

#### Justification for new endpoints

Studies with SAP250F were not included in the EU review and have been conducted to characterise the risk from the current formulation. The studies were conducted at higher tier and therefore include additional species. Based on the EU data, it was only considered necessary to test *C. carnea* in addition to the two sensitive indicator species, as it was the most sensitive additional species according to the EU review data. The indicator species *A. rhopalosiphi* and *T. pyri* were the most sensitive in the EU data set.

### Risk assessment

The evaluation of the risk for non-target arthropods was performed in accordance with the recommendations of the “Guidance Document on Terrestrial Ecotoxicology”, as provided by the Commission Services (SANCO/10329/2002 rev.2 (final), October 17, 2002), and in consideration of the recommendations of the guidance document ESCORT 2.

#### Risk assessment for in-field exposure

The potential risk of SAP250F to in-field non-target arthropods was assessed by calculation of the hazard quotient (HQ = exposure/toxicity) with the predicted environmental rate (PER) and the lowest lethal rate (LR50) values according to the following formula:

PERin-field = Application rate x MAF

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group cereals also covers the risk for non-target arthropods from all other intended uses in group OSR (see 9.1.2). The available studies were conducted as higher tier extended laboratory studies, so an HQ trigger of 1 is appropriate.

Table 9.7‑2: Higher-tier assessment of the in-field risk for non-target arthropods due to the use of SAP250F in cereals

|  |  |  |  |
| --- | --- | --- | --- |
| Intended use | Cereals | | |
| Active substance/product | SAP250F | | |
| Application rate (mL/ha) | 3 × 800 | | |
| MAF | 2.3 | | |
| Test species  Tier II (extended lab test) | ~~LR~~~~50~~ ~~(lab.)~~  ~~(mL/ha)~~ | ~~PER~~~~in‑field~~  ~~(mL/ha)~~ | ~~HQ~~~~in-field~~  ~~criterion: HQ ≤ 1~~ |
|  | LR50 (lab.) and ER50 (mL/ha) | PER in-field (mL/ha) | PERin field below rate with ≤ 50% effect? |
| *Typhlodromus pyri* | >1360 | 1840 | **No** |
| *Aphidius rhopalosiphi* | >1360 | **No** |
| *Chrysoperla carnea* | >1360 | **No** |

MAF: Multiple application factor; PER: Predicted environmental rate; HQ: Hazard quotient; DALT: Days after last treatment. Criteria values shown in bold breach the relevant trigger.

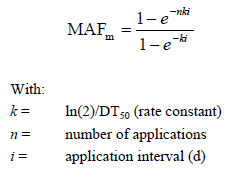
\* If an LR50 or ER50 from a relevant extended laboratory test is available, it should be considered in place of the rate with ≤ 50 % effect.

The in-field HQ value for exposure to maximum application rate for the representative species *T. pyri*, *A. rhopalosiphi,* and *C. carnea* is above the trigger value, although it should be noted that this is based on “greater than” endpoints and therefore results in “less than” HQ values. Further consideration is therefore required and is given below.

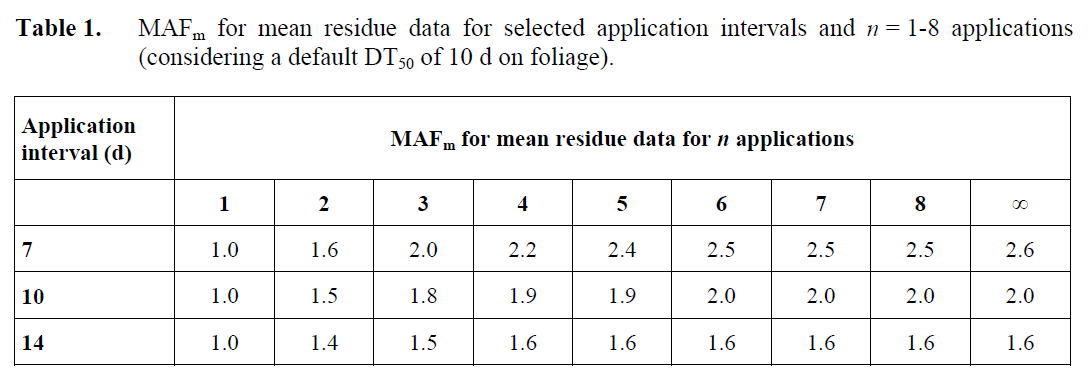
Refinement of MAF:

The MAF values in Appendix III of the ESCORT 2 guidelines (2001) are based on the ratio of DT50 : application interval, with a ratio of 2.3:1 being the default for foliar residues and giving MAF 2.3 for 3 applications.  The default MAF value does not take into account the actual ratio of DT50 : application interval and is used when either or both of those inputs is unknown.  According to ESCORT 3 guidance (2012), a default DT50 of 10 days can be used in accordance with the EFSA Bird and Mammal guidance (2009); this is conservative considering the foliar residues data presented at 9.3, above. The application interval is 14 days. This ratio of DT50 : interval (1 : 1.4) is not provided in the table at Appendix III of ESCORT 2. However, the exact value can be determined by other means.

The MAF values at Appendix III of ESCORT 2 are calculated using 1st order kinetics, in exactly the same way as the MAF used for long-term risk assessment in the EFSA Bird and Mammal risk assessment guidance (2009; Appendix H):



The MAF for use in the non-target arthropod risk assessment can therefore be calculated using the equation above, or taken from the Table 1 in Appendix H of the EFSA Bird and Mammal guidance document (provided below for convenience).



As a 14 day spray interval is given in the table, the MAF value for 3 applications can be taken directly from there without the need for calculation, i.e. MAF = 1.5.

This MAF value is then used in the risk assessment, as shown below.

Table 9.7‑3: Refined higher-tier assessment of the in-field risk for non-target arthropods due to the use of SAP250F in cereals

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Intended use | | Cereals | | |
| Active substance/product | | SAP250F | | |
| Application rate (mL/ha) | | 3 × 800, 14 day interval | | |
| MAF | | 1.5 ~~(refined)~~ | | |
| Test species  Tier II (extended lab test) | ~~LR~~~~50~~ ~~(lab.)~~  ~~(mL/ha)~~ | | ~~PER~~~~in‑field~~  ~~(mL/ha)~~ | ~~HQ~~~~in-field~~  ~~criterion: HQ ≤ 1~~ |
|  | LR50 (lab.) mL/ha | | PERin-field mL/ha | PERin field below rate with ≤ 50% effect? |
| *Typhlodromus pyri* | >1360 | | 1200 | Yes |
| *Aphidius rhopalosiphi* | >1360 | | Yes |
| *Chrysoperla carnea* | >1360 | | Yes |

MAF: Multiple application factor; PER: Predicted environmental rate; HQ: Hazard quotient; DALT: Days after last treatment. Criteria values shown in bold breach the relevant trigger.

\* If an LR50 or ER50 from a relevant extended laboratory test is available, it should be considered in place of the rate with ≤ 50 % effect.

Thus, the use of SAP250F has been shown to be ecologically acceptable and in agreement with the EU guidance document on terrestrial ecotoxicology SANCO/10329/2002 and ESCORT 2. It can be concluded that applications according to the GAP for SAP250F will not be harmful for a range of in-field populations of non-target arthropods.

|  |
| --- |
| **zRMS comments:**  The calculations of the risk assessment for in – field for Indofil for three species were verified by  zRMS-PL.  ~~After refined value of MAF =1.5 for three application based on DT~~~~50~~ ~~of 3.2 days in plants the~~  HQ in -field value (based on the extended laboratory studies) are below the rate with ≤ 50 % effects.  The risk assessment poses low risk to in-field to non-target arthropods following application according to the proposed use patterns. |

#### Risk assessment for off-field exposure

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group cereals also covers the risk for non-target arthropods from all other intended uses in group OSR (see 9.1.2).

PERoff-field = Application rate × MAF × (drift factor/vegetation distribution factor)

In order to assess the potential risk to off-field non-target arthropods, the predicted environmental rate (Table 10.5-3) is compared with the toxicity endpoints according to the following formula:



Table 9.7‑4: Higher-tier assessment of the off-field risk for non-target arthropods due to the use of SAP250F in cereals

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Intended use | | Cereals | | | | | |
| Active substance/product | | Prothioconazole / SAP250F | | | | | |
| Application rate (mL/ha) | | 3 × 800 | | | | | |
| MAF | | 2.3 | | | | | |
| vdf | | ~~10~~ 5 (for 2-D studies only) | | | | | |
| Test species  Tier II (extended lab tests) | LR50 (lab.)  (mL/ha) | | Drift rate | vdf | PERoff‑field (mL/ha) | CF | HQoff-field  criterion: HQ ≤ 1 |
| *Typhlodromus pyri* (2-D) | >1360 | | 2.01 | ~~10~~ 5 | ~~3.70~~ -7.3968 | 5 (Tier 2) | <~~0.014~~ 0.02 |
| *Aphidius rhopalosiphi* (3-D) | >1360 | | 1 | 37.0 | <0.14 |
| *Chrysoperla carnea* (2-D) | >1360 | | ~~10~~ 5 | ~~3.70~~ 7.3968 | <~~0.014~~ 0.02 |

MAF: Multiple application factor; vdf: Vegetation distribution factor; (corr.) PER: (corrected) Predicted environmental rate; CF: Correction factor; HQ: Hazard quotient. Criteria values shown in bold breach the relevant trigger.

\* If an LR50 or ER50 from a relevant extended laboratory test is available, it should be considered in place of the rate with ≤ 50 % effect.

The off-field HQ values for the standard species are well below the trigger of 1 for *T. pyri*, *A. rhopalosiphi*, and *C. carnea*, indicating no off-field unacceptable risk for non-target arthropods. This is additionally conservative considering that the MAF refinement has not been used.

|  |
| --- |
| **zRMS comment:**  The PERoff-field corrected for T.Pyri, A. rhopalosiphi and for additional species Chrysoperla carnea (based on the extended laboratory studies) are below the rate with ≤ 50 % effects.  Therefore, this assessment indicates that Indofil poses low risk off-field for non-target arthropods following application according to the proposed use patterns. |

#### Additional higher-tier risk assessment

Not relevant.

#### Risk mitigation measures

No risk mitigation needed.

### Overall conclusions

The in-field HQ values for the highest application rate are below the trigger of 1.0 for the three-standard species *Typhlodromus pyri*, *Aphidius rhopalosiphi* and *Chrysoperla carnea*. The off-field HQ values for all tested species, are below the trigger of 1.0, indicating that SAP250F is unlikely to pose an unacceptable risk to non-target-arthropods in or off-field.

## Effects on non-target soil meso- and macrofauna (KCP 10.4)

### Toxicity data

Studies on the toxicity to earthworms and other non-target soil organisms (meso- and macrofauna) have been carried out with Prothioconazole and its relevant metabolites. Full details of these studies are provided in the respective EU DAR and related documents as well as in Appendix 2 of this document (new studies).

Effects on earthworms and other non-target soil organisms (meso- and macrofauna) of SAP250F were not evaluated as part of the EU assessment of Prothioconazole. New data submitted with this application are listed in Appendix 1 and summarised in Appendix 2.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.8‑1: Endpoints and effect values relevant for the risk assessment for earthworms and other non-target soil organisms (meso- and macrofauna)

| Species | Substance | Exposure  System | Results | Reference |
| --- | --- | --- | --- | --- |
| *Eisenia foetida* | Prothioconazole | Acute  10 % peat content | LC50 > 1000 mg/kg dw  LC50,corr > 500 mg/kg dw\* | EFSA Scientific Report (2007) |
| *Eisenia foetida* | Prothioconazole  EC250 | Acute  10 % peat content | LC50 > 249.3 mg/kg dw  LC50,corr > 124.65 mg/kg dw\* | EFSA Scientific Report (2007) |
| *Eisenia foetida* | Prothioconazole  EC250 | Overspray  Chronic  10 % peat content  (Endpoint as mg/kg calculated from applied rate, using default assumption 5 cm incropration and soil bulk density 1.5 g/mL) | NOER = 1000 g a.s./ha  NOEC = 1.33 mg a.s./kg dw  NOECcorr = 0.665 mg a.s./kg dw\* | EFSA Scientific Report (2007) |
| *Folsomia candida* | Prothioconazole EC250 | Chronic  10 % peat content | NOEC = 64 mg/kg dw | EFSA Scientific Report (2007) |
| *Hypoaspis aculeifer* | Prothioconazole EC250 | Chronic | NOEC = 100 mg/kg dw | EFSA Scientific Report (2007) |
| Metabolites (spray application scenario) | | | | |
| *Eisenia fetida* | JAU 6476-desthio | Acute  10 % peat content | LC50 > 1000 mg/kg dw  LC50,corr > 500 mg/kg dw\* | EFSA Scientific Report (2007) |
| *Eisenia foetida* | JAU 6476-desthio | Long-term  10 % peat content | NOEC = 1 mg/kg dw  NOECcorr = 0.5 mg/kg dw\* | EFSA Scientific Report (2007) |
| *Eisenia foetida* | JAU 6476-S-methyl | Acute  10 % peat content | LC50 > 1000 mg/kg dw  LC50,corr > 500 mg/kg dw\* | EFSA Scientific Report (2007) |
| *Eisenia foetida* | JAU 6476-S-methyl | Chronic  10 % peat content | NOEC = 100 mg/kg dw  NOECcorr = 50 mg/kg dw\* | EFSA Scientific Report (2007) |
| *Folsomia candida* | JAU 6476-desthio | Combined spray application and seed treatment scenario Long-term  10 % peat content | NOEC = 62.5 mg/kg dw | EFSA Scientific Report (2007) |
| *Folsomia candida* | JAU 6476-S-methyl | Combined spray application and seed treatment scenario Long-term  10 % peat content | NOEC = 31.6 mg/kg dw | EFSA Scientific Report (2007) |
| *Folsomia candida* | Prothioconazole  FS100 | Seed treatment scenario  Long-term  10% peat content | NOEC = 230 kg seeds/ha (10 g a.s./dt seeds) equivalent to 24.38 g a.s./ha | EFSA Scientific Report (2007) |
| *Folsomia candida* | Prothioconazole  FS100 | Seed treatment scenario  Long-term  10% peat content | NOEC = 1150 kg seeds/ha (10 g a.s./dt seeds) equivalent to 112 g a.s./ha | EFSA Scientific Report (2007) |
| Field studies | | | | |
| *Lumbricius*  *terrestris,*  *L. rubellus,*  *L. castanea,*  *Aporrectodea*  *caliginosa,*  *A. terrestris*  *longa* | Prothioconazole  EC250 | 3 × 200 g a.s./ha  5 different species identified and assessed. 46% reduction in the number of A caliginosa juveniles 7 weeks after first application (2 weeks after final application). No adverse effect 5 month after first application. (Maximum measured soil PEC 0.052 mg prothioconazole/kg based on soil sampling depth of 10 cm which is equivalent to a soil PEC of 0.104 mg prothioconazole/kg over the standard 5 cm depth) | | EFSA Scientific Report (2007) |
| Range of species in an arable field study | FS 100  long-term | 1150 kg seeds/ha (10 g a.s./dt seeds) equivalent to 122 g a.s./ha | | EFSA Scientific Report (2007) |
| Litter bag test | | | | |
| Field Soil Litter Degradation | Prothioconazole  FS100 | 126 d,  FS 100 (23.2 g a.s./ha) followed by JAU 6476 EC 250 (3 @ 200 g a.s./ha during 26 day period) | Field soil litter degradation [%]  after 34 days:  test item: 51.7; control: 52.1  after 95 days:  test item: 74.3; control: 78.4  after 126 days  test item: 92.0; control 91.2 | EFSA Scientific Report (2007) |
| **SAP250F** | | | | |
| *Eisenia andrei* | SAP250F | Mixed into substrate  56 d, chronic  10 % peat content | NOEC (reproduction) = 21.1 mg PPP/kg sdw (equivalent to 5.3 mg a.s./kg sdw)  NOEC (reproduction) = 10.55 mg PPP/kg sdw\* (equivalent to 2.6 mg a.s./kg sdw) | KCP 10.4.1.1/01, Straube, D. (2019) |

\* Corrected value derived by dividing the endpoint by a factor of 2 in accordance with the EPPO earthworm scheme 2002.

