REGISTRATION REPORT

Part B

Section 6

Mammalian Toxicology

Detailed summary of the risk assessment

Product code: FHO04

Product name(s): Prothioconazole/Sulphur (50+625) SC, / Patton Supra

Chemical active substance(s): Prothioconazole 50 g/L, Sulphur 625 g/L

Central Zone

Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: UPL Holdings Coöperatief U.A.

Submission date: 31/05/2024

MS Finalisation date: November 2024 (initial Core Assessment)

February 2025 (final Core Assessment)

Version history

When	What
31 May 2024	Applicant version.
November 2024	Initial zRMS assessment The report in the dRR format has been prepared by the Applicant, therefore all comments, additional evaluations and conclusions of the zRMS are presented in grey commenting boxes. Minor changes are introduced directly in the text and highlighted in grey. Not agreed or not relevant information are ~~struck through~~ and shaded for transparency.
February 2025	Final report (Core Assessment updated following the commenting period) No additional information or assessments after the commenting period.

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Reviewer general comment:

This part of dossier (B6) summarizes data related to the toxicological profile and NDE assessment for the plant protection product Patton Supra (product code FHO04) containing the active substances Prothioconazole 50 g/L and Sulphur 625 g/L formulated as Suspension Concentrate. All information has been submitted to support registration according art. 33 of 1107/2009 in Poland also for zonal registration for which PL was designated zRMS. The intended use of the product is as a fungicide on wheat. The zRMS´s per-review all of the elements that are crucial for risk assessment and decision-making. Regarding evaluation of the toxicity profile of the product FHO04, in the absence of experimentally derived acute toxicity data for Patton Supra the Additivity Formula 3.1.3.6.1 has been used to classify a mixture based on acute toxicity estimates (ATE) or converted ATE (cATE) for each ingredient. (details of calculation are available in the Part C).

NDE assessment for operator, workers and B&R has been calculated using the EFSA calculator, on-line version 1.01 considering the worst-case exposure scenario to cover all the intended uses (highest application rate per application as well as the highest application rate per year with the shorter interval between each application). All NDE calculations provided for operator, workers and B&R resulting from use of PPP, considering all tasks according to the critical use(s), identify safe use of the product Patton Supra (product code FHO04).

6 Mammalian Toxicology (KCP 7)

6.1 Summary

Table 6.1-1: Information on FHO04

Product name and code	Prothioconazole/Sulphur (50+625) SC, 'Patton Supra' / code FHO04
Formulation type	SC
Active substance(s) (incl. content)	Prothioconazole 50 g/L + Sulphur 625 g/L
Function	Fungicide
Product already evaluated as the 'representative formulation' during the approval of the active substance(s)	No
Product previously evaluated in another MS according to Uniform Principles	No

* Information on the detailed composition of product code/name can be found in the confidential dRR Part C.

Justified proposals for classification and labelling

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

Table 6.1-2: Justified proposals for classification and labelling for FHO04 according to Regulation (EC) No 1272/2008

Hazard class(es), categories	Skin corrosion/irritation, Category 2
Hazard pictograms or Code(s) for hazard pictogram(s)	 GHS07
Signal word	Warning
Hazard statement(s)	H315 – Causes skin irritation
Precautionary statement(s)	P264 - Wash hands, forearms and face thoroughly after handling. ~~P273 – Avoid release to the environment.~~* P280 - ~~Wear eye protection, face protection~~, protective clothing, protective gloves. P302+P352 - IF ON SKIN: Wash with plenty of water. P332+P313 - If skin irritation occurs: Get medical advice/attention. P362+P364 - Take off contaminated clothing and wash it before reuse. ~~P391 – Collect spillage.~~* ~~P501 – Dispose of contents and container to hazardous or special waste collection point, in accordance with local, regional, national and/or international regulation~~. *
Additional labelling phrases	EUH401 - To avoid risks to human health and the environment, comply with the instructions for use. EUH208 - Contains 1,2-benzisothiazol-3(2H)-one; 1,2-benzisothiazolin-3-one. May produce an allergic reaction.

***zRMS Reviewer comment**: relevant Precautionary Statements has been mentioned in the Part A point 2.4.1 labelling information

Table 6.1-3: Summary of risk assessment for operators, workers, residents and bystanders for FHO04

	Result	PPE / Risk mitigation measures
Operators	Acceptable	Work wear (arms, body and legs covered) M/L and A ~~+ gloves~~
Workers	Acceptable	Work wear (arms, body and legs covered)
Residents	Acceptable	5 m buffer zone **or** 50% drift reduction technology
Bystanders	Acceptable	As addressed by resident risk mitigation measures

No unacceptable risk for operators, workers, residents and bystanders was identified when the product is used as intended and provided that the PPE/ risk mitigation measures stated in *zRMS Reviewer comment: relevant Precautionary Statements has been mentioned in the Part A point 2.4.1 labelling information

Table 6.1-3 are applied.

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

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

1	2	3	4	5	6	7	8	9	10			
Use-No.*	**Crops and situation (e.g. growth stage of crop)**	**F, Fn, Fpn G, Gn, Gpn or I ****	**Application**		**Application rate**		**PHI (d)**	**Remarks:** **(e.g. safener/synergist (L/ha))** **critical gap for operator, worker, resident or bystander exposure based on [Exposure model]**	**Acceptability of exposure assessment**			
			Method / Kind **(incl. application technique *****	**Max. number (min. interval between applications)** **a) per use** **b) per crop/ season**	**Max. application rate kg as/ha** **a) a.s. 1 (prothioconazole)** **b) a.s. 2 (sulphur)**	**Water L/ha** **min / max**			**Operator**	**Worker**	**Residents**	**Bystander**
1.	Winter wheat (TRZAW), Spring wheat (TRZAS), Durum wheat† (TRZDU), Spelt† (TRZSP), Winter triticale (TTLWI), Spring triticale (TTLSO)TTLSS	F	Foliar Spray	a) 1 b) 2	a) 0.2 + 2.5 b) 0.4 + 5	100 - 400	35	N/A				

† Minor crope according to Article 51

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

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

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

Explanation for column 10 “Acceptability of exposure assessment”

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

Data gaps

Noticed data gaps are:

- none.