#### Justification for new endpoints

The earthworm study with SAP250F was not included in the EU review and has been conducted to characterise the risk from the current formulation. Tests with *Folsomia* and *Hypoaspis* were not considered necessary in addition, as earthworms were clearly the most sensitive based on the active substance data.

### Risk assessment

The evaluation of the risk for earthworms and other non-target soil organisms (meso- and macrofauna) was performed in accordance with the recommendations of the “Guidance Document on Terrestrial Ecotoxicology”, as provided by the Commission Services (SANCO/10329/2002 rev 2 (final), October 17, 2002).

As stated in Commission Regulation EU No 284/2013 of 1 March 2013, “For plant protection products applied as a foliar spray, data on the relevant two non target arthropod species might be taken into account for a preliminary risk assessment. If effects do occur on either species, testing on *Folsomia candida* and *Hypoaspis aculeifer* shall be required (see point 10.4.2.1).

If data on *Aphidius rhopalosiphi* and *Typhlodromus pyri* are not available then the data outlined in point 10.4.2.1 shall be required.

For plant protection products applied as soil treatments directly to soil either as a spray or as a solid formulation, then testing shall be required on both *Folsomia candida* and *Hypoaspis aculeifer* (see point 10.4.2.1).”.

The formulated product SAP250F is not applied as a soil treatment but as a foliar spray one. As demonstrated above, no unacceptable risks are expected towards at least three non-target arthropod species (*Typhlodromus pyri*, *Aphidius rhopalosiphi* and *Chrysoperla carnea*). Besides, the formulated product is only composed by one active substance and enough data for such active substance is available. Therefore, performing the risk assessment with the data for the active substance can be used as a surrogate of effects of soil mesofauna organism’s exposure to SAP250F, and is considered conservative.

#### First-tier risk assessment

The relevant PECsoil for risk assessments covering the proposed use pattern are taken from Section 8 (Environmental Fate), Chapter 8.7.2, Table 8.7-3. According to the assessment of environmental-fate data, multi-annual accumulation in soil does not need to be considered for Prothioconazole.

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group cereals also covers the risk for earthworms and other non-target soil organisms (meso- and macrofauna) from all other intended uses in group OSR (see 9.1.2). Only a chronic risk assessment was carried out, in line with current data requirements.

Table 9.8‑2: First-tier assessment of the acute and chronic risk for earthworms and other non-target soil organisms (meso- and macrofauna) due to the use of SAP250F in cereals

|  |  |  |  |
| --- | --- | --- | --- |
| Intended use | Cereals | | |
| Chronic effects on earthworms | | | |
| Product/active substance | NOEC  (mg/kg dw) | PECsoil  (mg/kg dw) | TERlt  (criterion TER ≥ 5) |
| Prothioconazole | 0.665 | 0.220 | **3.0** |
| JAU 6476-desthio | 0.5 | 0.395 | **1.27** |
| JAU 6476-S-methyl | 50 | 0.260 | 192.31 |
| SAP250F | 10.55 (F.P.) | 0.836 | 12.62 |
| 2.6 (a.s.) | 0.220 | 11.82 |
| Chronic effects on other soil macro- and mesofauna | | | |
| Product/active substance | NOEC  (mg/kg dw) | PECsoil  (mg/kg dw) | TERlt  (criterion TER ≥ 5) |
| Prothioconazole  *Folsomia candida* | 64 | 0.220 | 290.9 |
| Prothioconazole  *Hypoaspis aculeifer* | 100 | 0.220 | 454.5 |
| JAU 6476-desthio  *Folsomia candida* | 62.5 | 0.395 | 158.2 |
| JAU 6476-desthio  *Hypoaspis aculeifer* | 10\* | 0.395 | 25.3 |
| JAU 6476-S-methyl  *Folsomia candida* | 31.6 | 0.260 | 121.5 |
| JAU 6476-S-methyl  *Hypoaspis aculeifer* | 10\* | 0.260 | 38.4 |

TER values shown in bold fall below the relevant trigger.

\* Endpoint was derived by assuming the toxicity of the metabolite to be 10 times larger than the active substance

From the derived TER values, unacceptable risks to earthworms are expected in the long-term scenario from prothioconazole and the metabolite JAU 6476-desthio, based on the EU data. However, no adverse effects are to be expected, as proven by the results of the field study (EFSA Scientific Report, 2007). Desthio-metabolite was confirmed as being present in field study after application of Prothioconazole with a maximum concentration recorded of 0.106 mg/kg at 7 days after second application. The depth of soil from which the sample cores were taken is not stated in the study report, but is highly unlikely to have been less than 5 cm and would more typically be expected to be 10 cm. As such, the maximum PEC for prothioconazole and the metabolite JAU 6476-desthio is likely to be an overestimation, with the level of exposure in the field study being considered more realistic. In the field study, from the 5 identified earthworm species, only the number of juveniles of 1 (*Aporrectodea caliginosa*) was affected. In fact, by the end of the study, an overall increase in the number and biomass of earthworms in the treated plots was observed (11 months of exposure with 3 applications of 200g a.s./ha).

It should also be noted that there is no risk predicted based on the results of the laboratory earthworm chronic study (the most sensitive species to prothioconazole) with formulation SAP250F.

Therefore, no unacceptable effects are expected in earthworms and other soil meso and macrofauna due to the application of SAP250F in the intended uses.

**zRMS comment:**

The chronic TER values for earthworms and other soil macro-organism for ppp Indofil were above the relevant Annex VI trigger of 5.

However in case of a.s. – prothioconazole and its metabolite M04 further refinement was needed.

Taking into account that the risk for a.s. calculated from ppp for earthworm was above the trigger value of 5, the risk is considered acceptable by zRMS.

In addition, no adverse effects are to be expected, as proven by the results of the field study (EFSA Scientific Report, 2007). Desthio-metabolite was confirmed as being present in field study after application of Prothioconazole with a maximum concentration recorded of 0.106 mg/kg at 7 days after second application. The depth of soil from which the sample cores were taken is not stated in the study report, but is highly unlikely to have been less than 5 cm and would more typically be expected to be 10 cm. As such, the maximum PEC for prothioconazole and the metabolite JAU 6476-desthio is likely to be an overestimation, with the level of exposure in the field study being considered more realistic. In the field study, from the 5 identified earthworm species, only the number of juveniles of 1 (Aporrectodea caliginosa) was affected. In fact, by the end of the study, an overall increase in the number and biomass of earthworms in the treated plots was observed (11 months of exposure with 3 applications of 200g a.s./ha).

**Therefore, it is concluded that Indofil and metabolites such as: M01 and M04 do not pose long-term risk to earthworms and other soil macro- and mesofauna when applied according to the proposed uses rates.**

#### Higher-tier risk assessment

Not relevant.

### Overall conclusions

No unacceptable acute risks are expected in earthworms due to exposure to either Prothioconazole or its metabolites (JAU 6476-desthio and JAU 6476-S-methyl). From the derived long-term TER values, unacceptable risks to earthworms are expected from Prothioconazole and the metabolite JAU 6476-desthio. However, in a field study, the occurrence of Prothioconazole and the Desthio-metabolite was confirmed slightly under the PECsoil derived. As the depth of soil from which the sample cores were taken is highly unlikely to have been less than 5 cm and would more typically be expected to be 10 cm, the maximum PEC values are likely to be an overestimation, with the level of exposure in the field study being considered more realistic. Besides, from the 5 identified earthworm species, only the number of juveniles of 1 (*Aporrectodea caliginosa*) was affected. In fact, by the end of the study, an overall increase in the number and biomass of earthworms in the treated plots was observed (11 months of exposure with 3 applications of 200g a.s./ha). Also, no unacceptable effects are expected when using the endpoint obtained in the chronic study with the formulation in question (TER value of 12.6, well above 5). Therefore, no unacceptable effects are expected in earthworms and other soil meso and macrofauna due to the application of SAP250F in the intended uses.

## Effects on soil microbial activity (KCP 10.5)

### Toxicity data

Studies on effects soil microorganisms have been carried out with Prothioconazole and its relevant metabolites. Full details of these studies are provided in the respective EU DAR and related documents.

Effects on soil microorganisms of SAP250F were not evaluated as part of the EU assessment of Prothioconazole.

However, the provision of further data on the formulation SAP250F is not considered essential, because enough data on the active substance and metabolites expected toxicity can be found in EFSA Scientific Report (2007).

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.9‑1: Endpoints and effect values relevant for the risk assessment for soil microorganisms

| Endpoint | Substance | Exposure  System | Results | Reference |
| --- | --- | --- | --- | --- |
| N-mineralisation | JAU 6476 a.s. | 28 d | No influence  2.0 kg a.s./ha | EFSA Scientific Report (2007) |
| N-mineralisation | JAU 6476-desthio | 28 d | No influence  0.2 kg p.m./ha | EFSA Scientific Report (2007) |
| N-mineralisation | JAU 6476-desthio | 28 d | No influence  1.0 kg p.m./ha | EFSA Scientific Report (2007) |
| N-mineralisation | JAU 6476-S-methyl | 28 d | No influence  2.0 kg p.m./ha | EFSA Scientific Report (2007) |

#### Justification for new endpoints

Not relevant.

### Risk assessment

As stated in Commission Regulation EU No 284/2013 of 1 March 2013, “The effects of plant protection products on soil microbial function shall be investigated if the toxicity of the plant protection product cannot be predicted on the basis of data for the active substance”. As the formulated product SAP250F is only composed by one active substance, interaction between substances (for example, synergism or antagonism) are not taken into consideration. Therefore, performing the risk assessment with the data for the active substance can be used as a surrogate of effects of microbial community exposure to SAP250F.

The evaluation of the risk for soil microorganisms was performed in accordance with the recommendations of the “Guidance Document on Terrestrial Ecotoxicology”, as provided by the Commission Services (SANCO/10329/2002 rev 2 (final), October 17, 2002).

The relevant PECsoil for risk assessments covering the proposed use pattern are taken from Section 8 (Environmental Fate), Chapter 8.7.2, Table 8.7-3 and were already used in the risk assessment for earthworms and other non-target soil organisms (meso- and macrofauna) (see 9.8).

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group cereals also covers the risk for the soil microorganisms from all other intended uses in group OSR (see 9.1.2).

Table 9.9‑2: Assessment of the risk for effects on soil micro-organisms due to the use of SAP250F in cereals

|  |  |  |  |
| --- | --- | --- | --- |
| Intended use | Cereals | | |
| N-mineralisation | | | |
| Product/active substance | Max. conc. with effects ≤ 25 % (mg/kg dw) | PECsoil  (mg/kg dw) | Risk acceptable? |
| Prothioconazole | 2000 (at28 d) | 0.220 | yes |
| JAU 6476-desthio | 200 (at 28 d) | 0.395 | yes |
| JAU 6476-S-methyl | 2000 (28 d) | 0.260 | yes |

### 

**zRMS comment:**

The risk assessment for soil micro-organism after exposure of both active substances and their metabolites has accepted by the zRMS. The effects on the nitrogen transformations are acceptable (<25%) at concentration which is higher than the maximum relevant PECs for the maximum application rate of active substances and their metabolites. The product data was not available. However, the risk for a.s. and its metabolite in this case covers risk from solo formulation Indofil from prothioconazole.

### Overall conclusions

The use of SAP250F according to the proposed use patterns will not have unacceptable effects on soil micro-organisms as more 1000-fold of the applied maximum concentration did not cause any significant effects on soil nitrogen transformation.

## Effects on non-target terrestrial plants (KCP 10.6)

### Toxicity data

Studies on the toxicity to non-target terrestrial plants have been carried out with Prothioconazole. Full details of these studies are provided in the respective EU DAR and related documents as well as in Appendix 2 of this document (new studies).

Effects on non-target terrestrial plants of SAP250F were not evaluated as part of the EU assessment of Prothioconazole. New data submitted with this application are listed in Appendix 1 summarised in Appendix 2.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.10‑1: Endpoints and effect values relevant for the risk assessment for non-target terrestrial plants

| Species | Substance | Exposure  System | Results | Reference |
| --- | --- | --- | --- | --- |
| *Amaranthus retroflexus* | JAU 6476 a.s. | Pre-emergence | Max phytotoxic effect 5% at 200 g a.s./ha | EFSA Scientific Report (2007) |
| *Amaranthus retroflexus*  *Beta vulgaris* | JAU 6476 a.s. | Post-emergence | Max phytotoxic effect 10% at 250 g a.s./ha | EFSA Scientific Report (2007) |
| *Amaranthus retroflexus* | JAU 6476  EC 250 | Pre-emergence | Max phytotoxic effect 5% at 200 g a.s./ha | EFSA Scientific Report (2007) |
| *-* | JAU 6476  EC 250 | Post-emergence | Max phytotoxic effect 0% at 250 g a.s./ha | EFSA Scientific Report (2007) |
| **SAP250F** | | | | |
| *Brassica oleracea*  *Helianthus annuus*  *Glycine max*  *Cucumis sativus*  *Allium cepa*  *Lolium perenne* | SAP250F | Seedling | ER50 > 1.6 L/ha  (400 g a.s./ha) | KCP 10.6.2/01, Stürtz, S., Kowalczyk, F. (2019) |
| *Brassica oleracea*  *Helianthus annuus*  *Glycine max*  *Cucumis sativus*  *Allium cepa*  *Lolium perenne* | SAP250F | Vegetative vigour | ER50 > 1.6 L/ha  (400 g a.s./ha) | KCP 10.6.2/02, Stürtz, S., Kowalczyk, F. (2019) |

m: monocotyledonous; d: dicotyledonous

#### Justification for new endpoints

Studies with the relevant formulation SAP250F have been conducted.

### Risk assessment

#### Tier-1 risk assessment (based screening data)

Not relevant.

#### Tier-2 risk assessment (based on dose-response data)

The risk assessment is based on the “Guidance Document on Terrestrial Ecotoxicology”, (SANCO/10329/2002 rev.2 final, 2002). It is restricted to off-field situations, as non-target plants are non-crop plants located outside the treated area.

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group cereals also covers the risk for non-target terrestrial plants from all other intended uses in group OSR (see 9.1.2). The endpoints with the relevant formulation SAP250 F have been used in the risk assessment; noting that there is no conflict between these and the endpoints from studies conducted with the active substance and EU representative formulation, as so strong phytotoxic effects have been observed at any tested rate in any study.

Table 9.10‑2: Assessment of the risk for non-target plants due to the use of SAP250F in cereals

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Intended use | | Cereals | | | |
| Active substance/product | | Prothioconazole / SAP250F | | | |
| Application rate | | 3 × 200 g a.s./ha | | | |
| MAF | | 2.3 a | | | |
| Test species | ER50  (g a.s./ha) | | Drift rate (%) | PERoff‑field  (g a.s./ha) | TER  criterion: TER ≥ 5 |
| *Brassica oleracea*  *Helianthus annuus*  *Glycine max*  *Cucumis sativus*  *Allium cepa*  *Lolium perenne* | ~~>1.6400~~  400 | | 2.~~01~~77 | ~~0.0421~~  12.74 | ~~38.04~~  31.40 |

MAF: Multiple application factor; PER: Predicted environmental rate; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

a The use of a MAF in the terrestrial non-target plant risk assessment is currently under debate but has been applied here for conservatism.

Table 9.10‑2a: Assessment of the risk for non-target plants due to the use of SAP250F in cereals

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Intended use | | Cereals | | | |
| Active substance/product | | Prothioconazole / SAP250F | | | |
| Application rate | | 3 × 200 g a.s./ha | | | |
| MAF | | 1 | | | |
| Test species | ER50  (g a.s./ha) | | Drift rate (%) | PERoff‑field  (g a.s./ha) | TER  criterion: TER ≥ 5 |
| *Brassica oleracea*  *Helianthus annuus*  *Glycine max*  *Cucumis sativus*  *Allium cepa*  *Lolium perenne* | 400 | | 2.77 | 5.54 | 72.2 |

MAF: Multiple application factor; PER: Predicted environmental rate; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

No unacceptable risks are expected due to application of SAP250F in the intended uses.

|  |
| --- |
| **zRMS comment:**  The risk assessment is based on the “Guidance Document on Terrestrial Ecotoxicology”, (SANCO/10329/2002 rev.2 final, 2002). It is restricted to off-field situations, as non-target plants are non-crop plants located outside the treated area.  To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group cereals also covers the risk for non-target terrestrial plants from all other intended uses in group OSR (see 9.1.2). The endpoints with the relevant formulation SAP250 F have been used in the risk assessment. No unacceptable risks are expected due to application of SAP250F in the intended uses as TERLT is above trigger of 5. |

#### Higher-tier risk assessment

Not relevant.

#### Risk mitigation measures

No risk mitigation needed.

### Overall conclusions

The worst-case TER values are well greater than the trigger value of 5 and therefore it is considered that risks to non-target plants after SAP250F applications are acceptable.

## Effects on other terrestrial organisms (flora and fauna) (KCP 10.7)

No available data.

## Monitoring data (KCP 10.8)

No available data.

## Classification and Labelling

**Prothioconazole Classification and Labelling**

~~No harmonized classification according to Regulation (EC) No 1272/2008.~~

|  |  |  |
| --- | --- | --- |
| **Environmental**  **hazards** | Aquatic chronic 1 | |
| **Hazard pictograms** |  | |
| **Signal word** | Warning | |
| **Hazard statements** | H410 | Very toxic to aquatic life with long lasting effects |

**SAP250F Classification and Labelling**

**Classification and labelling in accordance with Regulation (EC) No 1272/2008**

|  |  |  |
| --- | --- | --- |
| **Environmental**  **hazards** | Aquatic chronic 2 | |
| **Hazard pictograms** |  | |
| **Signal word** | No signal word is used. | |
| **Hazard statements** | H411 | Toxic to aquatic life with long lasting effects |
| **Precautionary statements –** | ~~P273: Avoid release to the environment.~~  P391: Collect spillage.  P501: Dispose of contents/container in accordance to local regulation. | |

Justification of the proposal of classification of the preparation based on the regulation 1272/2008:

Since the EC50 for *Daphnia magna* is 2.93 mg/L and the NOErC for *Lemna gibba* is < 0.274 mg/L, the formulation is not acutely classified and is classified as aquatic chronic 2.

|  |
| --- |
| **zRMS comment:**  We agree with the classification of the product: H411. |

1. Lists of data considered in support of the evaluation

List of data submitted by the applicant and relied on

| Data point | Author(s) | Year | Title Company Report No.  Source (where different from company) GLP or GEP status Published or not | Vertebrate study  Y/N | Owner |
| --- | --- | --- | --- | --- | --- |
| KCP 10.2.1/01 | Siche, O., Wydra, V. | 2019 | SAP250F: Acute toxicity to Daphnia magna in a semi-static 48-hour immobilisation test.  Ibacon Study No. 130811220.  GLP  Unpublished | N | ASCENZA AGRO S.A. |
| KCP 10.2.1/02 | Siche, O., Wydra, V. | 2019 | SAP250F: Toxicity to Pseudokirchneriella subcapitata in an algal growth inhibition test.  Ibacon Study No. 130811210.  GLP  Unpublished | N | ASCENZA AGRO S.A. |
| KCP 10.2.1/03 | Siche, O., Wydra, V. | 2019 | SAP250F: Toxicity to the aquatic plant Lemna gibba in a semi-static growth inhibition test.  Ibacon Study No. 130811240.  GLP  Unpublished | N | ASCENZA AGRO S.A. |
| KCP 10.3.1.1/01 | Schabio, S. | 2018 | SAP250F: Effects (Acute Contact and Oral) on Honey Bees (Apis mellifera L.) in the laboratory.  Ibacon Study No. 130811035.  GLP  Unpublished | N | ASCENZA AGRO S.A. |
| KCP 10.3.1.2/01 | Sekine, T., Kowalczyk, F. | 2019 | SAP250F: Chronic Oral Toxicity Test on the Honey Bee (Apis mellifera L.) in the Laboratory.  Ibacon Study No. 130811136.  GLP  Unpublished | N | ASCENZA AGRO S.A. |
| KCP 10.3.1.3/01 | Marin, M. | 2019 | SAP250F (Prothioconazole 250 g/L EC): Honey Bee (Apis mellifera L.) larval toxicity test following repeated exposure under laboratory conditions.  Trialcamp Study No. S19-20762.  GLP  Unpublished | N | ASCENZA AGRO S.A. |
| KCP 10.4/01 | Moll, M. | 2019 | SAP250F: Effects on the Predatory mite Typhlodromus pyri, Extended Laboratory Sutyd – Dose Response Test.  Ibacon Study No. 130811062.  GLP  Unpublished | N | ASCENZA AGRO S.A. |
| KCP 10.4/02 | Moll, M. | 2019 | SAP250F: Effects on the parasitoid Aphidius rhopalosiphi, Extended Laboratory Study – Dose Response Test.  Ibacon Study No. 130811002.  GLP  Unpublished | N | ASCENZA AGRO S.A. |
| KCP 10.4/03 | Moll, M. | 2019 | SAP250F: Effects on the Lacewing Chrysoperla carnea, Extended Laboratory Study – Dose Response Test.  Ibacon Study No. 130811047.  GLP  Unpublished | N | ASCENZA AGRO S.A. |
| KCP 10.4.1.1/01 | Straube,D. | 2019 | SAP250F: Effects on reproduction and growth of Earthworms Eisenia Andrei in artificial soil.  Ibacon Study No. 130811022.  GLP  Unpublished | N | ASCENZA AGRO S.A. |
| KCP 10.6.2/01 | Stürtz, S., Kowalczyk, F. | 2019 | SAP250F: Effects on Terrestrial (Non-Target) Plants: Seedling Emergence and Seedling Growth Test.  Ibacon Study No. 130811086.  GLP  Unpublished | N | ASCENZA AGRO S.A. |
| KCP 10.6.2/02 | Stürtz, S., Kowalczyk, F. | 2019 | SAP250F: Effects on Terrestrial (Non-Target) Plants: Vegetative Vigour Test.  Ibacon Study No. 130811087.  GLP  Unpublished | N | ASCENZA AGRO S.A. |

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 |
| --- | --- | --- | --- | --- | --- |
| KCP XX | Author | YYYY | Title  Company Report N  Source  GLP/non GLP/GEP/non GEP  Published/Unpublished | 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 |
| --- | --- | --- | --- | --- | --- |
| KCP XX | Author | YYYY | Title  Company Report N  Source  GLP/non GLP/GEP/non GEP  Published/Unpublished | 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 |
| --- | --- | --- | --- | --- | --- |
| KCP XX | Author | YYYY | Title  Company Report N  Source  GLP/non GLP/GEP/non GEP  Published/Unpublished | Y/N | Owner |
|  |  |  |  |  |  |

1. Detailed evaluation of the new studies
   1. KCP 10.1 Effects on birds and other terrestrial vertebrates
      1. KCP 10.1.1 Effects on birds
         1. KCP 10.1.1.1 Acute oral toxicity
         2. KCP 10.1.1.2 Higher tier data on birds
      2. KCP 10.1.2 Effects on terrestrial vertebrates other than birds
         1. KCP 10.1.2.1 Acute oral toxicity to mammals
         2. KCP 10.1.2.2 Higher tier data on mammals
      3. KCP 10.1.3 Effects on other terrestrial vertebrate wildlife (reptiles and amphibians)
   2. KCP 10.2 Effects on aquatic organisms
      1. KCP 10.2.1 Acute toxicity to fish, aquatic invertebrates, or effects on aquatic algae and macrophytes
         1. KCP 10.2.1/01 Study 1

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Comments of zRMS: | The study is considered acceptable. The validity criteria were met.   |  |  | | --- | --- | | Control Immobilisation Rate: | Was 0 % and furthermore no daphnid showed signs of disease or stress; thus the validity criterion was met. | | Dissolved Oxygen Concentration: | Was ≥ 8.1 mg O2/L in in all treatment groups at the end of the test; thus validity criterion was met. |   All reported results refer to geometric mean concentrations, since the test item concentrations were not within ± 20 % of the nominal concentrations during the test  **Agreed endpoints:**   |  |  |  | | --- | --- | --- | | Geomean concentration | % of immobilised Daphnids after | | | [mg test item/L] | 24 hours | 48 hours | | Control | 0 | 0 | | 0.0576 | 0 | 0 | | 0.240 | 0 | 0 | | 1.12 | 0 | 0 | | 3.13 | 5 | 60 | | 7.94 | 50 | 100 | | EC50 [mg test item/L]: | 7.93 | 2.93 | | 95 % CI [mg test item/L]: | 6.39 - > 7.94 | 2.48 - 3.47 | | EC20 [mg test item/L]: | 5.37 | 2.11 | | 95 % CI [mg test item/L]: | 3.98 - 7.25 | 1.67 - 2.65 | | EC10 [mg test item/L]: | 4.15 | 1.69 | | 95 % CI [mg test item/L]: | 2.64 - 6.52 | 1.24 - 2.31 | | NOEC [mg test item/L]: | 3.13 | 1.12 | | LOEC [mg test item/L]: | 7.94 | 3.13 | | Values refer to geometric mean measured test concentrations CI: Confidence interval | | | |

|  |  |
| --- | --- |
| **Reference:** | **KCP 10.2.1/01, Siche, O., Wydra, V. (2019)** |
| Report | SAP250F: Acute Toxicity to Daphnia magna in a Semi-Static 48-hour Immobilisation Test. Siche, O., Wydra, V., 2019, Ibacon Study No. 130811220. |
| Guideline(s): | Yes   * OECD Guideline for Testing of Chemicals No. 202: "Daphnia sp., Acute Immobilisation Test" adopted April 13, 2004 * Commission Regulation (EC) No 440/2008, Annex, Part C, C.2.: "Daphnia sp. Acute Immobilisation Test", Official Journal of the European Union (EN), dated May 30, 2008 * SANCO/3029/99 rev.4 11/07/00: Residues: Guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (part A; Section 4) and Annex III (part A; Section 5) of directive 91/414 |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |
| Duplication  (if vertebrate study) | No |

Objective

The purpose of this study was to determine the influence of the test item SAP250F on the mobility of Daphnia magna. For this purpose, young daphnids (< 24 hours old) were exposed in a semi-static test to various concentrations under defined conditions for 48 hours. The recorded effects were the mobility of the daphnids after 24 and 48 hours. The test method of application and the test system are recommended by the test guidelines and Daphnia magna is the recommended test species. The purpose of the analytical part of this study was to verify the concentrations of the test item in the test medium.

Materials and methods

|  |  |
| --- | --- |
| Test Item: | SAP250F; batch no.: R-DAA; content of a.i.: Prothioconazole:250 g/L(nominal); 257 g/L (analytical) according to certificate of analysis |
| Test Species: | Female *Daphnia magna*, clone 5; 2.75 to 19.75 hours old  Source: The daphnids introduced in the test were taken from ibacon's in-house laboratory culture. |
| Test Design: | This study encompassed 6 treatment groups (5 dose rates of the test item and a control) each containing 20 individuals. The mobility of the daphnids was determined in a semi-static 48-hour test by visual observation after 24 and 48 hours. |
| Endpoints: | Number of immobile organisms after 24 and 48 hours |
| Test Concentrations: | 10, 4.5, 2.1, 0.9 and 0.4 mg test item/L (spacing factor 2.2) and a control, corresponding to following geometric mean measured concentrations of the test item:  7.94, 3.13, 1.12, 0.115 and 0.0576 mg test item/L, and a control. |
| Test Conditions: | Water temperature: 20.0 to 20.9 °C; pH value: 7.9 to 8.2; dissolved oxygen concentration: 8.1 to 9.0 mg/L; photoperiod: 16 h light - 8 h dark; light intensity: 300 to 710 lux; and thus were within the ranges requested by guideline OECD 202 |

|  |  |  |  |
| --- | --- | --- | --- |
|  | Table 1. Summary of Biological Results | | |
|  | ~~Nominal~~ Geomean Concentration | % of immobilised daphnids after | |
|  | [mg test item/L] | 24 hours | 48 hours |
|  | Control | 0 | 0 |
|  | 0.0576 | 0 | 0 |
|  | 0.240 | 0 | 0 |
|  | 1.12 | 0 | 0 |
|  | 3.13 | 5 | 60 |
|  | 7.94 | 50 | 100 |
|  | EC50 [mg test item/L]: | 7.93 | 2.93 |
|  | 95 % CI [mg test item/L]: | 6.39 - > 7.94 | 2.48 - 3.47 |
|  | EC20 [mg test item/L]: | 5.37 | 2.11 |
|  | 95 % CI [mg test item/L]: | 3.98 - 7.25 | 1.67 - 2.65 |
|  | EC10 [mg test item/L]: | 4.15 | 1.69 |
|  | 95 % CI [mg test item/L]: | 2.64 - 6.52 | 1.24 - 2.31 |
|  | NOEC [mg test item/L]: | 3.13 | 1.12 |
|  | LOEC [mg test item/L]: | 7.94 | 3.13 |
|  | Values refer to geometric mean measured test concentrations CI: Confidence interval | | |
| Analytical test results: | The quantification of the active ingredient Prothioconazole of the test item SAP250F in the test samples was performed using liquid chromatography with MS/MS detection.  In the freshly prepared test media at the start of the test and at the renewal of the test media 90 % of the nominal test concentrations were found (average of nominal test concentrations 10, 4.5 and 2.1 mg test item/L). In the aged test media after 24 hours test duration, 76 % of the nominal value was determined (average of nominal test concentrations 10, 4.5 and 2.1 mg test item/L).  In the two lowest test concentrations of nominal 0.9 and 0.4 mg test item/L the measured values were partly below the limit of quantification of the analytical method. However this is regarded to have no negative effect on the outcome of the study, since these treatment groups were found to be below the 48-hour NOEC determined in this study. | | |

Conclusion

The toxic effect of the test item SAP250F to Daphnia magna was assessed in a semi-static concentration-response test. The 48-hour NOEC was determined to be 1.12 mg test item/L. The 48-hour LOEC was determined to be 3.13 mg test item/L and the 48-hour EC50 value was calculated to be 2.93 mg test item/L.

The initial concentrations and the maintenance of the exposure concentrations during the test were verified in the analytical part. All reported results refer to geometric mean concentrations, since the test item concentrations were not within ± 20 % of the nominal concentrations during the test.

Validity criteria

|  |  |
| --- | --- |
| Control Immobilisation Rate: | Was 0 % and furthermore no daphnid showed signs of disease or stress; thus the validity criterion was met. |
| Dissolved Oxygen Concentration: | Was ≥ 8.1 mg O2/L in in all treatment groups at the end of the test; thus validity criterion was met. |

* + - 1. KCP 10.2.1/02 Study 2

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Comments of zRMS: | The study is considered acceptable. The validity criteria were met.   |  |  | | --- | --- | | Cell Density Increase in Control Cultures: | 266.8-fold increase within 72 hours and thus | | Coefficient of Variation of Sectional (Daily) Growth Rates in Control Cultures: | 19.5 % and thus, the validity criterion was met. | | Coefficient of Variation of Average Growth between Control Replicates: | 1.1 % and thus, the validity criterion was met. |   At the start of the test recoveries of the nominal test concentration varied between 84 and 102% (all test concentrations considered). After 72 hours test duration, the recoveries of the nominal values varied between 24 and 101% (all test concentrations considered).  All reported results refer to geometric mean concentrations, since the test item concentrations were not within ± 20 % of the nominal and initial concentrations during the test.  **Agreed endpoints:**  72-hour EyC50 = 4.68 mg test item/L  72-hour NOEyC = 0.49 mg test item/L  72-hour LOEyC = 2.22 mg test item/L  72-hour ErC50 = 15.8 mg test item/L.  72-hour NOErC = 0.49 mg test item/L  72-hour LOErC = 2.22 mg test item/L. |

|  |  |
| --- | --- |
| **Reference:** | **KCP 10.2.1/02, Siche, O., Wydra, V. (2019)** |
| Report | SAP250F: Toxicity to *Pseudokirchneriella subcapitata* in an Algal Growth Inhibition Test. Siche, O., Wydra, V., 2019, Ibacon Study No. 130811210. |
| Guideline(s): | Yes   * OECD Guidelines for the Testing of Chemicals, Section 2, No. 201: "Freshwater Alga and Cyanobacteria, Growth Inhibition Test", adopted March 23, 2006, corrected July 28, 2011 * Commission Regulation (EC) No 761/2009, Annex, Part C, C.3.: "Freshwater Algae and Cyanobacteria, Growth Inhibition Test", Official Journal of the European Union (EN), dated August 24, 2009 * OECD Series on Testing and Assessment, No. 23, "Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures", December 15, 2000 * SANCO/3029/99 rev.4 11/07/00: Residues: Guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (part A; Section 4) and Annex III (part A; Section 5) of directive 91/414 |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |
| Duplication  (if vertebrate study) | No |

Objective

The purpose of this test was to determine the inhibitory effect of the test item SAP250F on the growth of the freshwater green algae *Pseudokirchneriella subcapitata*. For this purpose, exponentially growing cultures of this unicellular green algal species were exposed to various concentrations of the test item under defined conditions. The inhibition of growth in relation to control cultures was determined over a test period of 72 hours, and thus over several algal generations. The test method of application and the test system are recommended by the test guidelines and *Pseudokirchneriella subcapitata* is one of the recommended test species. The purpose of the analytical part of this study was to verify the concentrations of the test item in the test medium.