6.2 Toxicological Information on Active Substance(s)

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

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

	Prothioconazole	**Prothioconazole-desthio**	**Sulphur**
Common Name	Prothioconazole	Prothioconazole-desthio	Sulphur
CAS-No.	178928-70-6	N/A	7704-34-9
Classification and proposed labelling			
With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended)	Hazard classes (s), categories: None Code(s) for hazard pictogram(s): None Signal word: Warning Hazard statement(s): None Precautionary statement(s): None	No harmonised classification according to Regulation (EC) 1272/2008	Hazard classes (s), categories: Skin Irrit, Cat. 2 Code(s) for hazard pictogram(s):GHS07 Signal word: Warning Hazard statement(s): H315 Precautionary statement(s): None
Additional C&L proposal	Not applicable	Not applicable	Not applicable
Agreed EU endpoints			
AOEL systemic	0.2 mg/kg bw/d (with a 100-fold correction factor, no correction for oral absorption)	0.01 mg/kg (with a 100-fold correction factor)	26 mg/kg bw/d* (average background intake value)
Reference	EFSA Conclusion 2007	EFSA Conclusion 2007	EFSA Conclusion 2008
Conditions to take into account/critical areas of concern with regard to toxicology			
According to the Review Report and EFSA conclusion for active substance	The operator safety in spray applications. Conditions of use shall include adequate protective measures. The metabolite prothioconazole-desthio is more toxic than prothioconazole in the rat and rabbit developmental studies.	None	None

*Based on overall intake: 1.6 g/person/day, US National Academy of Medicine (EFSA Scientific Report (2008) 221, 9-70)

6.3 Toxicological Evaluation of Plant Protection Product

A summary of the toxicological evaluation for FHO04 is given in the following tables. Full summaries of studies on the product that have not been previously considered within an EU peer review process are described in detail in Appendix 2.

Table 6.3-1: Summary of evaluation of the studies on acute toxicity including irritancy and skin sensitisation for FHO04

Type of test, species, model system (Guideline)	**Result**	**Acceptability**	**Classification (acc. to the criteria in Reg. 1272/2008)**	**Reference**
LD_{50} oral	> 2000 mg/kg bw	Yes	None	Calculation method (refer Part C)
LD_{50} dermal	> 2000 mg/kg bw	Yes	None	Calculation method (refer Part C)

LC_{50} inhalation	> 5 mg/L	Yes	None	Calculation method (refer Part C)
Skin irritation	Irritant	Yes	**H315**	Calculation method (refer Part C)
Eye irritation	Non-irritant	Yes	None	Calculation method (refer Part C)
Skin sensitisation	Non-sensitising	Yes	None	Calculation method (refer Part C)
Supplementary studies for combinations of plant protection products	No data – not required	--	--	

Table 6.3-2: Additional toxicological information relevant for classification/labelling of FHO04

	Substance (concentration in product, % w/w)	**Classification of the substance (acc. to the criteria in Reg. 1272/2008)**	**Reference**	**Classification of product (acc. to the criteria in Reg. 1272/2008)**
Toxicological properties of active substance(s) (relevant for classification of product)	No data – not required – please refer to the Part C.			
Toxicological properties of non-active substance(s) (relevant for classification of product)	~~No data – not required – please refer to the Part C.~~ EUH208 - Contains 1,2-benzisothiazol-3(2H)-one; 1,2-benzisothiazolin-3-one. May produce an allergic reaction.			
Further toxicological information	No data – not required			

6.4 Toxicological Evaluation of Groundwater Metabolites

All metabolite concentrations are predicted to stay below 0.1 µg/L – no groundwater assessment is required.

6.5 Dermal Absorption (KCP 7.3)

A summary of the dermal absorption rates for the active substances in FHO04 are presented in the following table.

Table 6.5-1: Dermal absorption rates for active substances in FHO04

	Prothioconazole		**Prothioconazole-desthio**		**Sulphur**	
	Value	**Reference**	**Value**	**Reference**	**Value**	**Reference**
Concentrate	0.1%	KCP 7.3/01, Spa, S, 20202 Report No. 20321440. New study reported in Appendix 2	Not applicable*	KCP 7.3/01, Spa, S, 20202 Report No. 20321440. New study reported in Appendix 2	0.16%	KCP 7.3/02, [redacted], 20202 Report No. 20321446. New study reported in Appendix 2
Dilution (1:100) 6.25 g/L	3.3%		13%		1.7%	
Dilution (1:400) 1 g/L	3.3%		30%		2.4%	

* Prothioconazole-desthio is a product of degradation and is not present in the concentrate.

6.5.1 Justification for proposed values - prothioconazole

Proposed dermal absorption rates for prothioconazole are based on dermal absorption studies on a formulation identical to FHO04. The study results are summarised in the following table. Full summaries of studies on the dermal absorption of FHO04 that have not previously been evaluated within an EU peer review process are described in detail in Appendix 2.

Table 6.5-2: Summary of the results of submitted dermal absorption studies for prothioconazole

Test	Concentrate	Spray dilution (1:100)	Spray dilution (1:400)	Formulation in study	Acceptability of study	Justification provided on representativity of study formulation for current product	Acceptability of justification	Reference
In vitro (human)	0.1%	3.3%	3.3%	FHO04	Yes	Not required	Justification accepted. Endpoint can be used for current product	[redacted], 2022

6.5.2 Justification for proposed values – prothioconazole-desthio

Proposed dermal absorption rates for prothioconazole-desthio are based on dermal absorption studies on a formulation identical to FHO04. The study results are summarised in the following table. Full summaries of studies on the dermal absorption of FHO04 that have not previously been evaluated within an EU peer review process are described in detail in Appendix 2.

Table 6.5-2: Summary of the results of submitted dermal absorption studies for prothioconazole-desthio

Test	Concentrate	Spray dilution (1:100)	Spray dilution (1:400)	Formulation in study	Acceptability of study	Justification provided on representativity of study formulation for current product	Acceptability of justification	Reference
In vitro (human)	Not applicable	13%	30%	FHO04	Yes	Not required	Justification accepted. Endpoint can be used for current product	[redacted], 2022

6.5.3 Justification for proposed values - sulphur

Proposed dermal absorption rates for sulphur are based on dermal absorption studies on a formulation identical to FHO04. The study results are summarised in the following table. Full summaries of studies on the dermal absorption of FHO04 that have not previously been evaluated within an EU peer review process are described in detail in Appendix 2.