Materials and methods

|  |  |
| --- | --- |
| Test Item: | SAP250F; Batch No.: R-DAA; content of Prothioconazole: 257 g/L (analytical), according to certificate of analysis. |
| Test Species: | *Pseudokirchneriella subcapitata*, Strain No. 61.81 SAG formerly known as *Selenastrum capricornutum*, and recently renamed as *Raphidocelis subcapitata* (KORSHIKOV).  Cultivated in the laboratories of ibacon; original source: "Sammlung von Algenkulturen, Albrecht-von-Haller-Institut für Pflanzenwissen-schaften, Universität Göttingen", 37073 Göttingen, Germany. |
| Test Design: | This study encompassed 6 treatment groups (5 dose rates of the test item and a control) with three replicates per test concentration and six replicates for the control. At test start 50 mL of the test concentrations were inoculated with approximately 5000  algal cells per mL test medium and defined volumes of the algal suspensions were sampled after 24, 48 and 72  hours for determination of cell densities by spectrophotometrical measurement. |
| Endpoints: | Yield and growth rate of the algae |
| Test Concentrations: | Nominal 100, 32, 10, 3.2 and 1.0 mg test item/L (spacing factor 3.16) corresponding to geometric mean measured 98.3, 31.2, 8.18, 2.22 and 0.485 mg test item/L and a control. |
| Test Conditions: | Water temperature: 22 to 23.5°C; pH values at test start 7.8 to 8.0, at the end of the test 8.0 to 9.9; continuous illumination; mean light intensity: 6197 lux (5950 to 6480 lux). |

Results and discussions

|  |  |
| --- | --- |
| Biological Results: |  |

Table 1. Biological Results

|  |  |  |
| --- | --- | --- |
| Parameter | Yield [mg test item/L] | Growth rate [mg test item/L] |
| 72-hour EC50 | 4.68 | 15.8 |
| 95 % conf. interval | 4.28 – 5.11 | 15.14 – 16.56 |
|  |  |  |
| 72-hour EC20 | 2.11 | 6.69 |
| 95 % conf. interval | 1.82 - 2.39 | 6.23 – 7.14 |
|  |  |  |
| 72-hour EC10 | 1.39 | 4.26 |
| 95 % conf. interval | 1.14 – 1.63 | 3.88 - 4.64 |
|  |  |  |
| 72-hour NOEC | 0.49 | 0.49 |
| 72-hour LOEC | 2.22 | 2.22 |
| Values refer to geometric mean measured test concentrations | | |

|  |  |
| --- | --- |
| Analytical Results: | The quantification of the active ingredient Prothioconanzole of the test item SAP250F in the test samples was performed using liquid chromatography MS/MS detection.  At the start of the test recoveries of the nominal test concentration varied between 84 and 102% (all test concentrations considered). After 72 hours test duration, the recoveries of the nominal values varied between 24 and 101% (all test concentrations considered). The test item was dosed correctly but was not stable during the run of the test. |

Conclusion

The influence of SAP250F on the growth of the freshwater green algae Pseudokirchneriella subcapitata was assessed in a static concentration-response test. The 72-hour EyC50 was calculated to be 4.68 mg test item/L, and the 72-hour ErC50 value was calculated to be 15.8 mg test item/L. The 72-hour NOEyC was determined to be 0.49 mg test item/L and the associated 72-hour LOEyC was 2.22 mg test item/L. The 72-hour NOErC was determined to be 0.49 mg test item/L and the associated 72-hour LOErC was 2.22 mg test item/L.

The initial concentrations and the maintenance of the exposure concentrations during the test were verified in the analytical part.

All reported results refer to geometric mean concentrations, since the test item concentrations were not within ± 20 % of the nominal and initial concentrations during the test.

Validity criteria

After 72h:

|  |  |
| --- | --- |
| Cell Density Increase in Control Cultures: | 266.8-fold increase within 72 hours and thus, the validity criterion was met. |
| Coefficient of Variation of Sectional (Daily) Growth Rates in Control Cultures: | 19.5 % and thus, the validity criterion was met. |
| Coefficient of Variation of Average Growth between Control Replicates: | 1.1 % and thus, the validity criterion was met. |

* + - 1. KCP 10.2.1/03 Study 3

|  |  |
| --- | --- |
| Comments of zRMS: | The study is considered acceptable. The validity criteria were met.  -Doubling Time of Frond Number in Control: 1.7 days  At the start of the test and at the renewal of the test media recoveries of the nominal test concentration varied between 65 and 119% (all test concentrations considered). After 48 and 72 hours test duration, the recoveries of the nominal values va All reported results refer to geometric mean concentrations.  ried between 58 and 110% (all test concentrations considered).  **Agreed endpoints:**  7-day EyC50 = 3.15 and 2.50 mg test item/L for frond number and dry weight, respectively.  **7-day ErC50 =11.6 and 10.8 mg test item/L for frond number and dry weight, respectively.**  7-day NOEyC and the LOEyC < 0.274 and 0.274 mg test item/L for frond number and dry weight, respectively.  7-day NOErC and the LOErC < 0.274 and 0.274 mg test item/L for frond number and dry weight, respectively. |

|  |  |
| --- | --- |
| **Reference:** | **KCP 10.2.1/03, Siche, O., Wydra, V. (2019)** |
| Report | SAP250F: Toxicity to the Aquatic Plant Lemna gibba in a Semi-Static Growth Inhibition Test. Siche, O., Wydra, V., 2019, Ibacon Study No. 130811240. |
| Guideline(s): | Yes   * Commission Regulation (EC) No 761/2009, Annex, Part C, C.26.: "Lemna sp. Growth Inhibition Test", Official Journal of the European Union (EN), dated August 24, 2009 * OECD Guidelines for the Testing of Chemicals, No. 221: "Lemna sp. Growth Inhibition Test", adopted March 23, 2006 * SANCO/3029/99 rev.4 11/07/00: Residues: Guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (part A; Section 4) and Annex III (part A; Section 5) of directive 91/414 |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |
| Duplication  (if vertebrate study) | No |

Objective

The purpose of this study was to determine the inhibitory effect of the test item SAP250F on the growth of the freshwater aquatic plant *Lemna gibba*. For this purpose, cultures of *Lemna gibba* were exposed in a semi-static test to various concentrations under defined conditions. The inhibitions of growth in relation to control cultures were determined over a test period of 7 days. The test method of application and the test system are recommended by the test guidelines and *Lemna gibba* is the recommended test species. The purpose of the analytical part of this study was to verify the concentrations of the test item in the test medium.

Materials and methods

|  |  |
| --- | --- |
| Test Item: | SAP250F; batch no.: R-DAA; content of Prothioconazole: 250 g/L (nominal) and 257 g/L (analytical), according to certificate of analysis. |
| Test Species: | *Lemna gibba* G 3 |
| Test Design: | This study encompassed 6 treatment groups (5 dose rates of the test item and a control) with three replicates per test concentration and control.  At test start 12 fronds were introduced in each replicate and incubated for 7 days under semi-static conditions. The frond numbers were determined on day 3, 5 and 7. The dry weight of each replicate was determined at test termination. |
| Endpoints: | Yield and growth rate based on frond number and dry weight. |
| Test Concentrations: | 32, 10, 3.2, 1.0 and 0.32 mg test item/L (spacing factor 3.16), corresponding to geometric mean measured test concentrations of 31.2, 9.78, 3.30, 0.991 and 0.274 mg test item/L and a control. |
| Test Conditions: | Water temperature: 22.6 to 23.2°C; pH values at test start in the freshly prepared test media 7.5 to 7.8, at the end of the test in the aged test media 8.2 to 8.9; continuous illumination; mean light intensity: 7595 lux (6810 to 8130 lux). |

Results and discussions

|  |  |
| --- | --- |
| Biological Results: |  |

Table 1. Summary of Biological Results

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Parameter | Yield (frond number) [mg test item/L] | | Growth rate (frond number) [mg test item/L] | Yield (dry weight) [mg test item/L] | Growth rate (dry weight) [mg test item/L] |
| EC50 (7-day) | 3.15 | | 11.6 | 2.50 | 10.8 |
| 95 % conf. limits | 2.77 - 3.57 | | 11.1 - 12.1 | 2.13 - 2.93 | 9.93 - 11.7 |
|  |  | |  |  |  |
| EC20 (7-day) | 0.554 | | 5.54 | 0.436 | 4.25 |
| 95 % conf. limits | 0.446 - 0.688 | | 5.17 - 5.94 | 0.330 - 0.575 | 3.75 - 4.82 |
|  |  | |  |  |  |
| EC10 (7-day) | < 0.274 | | 3.77 | < 0.274 | 2.62 |
| 95 % conf. limits | n.d. | | 3.44 - 4.14 | n.d. | 2.21 - 3.10 |
|  |  | |  |  |  |
| 7-day NOEC | < 0.274 | | < 0.274 | < 0.274 | < 0.274 |
| 7-day LOEC | 0.274 | | 0.274 | 0.274 | 0.274 |
| Values refer to geometric mean measured test concentrations | | | | | |
|  | |  | | | |
| Analytical Results: | | The quantification of the active ingredient Prothioconazole of the test item SAP250F in the test samples was performed using liquid chromatography with MS/MS detection.  At the start of the test and at the renewal of the test media recoveries of the nominal test concentration varied between 65 and 119% (all test concentrations considered). After 48 and 72 hours test duration, the recoveries of the nominal values varied between 58 and 110% (all test concentrations considered). | | | |

Conclusion

The influence of SAP250F on the growth of the freshwater plant Lemna gibba was assessed in a semi-static concentration-response test.

The 7-day EyC50 was calculated to be 3.15 and 2.50 mg test item/L for frond number and dry weight, respectively.

The 7-day ErC50 was calculated to be 11.6 and 10.8 mg test item/L for frond number and dry weight, respectively.

The 7-day NOEyC and the LOEyC were determined to be < 0.274 and 0.274 mg test item/L for frond number and dry weight, respectively.

The 7-day NOErC and the LOErC were determined to be < 0.274 and 0.274 mg test item/L for frond number and dry weight, respectively.

The initial concentrations and the maintenance of the exposure concentrations during the test were determined the analytical part. All reported results refer to geometric mean concentrations.

Validity criteria

|  |  |
| --- | --- |
| Doubling Time of Frond Number in Control: | 1.7 days, validity criterion was met. |

KCP 10.2.2 Additional long-term and chronic toxicity studies on fish, aquatic invertebrates and sediment dwelling organisms

* + 1. KCP 10.2.3 Further testing on aquatic organisms
  1. KCP 10.3 Effects on arthropods
     1. KCP 10.3.1 Effects on bees
        1. KCP 10.3.1.1 Acute toxicity to bees
           1. KCP 10.3.1.1/01 Study 1

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Comments of zRMS: | The studies are considered acceptable. The validity criteria were met.   |  |  | | --- | --- | | Control Mortality: | Contact Test  water control:  6.7 %  Oral Test  sugar control:  0.0 % | | LD50 of Reference Item (24 hrs): | Contact Test: 0.17 μg a.i./bee  Oral Test: 0.15 μg a.i./bee | | Validity of the Tests: | The contact and oral tests are considered valid as the control mortality in each case was < 10 % and the LD50 values obtained with the reference item (dimethoate) were within the required ranges. |   **Agreed endpoints:**   |  |  |  | | --- | --- | --- | | Test Item | SAP250F | | | Exposure | Contact | Oral | | LD50 µg a.i./bee | 24 hours 267  48 hours 198  72 hours 158  96 hours 164 | 24 and 48 hours: > 84.2 | |

|  |  |
| --- | --- |
| **Reference:** | **KCP 10.3.1.1/01, Schabio, S. (2018)** |
| Report | SAP250F: Effects (acute contact and oral) on Honey bees (Apis mellifera L.) in the laboratory. Schabio, S., 2018, Ibacon Study No. 130811035. |
| Guideline(s): | Yes   * OECD (1998), *Test No. 213: Honeybees, Acute Oral Toxicity Test,* OECD Guidelines for the Testing of Chemicals, Section 2, OECD Publishing, Paris * OECD (1998), *Test No. 214: Honeybees, Acute Contact Toxicity Test,* OECD Guidelines for the Testing of Chemicals, Section 2, OECD Publishing, Paris |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |
| Duplication  (if vertebrate study) | No |

Objective

The purpose of this study was to determine the acute contact and oral toxicity of SAP250F to the honey bee (*A. mellifera* L.). Mortality of the bees was used as the toxic endpoint. Sublethal effects, such as changes in behaviour, were also assessed.

Materials and methods

|  |  |
| --- | --- |
| Test Item: | SAP250F, Batch No.: R-DAA, content: prothioconazole: nominal 250 g/L; analytical 257 g/L, according to certificate of analysis. |
| Test Species: | Honey bee *(Apis mellifera* L.); female worker bees; obtained from a healthy and queen-right colony, bred by ibacon, collected in the morning of use. |
| Test Design: | Dose response acute contact and oral toxicity test; test duration 96 h (contact test) and 48 h (oral test); 3 replicates for the contact and oral test, each consisting of 10 bees per cage per treatment; assessment of mortality after 4, 24 and 48 (oral and contact test) and additionally after 72 and 96 hours in the contact test, because of increasing mortality between 24/48 and 48/72 hr; reference item: dimethoate 400 g/L (nominal). |
| Test Concentrations: | Contact test: 600, 300, 150, 75 and 37.5 μg a.i. of SAP250F/bee\*  Oral test (nominal): 100, 50, 25, 12.5, 6.3 μg a.i. of SAP250F/bee\*  Oral test (measured): 84.2, 53.4, 26.8, 13.8 and 6.88 μg a.i. of SAP250F/bee\*  \*in the following, e.g. 100 μg a.i. of SAP250F/bee, will be referred to as 100 μg a.i./bee. The dose levels of the product are adjusted to reflect the percentage a.i. (analytical value), e.g. 100 μg a.i./bee = 100 μg prothioconazole/bee. |
| Test Conditions: | Temperature: 25 - 27 °C; relative humidity: 54 - 58 %; photoperiod: 24 h darkness. |

Results and discussions

Contact Test:

The contact test was prolonged for a further 48 hours up to 96 hours due to increasing mortality between 24/48 and 48/72 hours. Mortality occurred in all groups dosed with SAP250F, increasing with dose levels. The contact dose levels of 600 to 37.5 μg a.i./bee resulted in mortality ranging from 100 % to 10.0 % at the end of the test (96 hours after application). 6.7 % mortality occurred in the control group (water + 0.5 % Adhäsit).