Table 6.5-4: Summary of the results of submitted dermal absorption studies for sulphur

Test	Concentrate	Spray dilution (1:100)	Spray dilution (1:400)	Formulation in study	Acceptability of study	Justification provided on representativity of study formulation for current product	Acceptability of justification	Reference
In vitro (human)	0.16%	1.7%	2.4%	FHO04	Yes	Not required	Justification accepted. Endpoint can be used for current product	[redacted], 2022

6.6 Exposure Assessment of Plant Protection Product (KCP 7.2)

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

Product name and code	FHO04		
Formulation type	Suspension Concentrate (SC)		
Category	Fungicide		
Active substance(s) (incl. content)	**Prothioconazole** 50 g/L	**Sulphur** 625 g/L	**Prothioconazole-desthio** 45.34 g/L*
AOEL systemic	0.2 mg/kg bw/d	26 mg/kg bw/d**	0.01 mg/kg bw/d
Inhalation absorption	100%	100%	100%
Oral absorption	100%	100%	100%
Dermal absorption	Concentrate: 0.1% Dilution 1: 3.3% (1:100) Dilution 2: 3.3% (1:400) (Based on product (formulation)	Concentrate: 0.16% Dilution 1: 1.7% (1:100) Dilution 2: 2.4% (1:400) (Based on product (formulation)	Concentrate: Not applicable Dilution 1: 13% (1:100) Dilution 2: 30% (1:400) (Based on product (formulation)

*Based on the hypothetical and extreme assumption that 100% of prothioconazole is converted to prothioconazole-desthio, taking into account molar ratios (312.2/344.26)
**Based on overall intake: 1.6 g/person/day, US National Academy of Medicine (EFSA Scientific Report (2008) 221, 9-70)

6.6.1 Selection of critical use(s) and justification

The critical GAP used for the exposure assessment of the plant protection product is shown in Table 6.1-4. A list of all intended uses within the Northern zone is given in Part B, Section 0.

Justification

The intended use with the highest application rate has been used as the critical GAP for the exposure assessment.

Comments of zRMS:	NDE calculation (EFSA on-line model OPEX ver. 1.01) performed by the Applicant is acceptable and zRMS Reviewer agrees to the conclusions. The risk for operators is acceptable under conditions of intended uses and considering below mentioned risk mitigation measures such as Work wear (arms, body and legs covered) during M, L and A.

6.6.2 Operator exposure (KCP 7.2.1)

6.6.2.1 Estimation of operator exposure

A summary of the exposure model used for estimation of operator exposure to the active substances during application of FHO04 according to the critical use is presented in Table 6.6-2. The outcome of the estimation is presented in Table 6.6-3 (longer term exposure). Detailed calculations are in Appendix 3.

Table 6.6-2: Exposure models for intended uses

Critical use(s)	Field crops (max. 2 x 4 L product/ha)
Model(s)	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2022;20(1):7032 calculator version: 1.0.1 (2022)

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

		Prothioconazole	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
Application rate		2 x 0.2 kg a.s./ha	
Spray application (AOEM**;** 75th percentile) Body weight: 60 kg	Work wear (arms, body and legs covered) M/L and A	0.002	0.8
	Work wear (arms, body and legs covered) M/L and A + type of PPE/RPE	Not required	Not required

		Sulphur		Prothioconazole-desthio	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
Vehicle mounted, downward spraying, outdoor crops					
Application rate		2 x 2.5 kg a.s./ha		2 x 0.18 kg a.s./ha	
Spray application (AOEM**;** 75th percentile) Body weight: 60 kg	Work wear (arms, body and legs covered) M/L and A	0.01	0.04	0.003	32
	Work wear (arms, body and legs covered) M/L and A + gloves	Not required	Not required	Not required	Not required

6.6.2.2 Measurement of operator exposure

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

Comments of zRMS:	NDE calculation (EFSA on-line model OPEX ver. 1.01) performed by the Applicant is acceptable and zRMS Reviewer agrees to the conclusions. Exposure for workers (entry into a previously treated area or handling a crop according to the critical uses) is acceptable under conditions of intended uses considering below mentioned risk mitigation measures such as Work wear, (arms, body and legs covered) but no PPE is used.

6.6.3 Worker exposure (KCP 7.2.3)

6.6.3.1 Estimation of worker exposure

Table 6.6-4 shows the exposure model(s) used for estimation of worker exposure after entry into a previously treated area or handling a crop treated with FHO04 according to the critical use. Outcome of the estimation is presented in Table 6.6-5 (longer term exposure). Detailed calculations are in Appendix 3.

Table 6.6-4: Exposure models for intended uses

Critical use(s)	Field crops (max. 2 x 4 L product/ha)
Model	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2022;20(1):7032 calculator version: 1.0.1 (2022)

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

		Prothioconazole	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Field crops (max. 2 x 4 L product/ha) Inspection, irrigation Outdoor Work rate: 2 hours/day DT_{50}: 30 days DFR: 3 µg/cm^2/kg a.s./ha Interval between treatments: 14 days			
Number of applications and application rate		2 x 0.2 kg a.s./ha	
Body weight: 60 kg	Potential TC: 12500 cm^2/person/h	0.01	7.1
	Work wear (arms, body and legs covered) TC: 1400 cm^2/person/h	0.002	0.8
	Work wear (arms, body and legs covered) and gloves TC: 1250 cm^2/person/h	0.001	0.7

		Sulphur		Prothioconazole-desthio	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Field crops (max. 2 x 4 L product/ha) Inspection, irrigation Outdoor Work rate: 2 hours/day DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha Interval between treatments: 14 days					
Number of applications and application rate		2 x 2.5 kg a.s./ha		2 x 0.18 kg a.s./ha	
Body weight: 60 kg	Potential TC: 12500 cm²/person/h	0.09	0.4	0.05	**507**
	Work wear (arms, body and legs covered) TC: 1400 cm²/person/h	0.01	0.04	0.006	56.8
	Work wear (arms, body and legs covered) and gloves TC: 1250 cm²/person/h	0.009	0.04	0.005	50.7

6.6.3.2 Refinement of generic DFR value (KCP 7.2).

Not required.

6.6.3.3 Measurement of worker exposure

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

6.6.4 Resident and bystander exposure (KCP 7.2.2)

6.6.4.1 Estimation of resident and bystander exposure

No bystander risk assessment is required for PPPs that do not have significant acute toxicity or the potential to exert toxic effects after a single exposure. Exposure in this case will be determined by average exposure over a longer duration, and higher exposures on one day will tend to be offset by lower exposures on other days. Therefore, exposure assessment for residents also covers bystander exposure.

Table 6.6-6 shows the exposure model used for estimation of resident and bystander exposure to prothioconazole, sulphur, and prothioconazole-desthio. The outcome of the estimation is presented in Table 6.6-7 (acute bystander exposure). Detailed calculations are in Appendix 3. An acceptable risk to residents has been demonstrated for all components, with a buffer zone of 5 metres required to reduce resident exposure to prothioconazole-desthio.

Comments of zRMS:	Justification of waiving acute risk assessment discussed by the applicant is reliable thus, zRMS agrees to the conclusions. In the case of exposure to residents (children) calculated for prothioconazole-desthio, the additional RMM 5m buffer strip and 50% DRT (Drift reduction technology) proposed by the applicant have been accepted. However, it must be noted that when considering the 50% conversion factor from PTZ to PTZ-desthio, the mentioned RMM can be omitted. For the current registration process, the applicant proposed the worst-case scenario of 100% conversion, which was accepted by the Reviewer.

	Also no AAOEL has been set for all actives, therefore in line with *EFSA, 2022. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment of plant protection products. EFSA, Journal 2022;20(1):7032, 134 pp*. exposure assessment for residents also covers bystander exposure refer point 2.3.1 Step 1; Table 2. Risk for bystanders and residents is acceptable under conditions of intended uses.

Table 6.6-6: Exposure models for intended uses

Critical use(s)	Field crops (max. 2 x 4 L product/ha)
Model	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2022;20(1):7032 calculator version: 1.0.1 (2022)

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

		Prothioconazole	
Model data		**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Field crops (max. 2 x 4 L product/ha) Vehicle mounted, downward spraying, outdoor crops Buffer zone: 2-3 m Drift reduction technology: no DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha Interval between treatments: 14 days			
Number of applications and application rate		2 x 0.2 kg a.s./ha	
Resident child Body weight: 10 kg	Drift (75th perc.)	0.002	0.9
	Vapour (75th perc.)	0.0008	0.4
	Deposits (75th perc.)	0.0004	0.2
	Re-entry (75th perc.)	0.002	1
	Sum (mean)	0.004	1.8
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0004	0.2
	Vapour (75th perc.)	0.0003	0.1
	Deposits (75th perc.)	8×10^{-5}	0.04
	Re-entry (75th perc.)	0.001	0.5
	Sum (mean)	0.001	0.7

		Sulphur		**Prothioconazole-desthio**	
Model data		**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Field crops (max. 2 x 4 L product/ha) Vehicle mounted, downward spraying, outdoor crops Buffer zone: 2-3 m Drift reduction technology: no DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha Interval between treatments: 14 days					
Number of applications and application rate		2 x 2.5 kg a.s./ha		2 x 0.18 kg a.s./ha	
Resident child Body weight: 10 kg	Drift (75th perc.)	0.01	0.05	0.006	64.1
	Vapour (75th perc.)	8×10^{-4}	0.003	8×10^{-4}	8

	Deposits (75th perc.)	0.005	0.02	8 x10^{-4}	8.4
	Re-entry (75th perc.)	0.01	0.05	0.007	68.4
	Sum (mean)	0.02	0.08	0.01	**104**
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.003	0.01	0.002	15.2
	Vapour (75th perc.)	3 x10^{-4}	0.001	3 x10^{-4}	2.7
	Deposits (75th perc.)	5 x10^{-4}	0.002	3 x10^{-4}	2.8
	Re-entry (75th perc.)	0.007	0.03	0.004	38
	Sum (mean)	0.007	0.03	0.004	**42.2**

Table 6.6-8: Estimated resident exposure (longer term exposure) – 5m buffer zone

		Prothioconazole	
Model data		**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Field crops (max. 2 x 4 L product/ha) Vehicle mounted, downward spraying, outdoor crops **Buffer zone: 5 m** Drift reduction technology: no DT_{50}: 30 days DFR: 3 µg/cm^2/kg a.s./ha Interval between treatments: 14 days			
Number of applications and application rate		2 x 0.2 kg a.s./ha	
Resident child Body weight: 10 kg	Drift (75th perc.)	0.001	0.6
	Vapour (75th perc.)	0.0008	0.4
	Deposits (75th perc.)	0.0002	0.09
	Re-entry (75th perc.)	0.002	1
	Sum (mean)	0.003	1.6
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0002	0.1
	Vapour (75th perc.)	0.0003	0.1
	Deposits (75th perc.)	3 x10^{-4}	0.02
	Re-entry (75th perc.)	0.001	0.5
	Sum (mean)	0.001	0.6

		Sulphur		**Prothioconazole-desthio**	
Model data		**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Field crops (max. 2 x 4 L product/ha) Vehicle mounted, downward spraying, outdoor crops **Buffer zone: 5 m** Drift reduction technology: no DT_{50}: 30 days DFR: 3 µg/cm^2/kg a.s./ha Interval between treatments: 14 days					
Number of applications and application rate		2 x 2.5 kg a.s./ha		2 x 0.18 kg a.s./ha	
Resident child Body weight: 10 kg	Drift (75th perc.)	0.008	0.03	0.004	42.8
	Vapour (75th perc.)	8 x10^{-4}	0.003	8 x10^{-4}	8
	Deposits (75th perc.)	0.002	0.007	3 x10^{-4}	3.5

	Re-entry (75th perc.)	0.01	0.05	0.007	68.4
	Sum (mean)	0.02	0.06	0.009	88.7
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.001	0.006	8×10^{-4}	7.8
	Vapour (75th perc.)	3×10^{-4}	0.001	3×10^{-4}	2.7
	Deposits (75th perc.)	2×10^{-4}	8×10^{-4}	1×10^{-4}	1.1
	Re-entry (75th perc.)	0.007	0.03	0.004	38
	Sum (mean)	0.007	0.03	0.004	37.8

Table 6.6-9: Estimated resident exposure (longer term exposure) – 50% DRT

		Prothioconazole	
Model data		**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Field crops (max. 2 x 4 L product/ha) Vehicle mounted, downward spraying, outdoor crops Buffer zone: 2-3 m **Drift reduction technology: yes (50%)** DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha Interval between treatments: 14 days			
Number of applications and application rate		2 x 0.2 kg a.s./ha	
Resident child Body weight: 10 kg	Drift (75th perc.)	9×10^{-4}	0.5
	Vapour (75th perc.)	8×10^{-4}	0.4
	Deposits (75th perc.)	2×10^{-4}	0.1
	Re-entry (75th perc.)	0.002	1
	Sum (mean)	0.003	1.5
Resident adult Body weight: 60 kg	Drift (75th perc.)	2×10^{-4}	0.1
	Vapour (75th perc.)	3×10^{-4}	0.1
	Deposits (75th perc.)	4×10^{-5}	0.02
	Re-entry (75th perc.)	0.001	0.5
	Sum (mean)	0.001	0.6