In the 600 and 300 μg a.i./bee dosing groups all bees showed behavioural impairments (e.g. discoordinated movement or moribundity) or died until test end. In the 150, 75 and 37.5 μg a.i./bee treatment groups behavioural impairments such as apathy, discoordinated movement and moribundity appeared in a dose and time related pattern. After 48 hours no further affection occurred in the 75 and 37.5 μg a.i./bee dosing groups any more.

Oral Test:

In the oral toxicity test the maximum nominal test level of SAP250F (100 μg a.i./bee) could not be achieved, because the bees did not ingest the full volume of treated sugar solution even when offered over a period of 5 hours and 40 minutes. Actual oral doses of 84.2, 53.4, 26.8, 13.8 and 6.88 μg a.i./bee led to dose dependent mortality levels ranging from 43.3 to 0.0 % at test termination (48 hours after application). No mortality occurred in the control group (50 % w/v sucrose solution = 500 g sucrose/L tap water).

During the 4 hours assessment behavioural impairments such as apathy, discoordinated movement and moribundity occurred in a dose related pattern in all dosing groups, except of the lowest treatment group (6.88 μg a.i./bee). At the 24 and 48 hours assessment only single bees in the 84.2 and 53.4 μg a.i./bee dosing group appeared to be affected (e.g. discoordinated movement or moribund).

Table 1. Toxicity of SAP250F to honey bees; laboratory test

|  |  |  |
| --- | --- | --- |
| Test Item | SAP250F | |
| Test Species | *Apis mellifera* L. | |
| Exposure | contact  (solution in Adhäsit (0.5 %)/water) | oral  (50 % water/sucrose solution) |
| Application rate µg a.i./bee | 600, 300, 150, 75 and 37.5 | 84.2, 53.4, 26.8, 13.8 and 6.88 |
| LD50 µg a.i./bee | 24 hours 267  48 hours 198  72 hours 158  96 hours 164 | 24 and 48 hours: > 84.2 |
| The contact and oral LD50 (24 h) values for the reference item (dimethoate) were calculated to be 0.17 and 0.15 µg a.i./bee, respectively. | | |

Conclusion

The toxicity of SAP250F was tested in both an acute contact and an oral toxicity test on honey bees.

The lowest LD50 value in the contact test was 158 μg a.i./bee after 72 hours, during a study duration

of 96 hours.

The oral LD50 value (24 h + 48 h) was > 84.2 μg a.i./bee.

Validity criteria

|  |  |
| --- | --- |
| Control Mortality: | Contact Test  water control:  6.7 %  Oral Test  sugar control:  0.0 % |
| LD50 of Reference Item (24 hrs): | Contact Test: 0.17 μg a.i./bee  Oral Test: 0.15 μg a.i./bee |
| Validity of the Tests: | The contact and oral tests are considered valid as the control mortality in each case was < 10 % and the LD50 values obtained with the reference item (dimethoate) were within the required ranges. |

* + - * 1. KCP 10.3.1.1.1 Acute oral toxicity to bees
        2. KCP 10.3.1.1.2 Acute contact toxicity to bees
      1. KCP 10.3.1.2. Chronic toxicity to bees
         1. KCP 10.3.1.2/01 Study 1

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Comments of zRMS: | The studies are considered acceptable. The validity criteria were met.  In the present study the following results are obtained;   |  |  | | --- | --- | | Control Mortality: | Water control: 0.0 % (on day 10) | | Reference Item - | 100.0 % (on day 5) | |  |  |   The control mortality was < 15 % and the mortality of the reference item  (dimethoate) was within the required range.  **Agreed endpoints:**  The LC50 (10 days) =715.9 mg a.s./kg feeding solution.  The LDD50 (10 days) =12.3 µg a.s./bee/day.  The NOEC and NOEDD (10 days) =320 mg a.s./kg feeding solution and 6.18 µg a.s./bee/day, respectively. |

|  |  |
| --- | --- |
| **Reference:** | **KCP 10.3.1.2/01, Sekine, T., Kowalczyk, F. (2019)** |
| Report | SAP250F: Chronic Oral Toxicity Test on the Honey Bee (Apis mellifera L.) in the Laboratory. Sekine, T., Kowalczyk, F., 2019, Ibacon Study No. 130811136. |
| Guideline(s): | Yes   * OECD (2017), Test No. 245: Honey Bee (*Apis Mellifera* L.), Chronic Oral Toxicity Test (10-Day Feeding), OECD Publishing, Paris. |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |
| Duplication  (if vertebrate study) | No |

Objective

The purpose of this study will be to determine the chronic oral toxicity of SAP250F to the honey bee (*A. mellifera* L.) for a period of ten days. Mortality of the bees will be used as the toxic endpoint. Sublethal effects, such as changes in behaviour, will also be assessed. The purpose of the analytical part of this study is to verify proper dosing of the test item.

Materials and methods

|  |  |
| --- | --- |
| Test Item: | SAP250F, Batch Code: R-DAA, content:  Prothioconazole: 246.4 g/L (analytical), 250 g/L (nominal),  according to certificate of analysis. |
| Test Species: | Honey bee (*Apis mellifera* L.); freshly emerged young female worker bees; obtained from a healthy and queen-right colony, bred by ibacon. After hatch, the bees were collected and thereafter acclimatized under test conditions for one day. |
| Age of the Honey Bees: | Two days old worker bees. |
| Test Design: | 10 days chronic oral feeding test in the laboratory (dose response test). Young honey bees were provided with 5 concentrations of the test item treated sugar solutions *ad libitum* over a period of 10 days.  An untreated control and a reference item  (BAS 152 11 I; 400 g/L dimethoate) were included in this study.  3 replicates per treatment, each consisting of 10 bees per test cage. |
| Endpoints: | Daily assessment of mortality and behavioural abnormalities up to day 10.  Endpoints: LC50, LDD50, NOEC, NOEDD. |
| Test Concentrations: | Test item: 5000, 2000, 800, 320 and 128 mg a.i./kg feeding solution (ppm)  Reference item: 1 ppm (mg a.i./kg feeding solution) |
| Target Dose Level: | Test item: 100.0, 40.0, 16.0, 6.40 and 2.56 µg a.i./bee per day\*  Reference item: 0.02 µg a.i./bee per day\*  \* taking into account a mean uptake of feeding solution of 20 mg/bee/day; the exact dose per bee per day was calculated after determination of the definitive food uptake of the bees at test end (see “Actual Mean Dose Level”). |
| Actual Mean Dose Level: | Test item: 48.0, 24.9, 13.8, 6.18 and 2.79 µg a.i./bee/day\*\*  Reference item: 0.014 µg a.i./bee/day\*\*  \*\* based on daily actual intake taking into consideration loss by evaporation |
| Evaporation: | In order to adjust for possible evaporation of test solutions from the feeders, evaporation figure was subtracted from the calculated uptake to give the real uptake accounting the loss by evaporation. |
| Test Conditions: | Temperature: 31 - 33 °C; relative humidity: 51 - 70 % mean relative humidity: 60.8 %; photoperiod: 24 h darkness. |

Results and discussions

|  |
| --- |
| The test item was daily administered to the bees in sugar solution at the following concentrations: 5000, 2000, 800, 320 and 128 mg a.i./kg feeding solution. These concentrations led to a daily mean dose of 48.0, 24.9, 13.8, 6.18 and 2.79 µg a.i./bee/day (based on daily actual intake adjusted for evaporation) after 10 days.  Mortality occurred in all test item treated dose levels ranging from 3.3 to 100 % at test end (10 days following the start of chronic exposure). There was no mortality in the control (50 % w/v sucrose solution).  Discoordinated movements and/or apathy were observed in all test item treatments. On day 1, 2 and 3 behavioural abnormalities occurred in the 5000, 2000 and 800 mg a.i./kg feeding solution corresponding to 48.0, 24.9 and 13.8 µg a.i./bee/day dose levels. On day 4 one single bee in 2000 mg a.i./kg feeding solution was moribund. On day 5 some bees in the 800, 320 and 128 mg a.i./kg feeding solution were affected (= discoordinated movements). On day 6 bees in the 800 and 320 mg a.i./kg feeding solution were affected or moribund. One bee in the 2000 mg a.i./kg feeding solution was moribund on day 7 and affected on day 8. Day 9 and 10 no further behavioural abnormalities were found. |

Table 1. 10 days Chronic Oral Toxicity of SAP250F to young honey bees; laboratory test

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Test Organism | | | | *Apis mellifera* L. | | |
| Exposure | | | | Oral 10 days chronic exposure | | |
| Treatment Group | Concentration  [mg a.i./kg feeding solution] | | | Dose Level 1  [µg a.i./bee/day] | | Mortality at day 10 2  [%] |
| SAP250F | 5000 | | | 48.0 | | 100.0 (\*) |
| 2000 | | | 24.9 | | 100.0 (\*) |
| 800 | | | 13.8 | | 60.0 (\*) |
| 320 | | | 6.18 | | 6.7 (n.s.) |
| 128 | | | 2.79 | | 3.3 (n.s.) |
| Water control | 0.0 | | | 0.0 | | 0.0 |
| Reference Item | 1.0 | | | 0.014 | | 100.0 |
| **Endpoint at test termination (day 10)** | | | | | | |
| **LC50** | | **LDD50** | **NOEC** | | **NOEDD** | |
| **715.9 mg a.i./kg feeding solution** | | **12.3 µg a.i./bee/day** | **320 mg a.i./kg feeding solution** | | **6.18 µg a.i./bee/day** | |

1. mean dose per bee per day; dose measured based on consumed feeding solution adjusted for evaporation
2. Mortality at study termination 10 days after start of first feeding

Statistics:

LC50/LDD50: according to Weibull Analysis.

NOEC/NOEDD: was determined using Step-down Cochran-Armitage Test Procedure (one-sided greater, α = 0.05).

n.s. = no statistically significant difference compared to the control,

\* = statistically significant difference compared to the control

Conclusion

|  |
| --- |
| **The chronic oral toxicity of SAP250F was tested over 10 days.**  **The LC50 value (10 days) was 715.9 mg a.i./kg feeding solution.**  **The LDD50 value (10 days) was 12.3 µg a.i./bee/day.**  **The NOEC and NOEDD values (10 days) were 320 mg a.i./kg feeding solution and 6.18 µg a.i./bee/day, respectively.** |
|  |

The analytical recovery rates of the active ingredient SAP250F in the feeding solutions were as follows:

|  |  |
| --- | --- |
| Concentration 2 | Recovery rate [%] 1 |
| Feeding Solution Conc 5 DAA0 | 98 |
| Feeding Solution Conc 1 DAA0 | 97 |

1 recovery rate of the a.i. in feeding solution [ppm]  
2 nominal concentration of the a.i. in the feeding solution [ppm]  
3 DAA0 = freshly prepared feeding solution

Validity criteria

|  |  |
| --- | --- |
| Control Mortality: | Water control: 0.0 % (on day 10) |
| Reference Item Mortality: | 100.0 % (on day 5) |
| Validity of the Test: | The chronic oral test is considered valid as the control mortality was < 15 % and the mortality of the reference item (dimethoate) was within the required range. |

* + - 1. KCP 10.3.1.3 Effects on honey bee development and other honey bee life stages
         1. KCP 10.3.1.3/01 Study 1

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Comments of zRMS: | The studies are considered acceptable. The validity criteria were met.   |  |  | | --- | --- | | Control | The cumulative larval mortality from day 3 (D3) until day 8 (D8) was ≤ 15 % across all replicates (actual mean value 4.17 %).  On day 22 (D22) the adult emergence rate was ≥ 70 % across all replicates (actual mean value 72.92 %). | | Reference | The cumulative larval mortality was ≥ 50 % across all replicates on day 8 (D8) (actual mean value 68.75 %). |   The measured concentrations in the samples were within 20 % of nominal test concentrations. Thus the concentrations of the test item were confirmed and the endpoints are based on nominal concentrations  **Agreed endpoints:**   | **Endpoint** | **Value** | | --- | --- | | Statistical NOEC | 184.55 mg product./kg diet (203.01 mg product /L diet) | | NOEDᵃ | 28.42 µg product/larva (6.25 µg prothioconazole/larva) | | Empirical NOEC | 92.28 mg product/kg diet (101.50 mg prothioconazole//L diet) | | Empirical NOED | 14.21 µg product/larva (3.12 µg prothioconazole//larva) | | EC10, EC20 | n.d. | | ED10, ED20 | n.d. | | EC50 [c.l] | 1023.51 [866.32 – 1209.22] mg product./kg diet  (930.46 [ 787.56 – 1099.29] mg  product/L diet) | | ED50 [c.l] | 157.62 [133.41 – 186.22] µg product/larva  (34.66 [ 29.34-40.95] µg a.s./larva) | |

|  |  |
| --- | --- |
| **Reference:** | **KCP 10.3.1.3/01, Marin, M., (2019)** |
| Report | SAP250F (Prothioconazole 250 g/L EC): Honey Bee (*Apis mellifera* L.) larval toxicity test following repeated exposure under laboratory conditions. Marin, M., 2019, Ibacon Study No. S19-20762. |
| Guideline(s): | Yes   * OECD 239 (2016) Guidance Document on Honey Bee (Apis mellifer) larval toxicity test, repeated exposure * SANCO/3029/99, rev.4. |
| Deviations: | The reduction of the relative humidity conditions from 95 ± 5 % to 80 ± 5 % was done on day 7 (D7) of the test instead of on day 8 (D8). The reported deviation to the guideline has no impact on the outcome of the study since validity criteria for control were met |
| GLP: | Yes |
| Acceptability: | Yes |
| Duplication  (if vertebrate study) | No |

Objective

To determine the effects of SAP250F (Prothioconazole 250 g/L EC) on the honey bee (Apis mellifera L.) larvae after a repeated exposure in a 22 day test.

To determine the No Observed Effect Dose/Concentration (NOED\*/NOEC\*) for adult emergence (from D3 to D22).

To determine the Median Effect Dose/Concentration (ED50\*/EC50\*) and any EDx/ECx (i.e., ED10\*/EC10\* and ED20\*/EC20\*) for adult emergence (from D3 to D22).

\*Where possible.