		Sulphur		**Prothioconazole-desthio**	
Model data		**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Field crops (max. 2 x 4 L product/ha) Vehicle mounted, downward spraying, outdoor crops Buffer zone: 2-3 m **Drift reduction technology: yes (50%)** DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha Interval between treatments: 14 days					
Number of applications and application rate		2 x 2.5 kg a.s./ha		2 x 0.18 kg a.s./ha	
Resident child Body weight: 10 kg	Drift (75th perc.)	0.006	0.02	0.003	32
	Vapour (75th perc.)	0.0008	0.003	0.0008	8
	Deposits (75th perc.)	0.002	0.009	0.0004	4.2
	Re-entry (75th perc.)	0.01	0.05	0.007	68.4

	Sum (mean)	0.02	0.06	0.008	83.2
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.001	0.005	0.0008	7.6
	Vapour (75th perc.)	0.0003	0.001	0.0003	2.7
	Deposits (75th perc.)	0.0002	0.001	0.0001	1.4
	Re-entry (75th perc.)	0.0002	0.001	0.004	38
	Sum (mean)	0.007	0.03	0.004	37.6

6.6.4.2 Measurement of resident and/or bystander exposure

Since the resident exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) for prothioconazole, sulphur, and prothioconazole-desthio will not be exceeded under conditions of intended uses and considering above mentioned risk mitigation measures, a study to provide measurements of resident exposure was not necessary and was therefore not performed.

6.6.5 Combined exposure

The product is a mixture of two active substances. Therefore, a combined exposure assessment is presented below.

6.6.5.1 Exposure assessment of prothioconazole-desthio and sulphur in FHO04

The formulation of FHO04 is a mixture of two active substances: prothioconazole and sulphur. Furthermore, the conversion of prothioconazole to prothioconazole-desthio can occur. Since the toxicity of prothioconazole-desthio is greater than prothioconazole (with AOELs of 0.01 and 0.2 respectively), the worst case scenario of 100% conversion to prothioconazole-desthio with the combined exposure to sulphur has been investigated.

The combined toxicological effect of these active substances has not been investigated with regard to repeated dose toxicity. At the first tier, combined exposure is calculated as the sum of the component exposures without regard to the mode of action or mechanism/target of toxicity. Initially, the individual Hazard Quotients (HQ) are calculated for all active substances in the PPP by assessing the exposure according to appropriate models and dividing the individual exposure levels by the respective systemic AOEL. This is equivalent to the predicted exposure as % of systemic AOEL converted to decimal. The Hazard Index (HI) is the sum of the individual HQs.

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

Field crops (max. 2 x 4 L product/ha), 5m buffer zone		
Application scenario	**Active ingredient**	**Estimated exposure / AOEL (HQ)**
Operators – vehicle mounted, downward spraying, outdoor crops	Prothioconazole-desthio	0.32
	Sulphur	4×10^{-4}
	Cumulative risk operators (HI)	**0.3**
Workers – inspection, irrigation	Prothioconazole-desthio	0.51
	Sulphur	4×10^{-4}
	Cumulative risk workers (HI)	**0.5**
Resident - child	Prothioconazole-desthio	
	Drift	0.43
	Vapour	0.08
	Deposits	0.04

Field crops (max. 2 x 4 L product/ha), 5m buffer zone		
Application scenario	**Active ingredient**	**Estimated exposure / AOEL (HQ)**
	Re-entry	0.68
	Sum of all pathways	**0.89**
	Sulphur	
	Drift	3×10^{-4}
	Vapour	3×10^{-5}
	Deposits	7×10^{-5}
	Re-entry	5×10^{-4}
	Sum of all pathways	**6×10^{-4}**
	Cumulative risk resident – child (HI)	
	Drift	0.4
	Vapour	0.08
	Deposits	0.03
	Re-entry	0.7
	Sum of all pathways	**0.9**
Resident - adult	Prothioconazole-desthio	
	Drift	0.08
	Vapour	0.03
	Deposits	0.01
	Re-entry	0.38
	Sum of all pathways	0.38
	Sulphur	
	Drift	6×10^{-5}
	Vapour	1×10^{-5}
	Deposits	8×10^{-6}
	Re-entry	3×10^{-4}
	Sum of all pathways	**3×10^{-4}**
	Cumulative risk resident – adult (HI)	
	Drift	0.08
	Vapour	0.03
	Deposits	0.01
	Re-entry	0.4
	Sum of all pathways	**0.4**

When a 5 m buffer zone is applied, the Hazard Index is < 1. Thus, combined exposure to all active substances in FHO04 is not expected to present a risk for operators, workers, residents and bystanders. No further refinement of the assessment is required.

Table 6.6-10: Risk assessment from combined exposure (longer term exposure)

Field crops (max. 2 x 4 L product/ha), 50% DRT		
Application scenario	**Active ingredient**	**Estimated exposure / AOEL (HQ)**
Operators – vehicle mounted, downward spraying, outdoor crops	Prothioconazole-desthio	0.32
	Sulphur	0.0004
	Cumulative risk operators (HI)	**0.3**
Workers – inspection, irrigation	Prothioconazole-desthio	0.51
	Sulphur	0.0004
	Cumulative risk workers (HI)	**0.5**
Resident - child	Prothioconazole-desthio	
	Drift	0.43
	Vapour	0.08
	Deposits	0.04
	Re-entry	0.68
	Sum of all pathways	**0.89**
	Sulphur	
	Drift	0.0003
	Vapour	0.00003
	Deposits	0.00007
	Re-entry	0.0005
	Sum of all pathways	**0.0006**
	Cumulative risk resident – child (HI)	
	Drift	0.4
	Vapour	0.08
	Deposits	0.03
	Re-entry	0.7
	Sum of all pathways	**0.9**
Resident - adult	Prothioconazole-desthio	
	Drift	0.08
	Vapour	0.03
	Deposits	0.01
	Re-entry	0.38
	Sum of all pathways	**0.38**
	Sulphur	
	Drift	0.00006
	Vapour	0.00001
	Deposits	0.000008
	Re-entry	0.0003
	Sum of all pathways	0.0003
	Cumulative risk resident – adult (HI)	
	Drift	0.08
	Vapour	0.03

Field crops (max. 2 x 4 L product/ha), 50% DRT		
Application scenario	**Active ingredient**	**Estimated exposure / AOEL (HQ)**
	Deposits	0.01
	Re-entry	0.4
	Sum of all pathways	**0.4**

When 50% drift reduction technology is applied, the Hazard Index is < 1. Thus, combined exposure to all active substances in FHO04 is not expected to present a risk for operators, workers, residents and bystanders. No further refinement of the assessment is required.