Materials and methods

|  |  |
| --- | --- |
| **Test item:** | SAP250F (Prothioconazole 250 g/L EC)  Batch code: B-ACA Active ingredient: Prothioconazole Analysed content of a.i.: 239.7 g/L  Density: 1.09 g/mL. Expiry date: January, 2021 |
| **Reference item:** | BAS 152 I Batch code: COD-002332. Active ingredient: Dimethoate. Analysed content of a.i.: 99.7 % (w/w) |
| **Test organisms:** | Honey bee (*Apis mellifera* L.), synchronized first instar (L1) larvae not older than 30 hours at grafting time. |
| **Source:** | Commercial beehives from the in-house test facility stock, adequately fed, healthy and as far as possible disease-free and queen-right. The hives from which the larvae were obtained were not previously exposed to any chemical treatments within four weeks of test initiation. |
| **Preparation of test organisms and larvae collection:** | At D-3, the queen from at least three colonies was isolated for one day within a queen excluder placed on a single frame with empty cells in their own hive, to provide known-aged eggs and subsequent larvae.  At D-2, maximum 30 hours after isolation, the queens were released. Frames containing eggs were left in the excluder cages until hatching (D1). Three frames from different hives, containing the highest number of synchronized larvae, were selected for grafting in the laboratory. |
| **Test design:** | Dose response test with duration of 22 days from grafting on day 1 to the final assessment on day 22. From day 3 until day 6 of the test, 5 different concentrations of SAP250F were applied to the larvae of the test item groups and one single concentration of the reference item was applied to the larvae of the reference item group. Both, test and reference item, were supplied in diet B and C. The daily feeding volume increased from 20 µL to 50 µL diet per larva over the application period. The cumulative feeding volume from day 3 until day 6 (140 µL diet per larva), and the density of the diet (1.1 g/mL), were considered for the calculation of the cumulative doses per larva. One control group was included in the test and exposed for the same period of time under identical exposure conditions to the treatments. Each treatment group consisted of 48 larvae; 16 from each of three different colonies (each colony representing a replicate). Larval mortality assessments were on days 4, 5, 6, 7, and 8. The presence of uneaten food was qualitatively recorded on day 8. Assessment of mortality during pupation phase was on day 15 and assessment of emergence on day 22. |
| **Test concentrations and doses:** | Controls: C: Control group (untreated diet).  Test Item: 101.50, 203.01, 406.01, 812.03 and 1624.05 mg SAP250F/L diet (equivalent to 92.28, 184.55, 369.10, 738.20 and 1476.41 mg SAP250F/kg diet and 14.21, 28.42, 56.84, 113.68 and 227.37 µg SAP250F/larva).  Reference item: R: 52.80 mg Dimethoate/L diet (equivalent to 48.0 mg Dimethoate/kg diet and 7.39 µg Dimethoate/larva). |
| **Endpoints:** | NOEC/NOED and EC10,20,50/ED10,20,50 for adult emergence, where possible. |
| **Test conditions:** | Air Temperature: Min: 34.2 / Max: 35.4 °C\*  Relative humidity: Min: 56.1 / Max: 99.5 %\*  \*Deviations for Temperature (≥ 30 min. once every 24 h) and Relative Humidity (> 2 h) were recorded.  Exposure to light: Constant darkness except during feeding and assessments. |
| **Sampling:** | Samples of treated larval diet from the highest and lowest test item concentrations of the test item were taken from D3 until D6, directly after preparation. Additionally, samples of untreated diet and of the highest concentration solution used to treat the diets were taken on D6, directly after preparation. Samples were placed in the freezer at < -18 ºC until shipment. |
| **Analytical verification:** | An analytical study was performed as a phase of this multisite study. Prothioconazole residues were determined to verify the content of the active ingredient in the samples taken. Quantification was performed by HPLC. The limit of quantification (LOQ) of the analytical method was 1.10 µg prothioconazole/mL diet, with a limit of detection (LOD) set at 0.33 µg prothioconazole/mL diet (≤ 30 % of the LOQ).  Methods are summarized in section 5.10. Results of the analytical phase are shown in section 6.2. Detailed information is included in the Analytical Phase Report, included in the Annex 2 of this Final Report. |
| **Statistics:** | Statistical calculations were made using MS Excel 2010 v.14.0 and the statistical software ToxRat® Professional 3.2.1.  A statistical significance of α = 0.05 was considered for all the tests, except where stated.  Step-down Cochran-Armitage test was used to estimate the NOEC. The NOED was assumed to be the dose corresponding to the NOEC.  To estimate EC10/ED10 and EC20/EC20 a Probit analysis was performed. EC50 was estimated using the Spearman-Kärber method. ED50 was considered to be the dose corresponding to EC50, based on the cumulative volume per larva. |

Results and discussions

Validity criteria for the control group were met: the D8 mortality was lower than 15.00 % (actual value 4.17 %) and the D22 days emergence rate was greater than 70.00 % (actual value 72.92 %), across all replicates.

Validity criteria for the Reference Item group were also met (>50 % at day 8, actual value 68.75 %).

The measured concentrations in the samples were within 20 % of nominal test concentrations. Thus the concentrations of the test item were confirmed and the endpoints are based on nominal concentrations (see table below).

**Analytical results:**

|  |  |  |  |
| --- | --- | --- | --- |
| **Specimen** | **Prothioconazole Content (µg/g)** | **Expected Prothioconazole Content (µg/g)** | **Prothioconazole Recovery (%)** |
| S19-20762-D3-T1-A | 19.96 | 20.29 | 98.37 |
| S19-20762-D3-T5-A | 320.96 | 324.67 | 98.86 |
| S19-20762-D4-T1-A | 20.46 | 20.29 | 100.83 |
| S19-20762-D4-T5-A | 325.77 | 324.67 | 100.34 |
| S19-20762-D5-T1-A | 17.99 | 20.29 | 88.66 |
| S19-20762-D5-T5-A | 311.03 | 324.67 | 95.80 |
| S19-20762-D6-T1-A | 17.65 | 20.29 | 86.99 |
| S19-20762-D6-T5-A | 306.20 | 324.67 | 94.31 |
| S19-20762-D6-C-A | < LOQ | – | – |
| S19-20762-D6-St-A | 4042.92 µg/mL | 3571.31.00 | 113.21 |



|  |
| --- |
| Main results about mortality are shown in the tables below.  On day 8, one individual in treatment T5 (1624.05 mg t.i./L diet) was observed with uneaten food. That individual was recorded as dead from the D15 assessment. At the end of the test, in the final assessment of the emergence on day 22, no emerged bees were recorded as being affected (i.e. malformation). |

**The Effects of SAP250F (Prothioconazole 250 g/L EC) on Honey Bee (*Apis mellifera*L.) Larvae from Repeated Exposure.**

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Treatment Group** | **Concentration** | **Cumulative Mortality [%]** | | | | | | | **Emergence** |
| **[mg t.i./L diet]** | **D4** | **D5** | **D6** | **D7** | **D8** | **D15** | **D22** | **[%]** |
| Control | -- | 0.00 | 0.00 | 2.08 | 2.08 | 4.17 | 22.92 | 27.08 | 72.92 |
| Test item SAP250F | 101.50 | 2.08 | 2.08 | 2.08 | 2.08 | 4.17 | 27.08 | 27.08 | 72.92 |
| 203.01 | 2.08 | 6.25 | 8.33 | 8.33 | 10.42 | 41.67 | 41.67 | 58.33 |
| 406.01 | 0.00 | 0.00 | 0.00 | 0.00 | 6.25 | 39.58 | 39.58 | 60.42 |
| 812.03 | 0.00 | 0.00 | 0.00 | 0.00 | 8.33 | 39.58 | 39.58 | 60.42 |
| 1624.05 | 2.08 | 2.08 | 8.33 | 12.50 | 18.75 | 56.25 | 62.50 | 37.50 |
| Reference item (Dimethoate) | 52.8 ᵃ | 20.83 | 31.25 | 58.33 | 64.58 | 68.75 | 97.92 | 97.92 | 2.08 |

t.i.: test item

ᵃ mg Dimethoate/L diet.

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Treatment Group** | **Concentration** | **Corrected Mortality [%]ᵃ** | | | | | | |
| **[mg t.i./L diet]** | **D4** | **D5** | **D6** | **D7** | **D8** | **D15** | **D22** |
| Test item SAP250F | 101.50 | 2.08 | 2.08 | 0.00 | 0.00 | 0.00 | 5.41 | 0.00 |
| 203.01 | 2.08 | 6.25 | 6.38 | 6.38 | 6.52 | 24.32 | 20.00 |
| 406.01 | 0.00 | 0.00 | -2.13 | -2.13 | 2.17 | 21.62 | 17.14 |
| 812.03 | 0.00 | 0.00 | -2.13 | -2.13 | 4.35 | 21.62 | 17.14 |
| 1624.05 | 2.08 | 2.08 | 6.38 | 10.64 | 15.22 | 43.24 | 48.57 |
| Reference item (Dimethoate) | 52.8 ᵇ | 20.83 | 31.25 | 57.45 | 63.83 | 67.39 | 97.30 | 97.14 |

t.i.: test item

ᵃ Corrected for control mortality according Abbott modified by Schneider-Orelli.

ᵇ mg Dimethoate/L diet.

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| The NOEC for emergence on D22 was statistically determined to be 184.55 mg t.i./kg diet (step-down Cochran-Armitage test, α = 0.05, one-sided greater, equivalent to 203.01 mg t.i./L diet). The NOED, based on the supplied dose corresponding to the NOEC, was determined to be 28.42 µg t.i./larva (6.25 µg prothioconazole/larva). However, the corrected mortality for this treatment reached 20.00 %, so there can be concluded that an empirical NOEC for D22 was determined to be 92.28 mg t.i./kg diet, equivalent to 101.50 mg t.i./L diet and corresponding to 14.21 µg t.i./larva (3.12 µg prothioconazole/larva).  No statistically significant concentration/response was found (Probit analysis, p(F) > 0.05), so no reliable values for EC10/ED10 or EC20/ED20 could be determined.  EC50/ED50 values were estimated to be 1023.51 mg t.i./kg diet (with confidence limits 866.32 ‑ 1209.22 mg t.i./kg diet, Spearman-Kärber method, equivalent to 930.46 mg ti/L diet with confidence limits 787.56 – 1099.29 mg t.i./L diet) and 157.62 µg t.i./larva (with confidence limits 133.41 – 186.22 µg t.i./larva, based on a cumulative volume of diet of 140 µL/larva and a density of the diet of 1.1 g/mL; equivalent to 34.66 µg prothioconazole/larva with confidence limits 29.34 ‑ 40.95 µg a.i./larva ), respectively. |

Conclusion

The toxicity of SAP250F (Prothioconazole 250 g/L EC): to honey bee larvae after repeated exposure was tested under laboratory conditions over a period of 22 days.

All validity criteria were met and sensitivity of the test organisms was confirmed. Accordingly, the study was deemed valid.

The actual mean concentrations of prothioconazole in samples taken from test item feeding solutions were in the range from 80 to 120 % of the nominal concentrations, therefore the results are based on the nominal concentrations.

The 22-day NOEC on emergence was estimated to be 184.55 mg t.i./kg diet, or 203.01 mg t.i/L diet.

The NOED, based on the supplied dose corresponding to the NOEC, was determined to be 28.42 µg t.i./larva, equivalent to 6.25 µg prothioconazole/larva.

Empirical NOEC/NOED were estimated to be 92.28 mg t.i./kg diet (101.50 mg ti/L diet) and 14.21 µg  t.i./larva (3.12 µg t.i./larva), respectively.

No reliable values for EC10/ED10 or EC20/ED20 could be determined. EC50/ED50 values were estimated to be 1023.51 [866.32 – 1209.22] mg t.i./kg diet (930.46 [ 787.56 – 1099.29] mg t.i./L diet) and 157.62 [133.41 – 186.22] µg t.i./larva (34.66 [ 29.34-40.95] µg a.i./larva), respectively.

No affected emerged bees (i.e. malformation) were observed at the D22 emergence assessment.

**Endpoints:**

| **Endpoint** | **Value** |
| --- | --- |
| Statistical NOEC | 184.55 mg t.i./kg diet (203.01 mg t.i/L diet) |
| NOEDᵃ | 28.42 µg t.i./larva (6.25 µg prothioconazole/larva) |
| Empirical NOEC | 92.28 mg t.i./kg diet diet (101.50 mg ti/L diet) |
| Empirical NOED | 14.21 µg t.i./larva (3.12 µg t.i./larva), |
| EC10, EC20 | n.d. |
| ED10, ED20 | n.d. |
| EC50 [c.l] | 1023.51 [866.32 – 1209.22] mg t.i./kg diet  (930.46 [ 787.56 – 1099.29] mg t.i./L diet) |
| ED50 [c.l] | 157.62 [133.41 – 186.22] µg t.i./larva  (34.66 [ 29.34-40.95] µg a.i./larva) |

n.d.: not determined; t.i: test item; c.l.:confidence limits.

ᵃ Consumed dose for the treatment corresponding to the Statistical No Observed Effect Concentration (NOEC).

Validity criteria

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| Control | The cumulative larval mortality from day 3 (D3) until day 8 (D8) was ≤ 15 % across all replicates (actual mean value 4.17 %).  On day 22 (D22) the adult emergence rate was ≥ 70 % across all replicates (actual mean value 72.92 %). |
| Reference | The cumulative larval mortality was ≥ 50 % across all replicates on day 8 (D8) (actual mean value 68.75 %). |

* + - 1. KCP 10.3.1.4 Sub-lethal effects
      2. KCP 10.3.1.5 Cage and tunnel tests
      3. KCP 10.3.1.6 Field tests with honeybees
  1. KCP 10.4 Effects on non-target soil meso- and macrofauna
     1. KCP 10.4/01 Study 1

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| Comments of zRMS: | The studies are considered acceptable. The validity criteria were met.  Control Mortality: 18.3 % at day 7  Reference Item Mortality: 100.0 % corrected mortality at day 7  Control Reproduction:6.1 eggs per female for the second week  **Agreed endpoints:**  LR50 of SAP250F >1360 mL product/ha in 200 L water/ha.  No effect on reproduction up to and including 1360 mL product/ha. |

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| **Reference:** | **KCP 10.4/01, Moll, M. (2019)** |
| Report | SAP250F: Effects on the predatory mite Typhlodromus pyri, extended laboratory study – Dose response test. Moll, M., 2019, Ibacon Study No. 130811062. |
| Guideline(s): | Yes   * Blümel et al. 2000 * Oomen 1988 |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |
| Duplication  (if vertebrate study) | No |

Objective

The purpose of this study was to produce a dose-response curve for mortality effects seen over 7 days of exposure. From these the LR50 value was estimated. The effect of SAP250F on the predatory mite Typhlodromus pyri was measured via contact on treated leaf surfaces compared to a water treated control and to a reference item. Additionally, an assessment for significant sublethal effects (reproduction assessment) was done. Typhlodromus pyri is recommended as one of the most sensitive standard species for non-target arthropod regulatory testing for plant protection products (Candolfi et al., 2001).

Materials and methods

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| Test Item: | SAP250F; batch no.: R-DAA; content of a.s.: 257 g/L Prothioconazole. |
| Test Species: | Predatory mite *(Typhlodromus pyri),* protonymphs less than 24 hours old; source: Katz Biotech AG, Baruth, Germany. |
| Test Design: | This study encompassed 7 treatment groups (5 dose rates of the test item, control, reference item) with 6 replicates each containing 10 mites. The mites were exposed to dried residues on treated leaf surfaces (bean leaves). Survival of the mites was assessed after 3 and 7 days. For the reproduction assessment surviving mites from the control and from all test item groups where the corrected mortality was < 50 % were sexed and the number of eggs per females was recorded on 3 assessment days within one week. |
| Endpoints: | Mortality after 7 days of exposure; LR50: lethal rate producing 50 % mortality. Additionally, reproduction capacity for all variants with less than 50 % corrected mortality. |
| Reference Item: | Perfekthion (nominal: 400 g dimethoate/L). |

Results and discussions

Table 1. Mortality and reproduction of *Typhlodromus pyri*

|  | **Rate 1)  [mL/ha]** | **Mortality 2)  [%]** | | **Mortality corr. 3)  [%]** | **Reproduction 4)   [eggs/female]** | | **Effect on reproduction 5) [%]** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Control |  | 18.3 |  | -- | 6.1 |  | -- |
| SAP250F | 85.0 | 11.7 | n.s. | -8.2 | 8.0 | n.s. | -31.8 |
| SAP250F | 170 | 15.0 | n.s. | -4.1 | 7.1 | n.s. | -18.0 |
| SAP250F | 340 | 21.7 | n.s. | 4.1 | 4.5 | n.s. | 26.0 |
| SAP250F | 680 | 6.7 | n.s. | -14.3 | 4.2 | n.s. | 30.6 |
| SAP250F | 1360 | 21.7 | n.s. | 4.1 | 5.3 | n.s. | 11.8 |
| Endpoint | | | | | | | |
| LR50: > 1360 mL product/ha  EC 50 > 1360 mL product/ha | | | | | | | |

1) Application rate in 200 L water/ha

2) Mortality: after 7 days of exposure to spray residues on leaf surfaces (Bonferroni-Holm Fisher’s Exact Test, α = 0.05; n.s. = not significant)

3) Corrected mortality according to Abbott and improvements by Schneider-Orelli; negative values indicate better survivorship compared to control

4) Reproduction: mean number of eggs/female, (Williams t-test, α = 0.05; n.s. = not significant)

5) Calculated on the exact raw data; negative values indicate better performance compared to the control

The reference item applied at a rate of 40 mL Perfekthion/ha produced a statistically significant corrected mortality of 100.0 % after 7 days.

Conclusion

Under extended laboratory conditions the LR50 of SAP250F is estimated to be greater than 1360 mL product/ha in 200 L water/ha.

Reproduction of *Typhlodromus pyri* was assessed in the control and at all dose rates. There was no effect on reproduction up to and including 1360 mL product/ha.