Appendix 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 7.3/01	[redacted]	2022	Prothioconazole + Sulphur (50 + 625) g/L SC: The In Vitro Percutaneous Absorption of Radiolabelled Prothioconazole in a Concentrate Formulation and Two In-Use Dilutions and Prothioconazole-desthio in Two In-Use Dilutions through Human Split-Thickness Skin Company Report No. 20321440 [redacted] GLP Unpublished	N	UPL
KCP 7.3/02	[redacted]	2022	Prothioconazole + Sulphur (50 + 625) g/L SC: The In Vitro Percutaneous Absorption of Radiolabelled Sulphur in a Concentrate Formulation and Two In-Use Dilutions through Human Split-Thickness Skin Company Report No. 20321446 [redacted] GLP Unpublished	N	UPL

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
-	-	-	-	-	-

List of data submitted by the applicant and not relied on

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

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

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

Appendix 2 Detailed evaluation of the studies relied upon

A 2.1 Statement on bridging possibilities

Bridging was not necessary to support this application.

Comments of zRMS:	Bridging is not applicable. Hazard classification of the product has been based on content of ingredients of the currently registered product (FHO04).

The classification of FHO04 has been determined by calculation. The assessment of all acute toxicological properties of FHO04 is derived from the classification of the active substances and co-formulants. For confidentiality reasons, the calculations have been included in Part C of the dRR.

A 2.2 Acute oral toxicity (KCP 7.1.1)

Comments of zRMS:	Hazard assessment and proposed classification of the product based on content of ingredients of the mixture has been accepted (for details see Part C).

Please refer to the Part C.

A 2.3 Acute percutaneous (dermal) toxicity (KCP 7.1.2)

Comments of zRMS:	Hazard assessment and proposed classification of the product based on content of ingredients of the mixture has been accepted (for details see Part C).

Please refer to the Part C.

A 2.4 Acute inhalation toxicity (KCP 7.1.3)

Comments of zRMS:	Hazard assessment and proposed classification of the product based on content of ingredients of the mixture has been accepted (for details see Part C).

Please refer to the Part C.

A 2.5 Skin irritation (KCP 7.1.4)

Comments of zRMS:	Hazard assessment and proposed classification of the product based on content of ingredients of the mixture has been accepted (for details see Part C).

Please refer to the Part C.

A 2.6 Eye irritation (KCP 7.1.5)

Comments of zRMS:	Hazard assessment and proposed classification of the product based on content of ingredients of the mixture has been accepted (for details see Part C).

Please refer to the Part C.

A 2.7 Skin sensitisation (KCP 7.1.6)

Comments of zRMS:	Hazard assessment and proposed classification of the product based on content of ingredients of the mixture has been accepted (for details see Part C).

Please refer to the Part C.

A 2.8 Supplementary studies for combinations of plant protection products (KCP 7.1.7)

Not required.

A 2.9 Data on co-formulants (KCP 7.4)

A 2.9.1 Material safety data sheet for each co-formulant

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

A 2.9.2 Available toxicological data for each co-formulant

Available toxicological data for each co-formulant can be found in the confidential dossier of this submission (draft Registration Report - Part C).

A 2.10 Studies on dermal absorption (KCP 7.3)

A 2.10.1 Study 1 – Prothioconazole and Prothioconazole-desthio in Prothioconazole + Sulphur (50 + 625) g/L SC.

Comparative dermal absorption, in vitro using rat and human skin

Comments of zRMS:	The study ([redacted], 2022) was performed according to OECD 428 and is considered acceptable. The dermal absorption values proposed by the applicant are acceptable. The dermal penetration estimates for prothioconazole and prothioconazole-desthio in FHO04, to be used for risk assessment, are based on criteria laid down in the EFSA Journal guidance, 2017. The study is accepted

Reference	KCP 7.3/01
Report	Prothioconazole + Sulphur (50 + 625) g/L SC: The In Vitro Percutaneous Absorption of Radiolabelled Prothioconazole in a Concentrate Formulation and Two In-Use Dilutions and Prothioconazole-desthio in Two In-Use Dilutions through Human Split-Thickness Skin. [redacted] Study No. 20321440 Sponsor Reference No. UPL/2021/0519
Guideline(s)	• OECD Guideline for Testing of Chemicals, Guideline 428: Skin Absorption: In Vitro Method (2004). • OECD Guidance Notes on Dermal Absorption No. 156, ENV/JM/MONO (2011) 36, 2011. • Council Regulation (EC) No. 440/2008, Method B.45; Skin Absorption: In Vitro Method, Brussels, May 2008. • OECD Environmental Health and Safety Publications Series on Testing and Assessment No. 28. Guidance Document for the Conduct of Skin Absorption Studies (2004). • European Commission Guidance Document on Dermal Absorption – Sanco/222/2000/Rev. 7 (19 March 2004). • Guidance on Dermal Absorption (EFSA Journal, 2017, 15(6): 4873)
Deviations	No
GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	N/A

Materials and methods

Test material	Name (Lot/Batch No.)	Prothioconazole technical (200713)
	Test preparation	radioformulation
	Specific activity	1845 MBq/mmol (= 5.33 MBq/mg)
	Radiochemical purity	98.8%
Test material	Name (Lot/Batch No.)	Prothioconazole-desthio (FCC3159872)
	Test preparation	radioformulation
	Specific activity	1978 MBq/mmol (= 6.30 MBq/mg)
	Radiochemical purity	99.6%

Product	Name (Lot/Batch No.)	FHO04
	Company code	FHO04
	Concentration a.s.	50+625 g/L
	Formulation type	SC
Blank product	Name (Lot/Batch No.)	Prothioconazole/Sulphur (50+625) g/L SC Blank (no Prothioconazole (027121)
	Concentration a.s.	50+625 g/L