Validity criteria

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| --- | --- |
| Control Mortality: | 18.3 % at day 7, validity criterion was met |
| Reference Item Mortality: | 100.0 % corrected mortality at day 7, validity criterion was met |
| Control Reproduction: | 6.1 eggs per female for the second week, validity criterion was met |

* + 1. KCP 10.4/02 Study 2

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| --- | --- | --- | --- | --- | --- | --- | --- |
| Comments of zRMS: | The studies are considered acceptable. The validity criteria were met.   |  |  | | --- | --- | | Control Mortality: | 0.0 % | | Reference Item Mor | 96.7 % corrected mortality | | Control Reproduction Rate: | 46.0 mummies per female  No parasitoid produced zero values |   **Agreed endpoints:**  LR50 of SAP250F >1360 mL product/ha in 200 L water/ha.  There was no effect on reproduction up to and including 1360 mL product/ha compared to the control. |

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| --- | --- |
| **Reference:** | **KCP 10.4/02, Moll, M. (2019)** |
| Report | SAP250F: Effects on the parasitoid Aphidius rhopalosiphi, Extended Laboratory Study – Dose Response Test. Moll, M., 2019, Ibacon Study No. 130811002. |
| Guideline(s): | Yes   * Mead-Briggs et al. 2010 |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |
| Duplication  (if vertebrate study) | No |

Objective

The purpose of this study was to produce a dose-response curve for mortality effects seen over 48 h of exposure. From these the LR50 value was estimated. The effect of SAP250F on the parasitoid Aphidius rhopalosiphi was measured in the laboratory via contact on treated plant surfaces (exposure period), compared to a water treated control and to a reference item. Additionally, an assessment for sublethal effects on parasitisation activity of the female survivors (post-exposure period) was done. A. rhopalosiphi is recommended as one of the most sensitive standard species for non-target arthropod regulatory testing for plant protection products (Candolfi et al. 2001).

Materials and methods

Test Item: SAP250F; batch no.: R-DAA; content of a.s.: 257 g/L Prothioconazole.

Test Species: Parasitoid *(Aphidius rhopalosiphi),* adults not older than 48 hours; source: Katz Biotech AG, Baruth, Germany.

Test Design: This study encompassed 7 treatment groups (5 dose rates of the test item, control, reference item) with 6 replicates each containing 5 female parasitoids. The parasitoids were exposed to dried residues on treated plant surfaces (barley plants). Survival of the parasitoids was assessed after 2, 24 and 48 hours. At 48 hours, for treatment groups with < 50 % corrected mortality survived females were removed and their reproductive capacity was assessed by confining them individually over untreated barley plants infested with the host cereal aphids, *Rhopalosiphum padi*. The adult parasitoids were removed after 24 hours and the aphid-infested plants left for further 11 - 12 days before the numbers of aphid mummies that had developed were assessed.

Endpoints: Mortality of exposed parasitoids; LR50: lethal rate producing 50 % mortality after 48 h of exposure. Additionally reproductive capacity for female survivors was assessed.

Reference Item: Perfekthion (nominal: 400 g dimethoate/L).

Test Rates: Control, 85.0, 170, 340, 680 and 1360 mL product/ha and reference item. The reference item was applied at an application rate of 10.0 mL Perfekthion/ha. All treatments were applied in 400 L water/ha. The spraying dilutions were sprayed onto barley plants *via* laboratory spraying equipment, which were then air dried.

Test Conditions: Temperature: 19 - 21 °C; relative humidity: 69 - 72 % (acclimatisation and exposure period), 75 - 84 % (post-exposure period, within the test units); photoperiod: 16 h light : 8 h dark; light intensity: 610 - 890 lux (acclimatisation and exposure period), 1970 - 2100 lux (parasitisation period), 12050 - 15360 lux (post-parasitisation period).

Results and discussions

Table 1. Mortality and parasitisation efficiency of *Aphidius rhopalosiphi*

|  | **Rate 1)  [mL/ha]** | **Mortality 2)  [%]** | | **Mortality corr. 3)  [%]** | **Reproduction 4)   [mummies/female]** | | **Effect on reproduction 5) [%]** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Control | - | 0.0 |  | -- | 46.0 |  | -- |
| SAP250F | 85.0 | 0.0 | n.s. | 0.0 | 55.7 | n.s. | -21.3 |
| SAP250F | 170 | 0.0 | n.s. | 0.0 | 46.6 | n.s. | -1.3 |
| SAP250F | 340 | 0.0 | n.s. | 0.0 | 47.6 | n.s. | -3.6 |
| SAP250F | 680 | 0.0 | n.s. | 0.0 | 56.9 | n.s. | -23.7 |
| SAP250F | 1360 | 3.3 | n.s. | 3.3 | 53.4 | n.s. | -16.2 |
| Endpoint | | | | | | | |
| LR50: > 1360 mL product/ha  EC 50 > 1360 mL product/ha | | | | | | | |

1) Application rate in 400 L water/ha

2) Mortality: after 48 hours of exposure to spray residues on plant surfaces (Bonferroni-Holm Fisher’s Exact Test, α = 0.05; n.s. = not significant)

3) Corrected mortality according to Abbott and improvements by Schneider-Orelli

4) Reproduction: mean number of parasitised aphids/female (Dunnett’s t-test, α = 0.05; n.s. = not significant)

5) Calculated on the exact raw data; negative values indicate better performance compared to the control

The reference item applied at a rate of 10.0 mL Perfekthion/ha produced a statistically significant corrected mortality of 96.7 % after 48 hours.

Conclusion

Under extended laboratory conditions the LR50 of SAP250F is estimated to be greater than 1360 mL product/ha in 200 L water/ha.

No repellent effect of the test item was observed compared to the control. The settling rate of the parasitoids on the plants was > 30 % at all dose rates.

The reproductive capacity of *A. rhopalosiphi* was tested at all dose rates. There was no effect on reproduction up to and including 1360 mL product/ha compared to the control.

Validity criteria

|  |  |
| --- | --- |
| Control Mortality: | 0.0 %, validity criterion was met |
| Reference Item Mortality: | 96.7 % corrected mortality, validity criterion was met |
| Control Reproduction Rate: | − 46.0 mummies per female, validity criterion was met  − No parasitoid produced zero values, validity criterion was met |

* + 1. KCP 10.4/03 Study 3

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Comments of zRMS: | The studies are considered acceptable. The validity criteria were met.   |  |  | | --- | --- | | Control Mortality: | 20.0 %, validity criterion was met | | Reference Item Mortality: | 93.8 % corrected mortality, validity criterion was met | | Fecundity in the Control Group: | 24.7 eggs per female per day (mean number), validity criterion was met | | Fertility in the Control Group: | 98.5 % larval hatching rate (mean value), validity criterion was met |   **Agreed endpoints:**  The LR50 of SAP250F >1360 mL product/ha in 200 L water/ha.  There was no negative effect of the test item on reproductive performance of *C. carnea* up to and including 1360 mL product/ha. |

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| --- | --- |
| **Reference:** | **KCP 10.4/01, Moll, M. (2019)** |
| Report | SAP250F: Effects on the Lacewing Chrysoperla carnea, Extended Laboratory Study – Dose Response Test. Moll, M., 2019, Ibacon Study No. 130811047. |
| Guideline(s): | Yes   * Vogt et al. 2000; this guideline was modified for exposure of C. carnea on natural substrate. |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |
| Duplication  (if vertebrate study) | No |

Objective

The purpose of this study was to produce a concentration-response curve for mortality effects. From this the LR50 value was estimated. The effect of SAP250F on the larvae of the lacewing Chrysoperla carnea was determined in the laboratory by contacting substance treated leaf surfaces (exposure period) compared to a water treated control and a reference item. Additionally, an assessment for sublethal effects on reproduction of the survivors (reproduction) was made. Chrysoperla carnea is recommended as standard species for non-target arthropod regulatory testing for plant protection products (Candolfi et al. 2001).

Materials and methods

Test Item: SAP250F; batch-no.: R-DAA; content of a.s.: 257 g/L Prothioconazole.

Test Species: Lacewing (*Chrysoperla carnea*), 2 - 3 day old larvae; source: Katz Biotech AG, Baruth, Germany.

Test Design: This study encompassed 7 treatment groups (5 dose rates of the test item, control, reference item) with 40 replicates each containing 1 larva. The larvae were exposed to dried residues on treated leaf surfaces (beanleaves). Exposure lasted until pupae were transferred to the reproduction units for development of adults. Mortality checks were carried out regularly until hatching of adult lacewings. In addition, for the control and the test item treatment groups where the corrected mortality was < 50 %, the reproduction performance, *i.e.* egg deposition and larval hatching rate, was determined (2 checks/week, 24 hours period each check).

Endpoints: Larval and pupal mortality, LR50: lethal rate producing 50 % pre-imaginal mortality. Additionally reproductive capacity of female survivors.

Reference Item: Perfekthion (nominal: 400 g dimethoate/L).

Test Rates: Control, 85.0, 170, 340, 680 and 1360 mL product/ha and reference item. The reference item was applied at an application rate of 140 mL Perfekthion/ha. All treatments were applied in 200 L water/ha. The spraying dilutions were sprayed onto leaves *via* laboratory spraying equipment, which were then air dried.

Test Conditions: Temperature: 24 - 26 °C; relative humidity: 65 - 82 %; photoperiod: 16 h light : 8 h dark; light intensity: 1130 - 1340 lux.

Results and discussions

| Table 1. Pre-imaginal mortality and reproduction of *Chrysoperla carnea* | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Rate 1)  [mL/ha]** | **Mortality 2)  [%]** | | **Mortality corr. 3)  [%]** | **Reproduction  [eggs/female/day]** | **Larval hatching rate [%]** |
| Control | -- | 20.0 |  | -- | 24.7 | 98.5 |
| SAP250F | 85.0 | 20.0 | n.s. | 0.0 | 21.2 | 98.4 |
| SAP250F | 170 | 27.5 | n.s. | 9.4 | 19.4 | 95.3 |
| SAP250F | 340 | 25.0 | n.s. | 6.3 | 26.7 | 97.5 |
| SAP250F | 680 | 27.5 | n.s. | 9.4 | 28.0 | 96.4 |
| SAP250F | 1360 | 12.5 | n.s. | -9.4 | 17.7 | 99.0 |
| Endpoint | | | | | | |
| LR50: > 1360 mL product/ha  EC 50 > 1360 mL product/ha | | | | | | |

1) Application rate in 200 L deionised water/ha

2) Pre-imaginal mortality after exposure to spray residues on leaf surfaces  
(Bonferroni-Holm Fisher’s Exact Test, α = 0.05: n.s. = not significant)

3) Corrected pre-imaginal mortality according to Abbott and improvements by Schneider-Orelli; negative value indicates better survivorship compared to control

The reference item applied at a rate of 140 mL Perfekthion/ha produced a statistically significant mortality of 95.0 % (93.8 % corrected mortality).

Conclusion

Under extended laboratory conditions the LR50 of SAP250F is estimated to be greater than 1360 mL product/ha in 200 L water/ha.

The reproductive capacity of *C. carnea* was tested at all dose rates. Reproduction was > 15 eggs per female per day and the mean hatching rate was > 70 % at all dose rates. This indicates that there was no negative effect of the test item on reproductive performance of *C. carnea* up to and including 1360 mL product/ha.

Validity criteria

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| --- | --- |
| Control Mortality: | 20.0 %, validity criterion was met |
| Reference Item Mortality: | 93.8 % corrected mortality, validity criterion was met |
| Fecundity in the Control Group: | 24.7 eggs per female per day (mean number), validity criterion was met |
| Fertility in the Control Group: | 98.5 % larval hatching rate (mean value), validity criterion was met |

* + 1. KCP 10.4.1 Earthworms
       1. KCP 10.4.1.1 Earthworms - sub-lethal effects
          1. KCP 10.4.1.1/01 Study 1

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Study Comments: KCP 10.4.1.1/01 | The studies are considered acceptable. The validity criteria were met.   |  |  | | --- | --- | | Control Mortality: | Control mortality 1.3% | | Reproduction of Control: | The number of juvenile earthworms per replicate was 143 to 185. | | Coefficient of Variation of Reproduction in Control: | 8.0% |   **Agreed endpoints:**  The NOECmortality and weight changes ≥42.1 mg test item/kg soil, *i.e.* the highest concentration tested.  The LOEC mortality and weight changes >42.1 mg test item/kg soil.  The LC50 >42.1 mg test item/kg soil.  The NOEC reproduction = 21.1 mg test item/kg soil.  The LOEC reproduction =42.1 mg test item/kg soil.  The EC50 >42.1 mg test item/kg soil. |

|  |  |
| --- | --- |
| **Reference:** | **KCP 10.4.1.1/01, Straube, D. (2019)** |
| Report | SAP250F: Effects on reproduction and growth of Earthworms Eisenia Andrei in artificial soil. Straube, D., 2019, Ibacon Study No. 130811022. |
| Guideline(s): | Yes   * - OECD, Guideline for the testing of chemicals No. 222, Earthworm, Reproduction Test (adopted July 29, 2016) * - ISO-Guideline 11268-2, Soil quality - Effects of pollutants on earthworms - Part 2: Determination of effects on reproduction of Eisenia fetida/Eisenia andrei, International Organization for Standardization, 2012. |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |
| Duplication  (if vertebrate study) | No |

Objective

The purpose of this study was to investigate the effects of SAP250F on the mortality, body weight, feeding activity and reproduction of the adult earthworm Eisenia andrei.

Materials and methods

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| Test Item: | SAP250F; batch no.: R-DAA; content of a.i.: Prothioconazole: 250 g/L (nominal), 257 g/L (analytical) |
| Test Species: | Earthworm (*Eisenia andrei*), adult earthworms (with clitellum and weight range 300 to 587 mg), approximately7 months old, source: from an in-house culture. |
| Test Design: | 56-day test in treated artificial soil prepared according to OECD 222; different concentrations of the test item were incorporated into the soil; 6 treatment groups (5 test item concentrations, control); 4 replicates for the test item treatments and 8 replicates for the control with 10 earthworms each.  Assessment of adult earthworm mortality, behavioural effects and biomass development was carried out after 28 days exposure of adult earthworms in treated artificial soil. Reproduction rate (number of offspring) was assessed after additional 28 days (assessed 56 days after application). |
| Endpoints: | Mortality, weight change, feeding activity and reproduction rate were determined. |
| Reference Item: | Carbendazim 600 g/L SC (600 g/L nominal). The effects of the reference item were investigated in a separate study. |
| Test Concentrations: | Control, 2.63, 5.26, 10.5, 21.1 and 42.1 mg SAP250F/kg soil[[5]](#footnote-5). |
| Test Conditions: | Artificial soil according to OECD 222; initial pH 5.7, pH at experimental end 5.9 to 6.0; water content 29.0% to 30.8% (50.1% to 53.0% of maximum water holding capacity, WHC) at experimental start and 31.8% to 33.7% (54.8% to 58.2% of the maximum WHC) at experimental end; temperature: within the range of 18 °C to 22 °C; photoperiod: 16 h light : 8 h dark, light intensity: within the range of 400 lux to 800 lux. |
| Statistics: | Standard procedures, Fisher’s Exact Test (mortality), Dunnett’s t-test (body weight changes), Williams t-test (reproduction). |

Results and discussions

All study validity criteria were met.

No mortality was observed in any test item treatment group. One worm died at the control (1.3%).

The body weight changes of the earthworms after 4 weeks exposure to SAP250F were not statistically significantly different compared to the control up to and including the highest test concentration of 42.1 mg test item/kg soil (Dunnett’s t-test, α = 0.05, one-sided smaller).

The reproduction rates were not statistically significantly different compared to the control up to and including the test concentration of 2.11 mg test item/kg soil (Williams t-test, α = 0.05, one-sided smaller). At the test concentration of 42.1 mg test item/kg soil, the reproduction was statistically significantly reduced compared to the control. No behavioural abnormalities were observed in any of the treatment groups. The feeding activity in all the treated groups was comparable to the control (see Table 1).

| Table 1. Effect of SAP250F on earthworms (*Eisenia andrei*) in a 56-day reproduction study | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **SAP250F [mg test item/kg soil]** | **Control** | **2.63** | **5.26** | **10.5** | **21.1** | **42.1** |
| Mortality (day 28) [%] | 1.3 | 0 | 0 | 0 | 0 | 0 |
| Statistical Significance 1) | - | n.s. | n.s. | n.s. | n.s. | n.s. |
| Body weight change (day 28) [%] | 35.8 | 30.6 | 37.4 | 31.4 | 38.0 | 36.3 |
| Statistical Significance 2) | - | n.s. | n.s. | n.s. | n.s. | n.s. |
| Mean No. of juveniles (day 56) | 174 | 204 | 145 | 187 | 177 | 142 |
| Statistical Significance 3) | - | n.s. | n.s. | n.s. | n.s. | \* |
| Reproduction in [%] of control (day 56) | - | 118 | 83 | 108 | 102 | 82 |
| Food consumption [g] | 25.0 | 25.0 | 25.0 | 25.0 | 25.0 | 25.0 |
|  | **Endpoints [mg test item/kg soil]** | | | | | |
| NOEC (day 28 mortality) | ≥42.1 | | | | | |
| LOEC (day 28 mortality) | >42.1 | | | | | |
| LC50 4) | >42.1 | | | | | |
| NOEC (day 28 weight) | ≥42.1 | | | | | |
| LOEC (day 28 weight) | >42.1 | | | | | |
| NOEC (day 56 reproduction) | 21.1 | | | | | |
| LOEC (day 56 reproduction) | 42.1 | | | | | |
| EC50 4) | >42.1 | | | | | |

The results represent rounded values calculated on the exact raw data.  
n.s. = not significantly different compared to the control \* = significantly different compared to the control  
1) Fisher’s Exact Test, α = 0.05, one-sided greater 2) Dunnett´s t-test, α = 0.05, one-sided smaller  
3) Williams t-test, α = 0.05, one-sided smaller 4) estimated value - = not applicable

Conclusion

In an earthworm reproduction and growth study with SAP250F the No Observed Effect Concentration (NOEC) for mortality and weight changes of the earthworm *Eisenia andrei* was determined to be ≥42.1 mg test item/kg soil, *i.e.* the highest concentration tested. The LOEC for mortality and weight changes was estimated to be >42.1 mg test item/kg soil. The LC50 was estimated to be >42.1 mg test item/kg soil. The NOEC for reproduction was determined to be the concentration of 21.1 mg test item/kg soil. The LOEC for reproduction was determined to be 42.1 mg test item/kg soil. The EC50 was estimated to be >42.1 mg test item/kg soil.

**Reference Item Test:**

In the most recent test with the reference item Carbendazim 600 g/L SC (performed under ibacon Study No. 105684022 from June to September 2018), there were statistically significant effects on reproduction at a concentration of 1.00 mg carbendazim/kg soil and higher, which is in line with the guideline OECD 222 (effects should be observed between 1 and 5 mg carbendazim/kg soil). The EC50 for reproduction was calculated as 0.94 mg carbendazim/kg soil. The results are shown in Appendix 2.

Validity criteria

|  |  |
| --- | --- |
| Control Mortality: | Control mortality was 1.3% and so this validity criterion was met. |
| Reproduction of Control: | The number of juvenile earthworms per replicate was 143 to 185 and so this validity criterion was met. |
| Coefficient of Variation of Reproduction in Control: | Was 8.0% and so this validity criterion was met. |

* + - 1. KCP 10.4.1.2 Earthworms - field studies
    1. KCP 10.4.2 Effects on non-target soil meso- and macrofauna (other than earthworms)
       1. KCP 10.4.2.1 Species level testing
       2. KCP 10.4.2.2 Higher tier testing
  1. KCP 10.5 Effects on soil nitrogen transformation
  2. KCP 10.6 Effects on terrestrial non-target higher plants
     1. KCP 10.6.1 Summary of screening data
     2. KCP 10.6.2 Testing on non-target plants
        1. Study 1

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study Comments: | The studies is considered acceptable. The validity criteria were met.   |  |  | | --- | --- | | Germination Rate of the Control Seeds: | 80 -100%, validity criterion was met. | | Mean Survival of Emerged Control Seedlings: | 100%, validity criterion was met. | | Growth and Morphology of the Control Seedlings: | The control seedlings exhibited no visible phytotoxic effects and the plants exhibited only normal variation in growth and morphology for that particular species; validity criterion was met. |   **Agreed endpoints:**   |  |  |  |  | | --- | --- | --- | --- | |  | NOER | LOER | Statistical | |  | [L product/ha] | | Analysis | | *Brassica oleracea* | ≥ 1.6 | > 1.6 | n.s1 | | *Helianthus annuus* | ≥ 1.6 | > 1.6 | n.s1 | | *Glycine max* | ≥ 1.6 | > 1.6 | n.s1 | | *Cucumis sativus* | ≥ 1.6 | > 1.6 | n.s1 | | *Allium cepa* | ≥ 1.6 | > 1.6 | n.s1 | | *Lolium perenne* | ≥ 1.6 | > 1.6 | n.s1 |   Results represent nominal values  1 pair-wise comparison Student t-test, α = 0.05  n.s.: no significant difference between control and test rate  Phytotoxic effects observed were growth reduction and deformation of the leaves for *Helianthus annuus* (5%), growth reductionand deformation of the stems for *Glycine max* (18%), growth reduction for *Allium cepa* (1%) and necrosis for *Brassica oleracea* (4%). |

|  |  |
| --- | --- |
| **Reference:** | **KCP 10.6.2/01, Stürtz, S., Kowalczyk, F. (2019)** |
| Report | SAP250F: Effects on Terrestrial (Non-Target) Plants: Seedling Emergence and Seedling Growth Test. Stürtz, S., Kowalczyk, F., 2019, Ibacon Study No. 130811086. |
| Guideline(s): | Yes   * OECD Guideline for the Testing of Chemicals No. 208 “Terrestrial Plant Test: Seedling Emergence and Seedling Growth Test” (adopted July 19, 2006) |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |
| Duplication  (if vertebrate study) | No |

Objective

Non-target plant phytotoxicity data are routinely used to conduct ecological risk assessments for the registration of pesticides.

The purpose of this study was to determine a possible effect of the test item on the seedling emergence and seedling growth of six non-target plant species representing six plant families. Parameters measured were plant fresh weight, phytotoxicity, germination and mortality.

Materials and methods

|  |  |
| --- | --- |
| Test Item: | SAP250F; batch code: R-DAA; content of a.s.: 246.4 g/L prothioconazole (nominal: 250 g/L prothioconazole). |
| Test Species and Rates: | Six plant species from six different plant families were tested: *Brassica oleracea, Helianthus annuus, Glycine max, Cucumis sativus, Allium cepa, Lolium perenne.*  The following rate was tested: 1.6 L product/ha. |
| Test Design: | On the day after sowing the test item was sprayed in 150 L/ha of deionised water onto the soil. At least 20 seeds were tested per rate and species. The exposure time was 14 or 21 days after 50% germination in the control depending on the growth of the seedlings. The concentration of the active ingredient in the stock solution was verified analytically. |
| Endpoints: | NOER based on fresh weight or germination.  Observation of germination, mortality and phytotoxicity. |
| Test Conditions: | The study was performed in a growth chamber. Exposure conditions were as follows:  Mean temperature was 21.6 °C (16.6 °C to 26.6 °C). Mean humidity was 63% (41% to 94%). Photoperiod: 16 hours light / 8 hours dark. Mean light intensity during the day was 288 µE/m2/s (201 µE/m2/s to 480 µE/m2/s). |

Results and discussions

Table 1. Summary of effect rates (based on fresh weight/germination)

|  |  |  |  |
| --- | --- | --- | --- |
|  | NOER | LOER | Statistical |
|  | [L product/ha] | | Analysis |
| *Brassica oleracea* | ≥ 1.6 | > 1.6 | n.s1 |
| *Helianthus annuus* | ≥ 1.6 | > 1.6 | n.s1 |
| *Glycine max* | ≥ 1.6 | > 1.6 | n.s1 |
| *Cucumis sativus* | ≥ 1.6 | > 1.6 | n.s1 |
| *Allium cepa* | ≥ 1.6 | > 1.6 | n.s1 |
| *Lolium perenne* | ≥ 1.6 | > 1.6 | n.s1 |

Results represent nominal values

1 pair-wise comparison Student t-test, α = 0.05

n.s.: no significant difference between control and test rate

Conclusion

SAP250F was tested for effects on seedling emergence and seedling growth of six plant species out of six different plant families.

The analytical recovery rate of the active ingredient prothioconazole in the stock solution was 107% of the nominal value.

All plant species showed a NOER in terms of fresh weight or germination of ≥ 1.6 L SAP250F/ha (400 g a.s./ha).

The germination rate was not statistically significantly reduced for any species tested*.*

No or no statically significant mortality was observed for any species tested.

Phytotoxic effects observed were growth reduction and deformation of the leaves for *Helianthus annuus* (5%), growth reductionand deformation of the stems for *Glycine max* (18%), growth reduction for *Allium cepa* (1%) and necrosis for *Brassica oleracea* (4%).

Validity criteria

|  |  |
| --- | --- |
| Germination Rate of the Control Seeds: | 80 -100%, validity criterion was met. |
| Mean Survival of Emerged Control Seedlings: | 100%, validity criterion was met. |
| Growth and Morphology of the Control Seedlings: | The control seedlings exhibited no visible phytotoxic effects and the plants exhibited only normal variation in growth and morphology for that particular species; validity criterion was met. |

* + - 1. Study 2

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study Comments: | The studies are considered acceptable. The validity criteria were met.   |  |  | | --- | --- | | Germination Rate of the Control Seeds: | 80 -100%, validity criterion was met. | | Mean Survival of Emerged Control Seedlings: | 100%, validity criterion was met. | | Growth and Morphology of the Control Seedlings: | The control seedlings exhibited no visible phytotoxic effects and the plants exhibited only normal variation in growth and morphology for that particular species; validity criterion was met. |   **Agreed endpoints:**  Effect rates (based on fresh weight)   |  |  |  |  | | --- | --- | --- | --- | |  | NOER | LOER | Statistical | |  | [L product/ha] | | Analysis | | *Brassica oleracea* | ≥ 1.6 | > 1.6 | n.s1 | | *Helianthus annuus* | ≥ 1.6 | > 1.6 | n.s1 | | *Glycine max* | ≥ 1.6 | > 1.6 | n.s1 | | *Cucumis sativus* | ≥ 1.6 | > 1.6 | n.s1 | | *Allium cepa* | ≥ 1.6 | > 1.6 | n.s1 | | *Lolium perenne* | ≥ 1.6 | > 1.6 | n.s1 |   Results represent nominal values  1 pair-wise comparison Student t-test, α = 0.05  n.s.: no significant difference between control and test rate  Phytotoxic effects observed were necrosis for *Brassica oleracea* (4%)*, Helianthus annuus* (4%)and *Glycine max* (3%).Necrosis and growth reduction were observed for *Cucumis sativus* (6%). |

|  |  |
| --- | --- |
| **Reference:** | **KCP 10.6.2/02, Stürtz, S., Kowalczyk, F. (2019)** |
| Report | SAP250F: Effects on Terrestrial (Non-Target) Plants: Vegetative Vigour Test. Stürtz, S., Kowalczyk, F., 2019, Ibacon Study No. 130811087. |
| Guideline(s): | Yes   * OECD Guideline for the Testing of Chemicals No. 227 "Terrestrial Plant Test: Vegetative Vigour Test" (adopted July 19, 2006) |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |
| Duplication  (if vertebrate study) | No |

Objective

The purpose of this study was to determine a possible effect of the test item on the vegetative vigour of six non-target plant species representing six plant families. Parameters measured were plant fresh weight, phytotoxicity and mortality.

Materials and methods

|  |  |
| --- | --- |
| Test Item: | SAP250F; batch code: R-DAA; content of a.s.: 246.6 g/L prothioconazole (nominal: 250 g/L prothioconazole). |
| Test Species and Rates: | Six plant species from six different plant families were tested: *Brassica oleracea, Helianthus annuus, Glycine max, Cucumis sativus, Allium cepa, Lolium perenne.*  The following rate was tested: 1.6 L product/ha. |
| Test Design: | The plants were grown until they had reached the 2 to 4 true leaf stage prior to dosing. Test rates were calculated for a water amount of 150 L/ha and were administered onto the plants using laboratory spraying equipment. At least 20 plants were tested per rate and species. The concentration of the active ingredient in the stock solution was verified analytically. The exposure time was 21 days. |
| Endpoints: | NOER based on fresh weight.  Observation of mortality and phytotoxicity. |
| Test Conditions: | The study was performed in a growth chamber.  Pre-application conditions were as follows:  Mean temperature was 21.3 °C (16.7 °C to 26.9 °C). Mean humidity was 70% (46% to 100%). Photoperiod: 16 hours light / 8 hours dark. Mean light intensity during the day was 239 µE/m2/s (202 µE/m2/s to 383 µE/m2/s).  Exposure conditions were as follows:  Mean temperature was 22.3 °C (16.6 °C to 26.6 °C). Mean humidity was 59% (41% to 85%). Photoperiod: 16 hours light / 8 hours dark. Mean light intensity during the day was 286 µE/m2/s (202 µE/m2/s to 490 µE/m2/s). |

Results and discussions

Table 1. Summary of effect rates (based on fresh weight)

|  |  |  |  |
| --- | --- | --- | --- |
|  | NOER | LOER | Statistical |
|  | [L product/ha] | | Analysis |
| *Brassica oleracea* | ≥ 1.6 | > 1.6 | n.s1 |
| *Helianthus annuus* | ≥ 1.6 | > 1.6 | n.s1 |
| *Glycine max* | ≥ 1.6 | > 1.6 | n.s1 |
| *Cucumis sativus* | ≥ 1.6 | > 1.6 | n.s1 |
| *Allium cepa* | ≥ 1.6 | > 1.6 | n.s1 |
| *Lolium perenne* | ≥ 1.6 | > 1.6 | n.s1 |

Results represent nominal values

1 pair-wise comparison Student t-test, α = 0.05

n.s.: no significant difference between control and test rate

Conclusion

SAP250F was tested for effects on the vegetative vigour using six plant species out of six different plant families.

The analytical recovery rate of the active ingredient prothioconazole in the stock solution was 107% of the nominal value.

All plant species showed a NOER in terms of fresh weight of 1.6 L SAP250F/ha (400 g a.s./ha).

No mortality was observed for any species tested.

Phytotoxic effects observed were necrosis for *Brassica oleracea* (4%)*, Helianthus annuus* (4%)and *Glycine max* (3%).Necrosis and growth reduction were observed for *Cucumis sativus* (6%).

Validity criteria

|  |  |
| --- | --- |
| Germination Rate of the Seeds: | 85 - 100%, validity criterion was met. |
| Mean Survival of Control Plants: | 100%, validity criterion was met. |
| Growth and Morphology of the Control Plants: | The control plants exhibited no visible phytotoxic effects and the plants exhibited only normal variation in growth and morphology for that particular species; validity criterion was met. |

* + 1. KCP 10.6.3 Extended laboratory studies on non-target plants
  1. KCP 10.7 Effects on other terrestrial organisms (flora and fauna)
  2. KCP 10.8 Monitoring data

1. Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters (EFSA Journal 2013;11(7):3290) [↑](#footnote-ref-1)
2. EPPO/OEPP (2010). Environmental risk assessment scheme for plant protection products, Chapter 10: Honeybees (PP 3/10(3)). Bulletin OEPP/EPPO Bulletin 40: 323-331. [↑](#footnote-ref-2)
3. EPPO/OEPP (2010). Environmental risk assessment scheme for plant protection products, Chapter 10: Honeybees (PP 3/10(3)). Bulletin OEPP/EPPO Bulletin 40: 323-331. [↑](#footnote-ref-3)
4. Agnès RORTAIS, Gérard ARNOLD, Marie-Pierre HALM, Frédérique TOUFFET-BRIENS (2005). Modes of honeybees exposure to systemic insecticides: estimated amounts of contaminated pollen and nectar consumed by different categories of bees. Apidologie 36 (2005) 71–83 [↑](#footnote-ref-4)
5. All concentrations are indicated per kg soil dry weight. [↑](#footnote-ref-5)