Test system		
Diffusion cell	Cell type	dynamic
	(if dynamic) Flow rate	1.5 ml/h
	Exposed skin area	0.64 cm²
	Cover	open
Membrane	Skin type	dermatomed
	Skin thickness range	200-400 µm
	Skin donors age	39-65
	Skin donors sex	f
	Location	abdomen / breast
	Source	ex vivo
	Integrity test	Yes - Saline (0.9% (w/v) NaCl in water)
Receptor	Receptor medium	Phosphate buffered saline (PBS)
	Solubility in receptor medium	y
Sample Time	Exposure time	8h
	Observation time	24h
Sampling	Sample intervals	0-1 h, 1-2 h, 2-4 h, 4-6 h, 6-8 h, 8-10 h, 10-12 h, 12-16 h, 16-20 h and 20-24 h
Washing		post exposure & post observation
Final Procedure	Tape stripping	y
	TS1-2 analysed separately	y
Remarks:		

Tested doses (PTZ)	Concentrate	Spray dilution 1	Spray dilution 2
Target concentration [g/L]	50	0.5	0.125
Area dose [µg/cm²]	490	4.85	1.29
Total dose [µg/cell]	497	4.26	1.16
Specific activity [kBq/ml]	2.51	2.96	0.72
No. of donors	4	4	4
No of cells used/valid cells*	8/8	8/8	8/8

* Justification for excluded cells, if applicable

Tested doses (PTZ-desthio)	Concentrate	Spray dilution 1	Spray dilution 2
Target concentration [mg/ml]	Not tested	0.45	0.113
Area dose [µg/cm²]	Not tested	4.25	1.01
Total dose [µg/cell]	Not tested	3.76	0.85
Specific activity [kBq/ml]	Not tested	2.70	2.85
No. of donors	Not tested	4	4
No of cells used/valid cells*	Not tested	8/7	8/7

* Justification for excluded cells, if applicable

Results and discussions

In-vitro dermal penetration of active substance 1 (PTZ) formulated as product FHO04 through human skin - Recovery data

Summary of the Mean Dermal Absorption Results for PTZ

Test preparation:	1: Formulation Concentrate	2: Spray Dilution I	3: Spray Dilution II

Target PTZ Concentration	50 g/L	0.50 g/L	0.125 g/L
Actual PTZ Concentration	49 g/L	0.48 g/L	0.129 g/L
Number of replicates	8	8	8
Did >75% Absorption into receptor Fluid Occur in First Half of Study?	No (76.6 ± 6.0%) [1]	Yes (79.2 ± 4.8%)	Yes (81.0 ± 7.7%)
	(% Applied Dose, mean ± SD)		
Dislodgeable Dose 8 h	101 ± 3	83.0 ± 4.7	86.0 ± 3.0
Dislodgeable Dose 24 h	0.040 ± 0.013	4.14 ± 0.95	3.65 ± 1.05
Total Dislodgeable Dose	101 ± 3	87.8 ± 4.1	90.0 ± 2.3
Stratum Corneum 1-2	0.012 ± 0.011	2.38 ± 1.18	2.50 ± 2.30
Stratum Corneum 3-last	0.025 ± 0.006	5.86 ± 2.02	6.97 ± 2.15
Total Unabsorbed dose	101 ± 3	96.0 ± 2.0	99.4 ± 1.1
Total absorbed dose	0.033 ± 0.012	1.99 ± 0.78	1.43 ± 0.42
Dermal Delivery	0.043 ± 0.016	2.44 ± 1.00	2.52 ± 0.95
Potentially Absorbable Dose	0.068 ± 0.017	N/A	N/A
Mass Balance	102 ± 3	98.5 ± 1.3	102 ± 1
	(µg equiv./cm^2, mean ± SD)		
Dislodgeable Dose 8 h	497 ± 12	4.02 ± 0.23	1.11 ± 0.04
Dislodgeable Dose 24 h	0.20 ± 0.06	0.20 ± 0.05	0.047 ± 0.013
Total Dislodgeable Dose	497 ± 12	4.26 ± 0.20	1.16 ± 0.03
Stratum Corneum 1-2	0.056 ± 0.052	0.12 ± 0.06	0.032 ± 0.030
Stratum Corneum 3-last	0.12 ± 0.03	0.28 ± 0.10	0.090 ± 0.028
Total Unabsorbed dose	497 ± 12	4.66 ± 0.10	1.28 ± 0.01
Total absorbed dose	0.16 ± 0.06	0.10 ± 0.04	0.018 ± 0.005
Dermal Delivery	0.21 ± 0.08	0.12 ± 0.05	0.032 ± 0.012
Potentially Absorbable Dose	0.33 ± 0.08	N/A	N/A
Mass Balance	498 ± 12	4.77 ± 0.06	1.31 ± 0.01

[1]Since $t_{0.5}$ was near 75% and the lower confidence interval was below 75%, the absorption was considered 'incomplete', as defined by the EFSA Scientific Opinion – Guidance on Dermal Absorption 2017; 15(6):4873 Dislodgeable Dose 8 h= Skin Wash 8 h + Cotton Swab 8 h + Dry Cotton Swab 8 h
Dislodgeable Dose 24 h = Skin Wash 24 h + Cotton Swab 24 h + Dry Cotton Swab 24 h
Total Dislodgeable Dose = Donor Wash + Dislodgeable Dose 8 h + Dislodgeable Dose 24 h
Stratum Corneum 1-2 = Tape Strips 1 and 2
Stratum Corneum 3-last = Tape Strips 3 until the last strip collected
Total Unabsorbed dose = Total Dislodgeable Dose + *Stratum Corneum* + Unexposed Skin
Total absorbed dose = Cumulative Receptor fluid + Receptor Chamber Wash
Dermal Delivery = Total absorbed dose + Exposed Skin
Potentially Absorbable Dose = Dermal Delivery + *Stratum Corneum* 3-last
Mass Balance = Total Unabsorbed dose + Dermal Delivery
N/A = not applicable. The potentially absorbable dose is not applicable when the absorption was "complete" as defined in the EFSA Scientific Opinion – Guidance on Dermal Absorption 2017; 15(6):4873. Absorption is defined as incomplete if less than 75% of the absorption occurs within the first half of the experiment

In-vitro dermal penetration of active substance 2 (PTZ-DESTHIO) formulated as product code/name through human skin - Recovery data

Summary of the Mean Dermal Absorption Results for PTZ-desthio

Test preparation:	4: Spray Dilution I	5: Spray Dilution II
Target PTZ-desthio Concentration	0.45 g/L	0.113 g/L
Actual PTZ-desthio Concentration	0.43 g/L	0.114 g/L
Number of replicates	8	7 [1]
Did >75% Absorption into receptor Fluid Occur in First Half of Study?	Yes (92.1 ± 3.2%)	Yes (93.2 ± 6.5%)
	(% Applied Dose, mean ± SD)	
Dislodgeable Dose 8 h	86.5 ± 3.6	74.1 ± 7.8
Dislodgeable Dose 24 h	1.19 ± 0.78	1.46 ± 0.77
Total Dislodgeable Dose	88.3 ± 2.9	76.4 ± 8.4
Stratum Corneum 1-2	0.063 ± 0.081	0.067 ± 0.074
Stratum Corneum 3-last	0.060 ± 0.032	0.14 ± 0.05
Total Unabsorbed dose	88.5 ± 2.8	76.7 ± 8.4
Total absorbed dose	10.2 ± 3.2	21.2 ± 8.9
Dermal Delivery	10.4 ± 3.3	21.5 ± 8.8
Potentially Absorbable Dose	N/A	N/A
Mass Balance	98.8 ± 1.0	98.1 ± 1.2
	(µg equiv./cm^2, mean ± SD)	
Dislodgeable Dose 8 h	3.68 ± 0.16	0.82 ± 0.09
Dislodgeable Dose 24 h	0.050 ± 0.033	0.016 ± 0.009
Total Dislodgeable Dose	3.76 ± 0.13	0.85 ± 0.10
Stratum Corneum 1-2	0.003 ± 0.003	0.001 ± 0.001
Stratum Corneum 3-last	0.003 ± 0.001	0.002 ± 0.001
Total Unabsorbed dose	3.76 ± 0.12	0.85 ± 0.10
Total absorbed dose	0.43 ± 0.14	0.23 ± 0.10
Dermal Delivery	0.44 ± 0.14	0.24 ± 0.10
Potentially Absorbable Dose	N/A	N/A
Mass Balance	4.20 ± 0.05	1.09 ± 0.02

[1] One cell replicate was excluded from the calculations of the mean because of an apparent dosing error.
Dislodgeable Dose 8 h= Skin Wash 8 h + Cotton Swab 8 h + Dry Cotton Swab 8 h
Dislodgeable Dose 24 h = Skin Wash 24 h + Cotton Swab 24 h + Dry Cotton Swab 24 h
Total Dislodgeable Dose = Donor Wash + Dislodgeable Dose 8 h + Dislodgeable Dose 24 h
Stratum Corneum 1-2 = Tape Strips 1 and 2
Stratum Corneum 3-last = Tape Strips 3 until the last strip collected
Total Unabsorbed dose = Total Dislodgeable Dose + *Stratum Corneum* + Unexposed Skin
Total absorbed dose = Cumulative Receptor fluid + Receptor Chamber Wash
Dermal Delivery = Total absorbed dose + Exposed Skin
Potentially Absorbable Dose = Dermal Delivery + *Stratum Corneum* 3-last
Mass Balance = Total Unabsorbed dose + Dermal Delivery

N/A = not applicable. The potentially absorbable dose is not applicable when the absorption was "complete" as defined in the EFSA Scientific Opinion – Guidance on Dermal Absorption 2017; 15(6):4873. Absorption is defined as incomplete if less than 75% of the absorption occurs within the first half of the experiment

Conclusion/endpoint:

In conclusion, following topical application of [^{14}C]PTZ in test preparation 1 (actual concentration 49.0 g/L), test preparation 2 (actual concentration 0.48 g/L) and test preparation 3 (actual concentration 0.129 g/L) to human skin in vitro, the total absorbed dose of [^{14}C]PTZ was 0.033% (0.16 µg equiv./cm^2), 1.99% (0.10 µg equiv./cm^2) and 1.43% (0.018 µg equiv./cm^2) of the applied dose, respectively.

The 8 h dislodgeable dose was 101%, 83.0% and 86.0% of the applied dose for test preparations 1, 2 and 3, respectively. The recovery of radioactivity from the individual washing steps at 8 h showed appropriate decontamination of the skin with, on average, less than 1% of the applied dose recovered in the last washing step.

The 24 h dislodgeable dose was 0.040%, 4.14% and 3.65% of the applied dose for test preparations 1, 2 and 3, respectively. The dermal delivery of [^{14}C]PTZ was 0.043% (0.21 µg equiv./cm^2) of the applied dose for test preparation 1, 2.44% (0.12 µg equiv./cm^2) of the applied dose for test preparation 2 and 2.52% (0.032 µg equiv./cm^2) of the applied dose for test preparation 3. The potentially absorbable dose of [^{14}C]PTZ was 0.068% (0.33 µg equiv./cm^2) of the applied dose for test preparation 1. The potentially absorbed dose is not applicable for Test Preparation 2 and 3 because the absorption was deemed "complete" as defined in the EFSA Scientific Opinion – Guidance on Dermal Absorption 2017; 15(6):4873.

The mass balance for [^{14}C]PTZ was 102% (498 µg equiv./cm^2) of the applied dose for test preparation 1, 98.5% (4.77 µg equiv./cm^2) of the applied dose for test preparation 2 and 102% (1.31 µg equiv./cm^2) of the applied dose for test preparation 3. Following topical application of [^{14}C]PTZ-desthio in test preparation 4 (actual concentration 0.43 g/L) and test preparation 5 (actual concentration 0.114 g/L)) to human skin in vitro, the total absorbed dose of [^{14}C]PTZ-desthio was 10.2% (0.43 µg equiv./cm^2) and 21.2% (0.23 µg equiv./cm^2) of the applied dose, respectively.

The 8 h dislodgeable dose was 86.5% and 74.1% of the applied dose for test preparations 4 and 5, respectively. The 24 h dislodgeable dose was 1.19% and 1.46% of the applied dose for test preparations 4 and 5, respectively, confirming appropriate decontamination of the skin at 8 h post dose. The dermal delivery of [^{14}C]PTZ-desthio was 10.4% (0.44 µg equiv./cm^2) of the applied dose for test preparation 4, and 21.5% (0.24 µg equiv./cm^2) of the applied dose for test preparation 5. Potentially absorbed dose is not applicable for Test Preparation 4 and 5 because the absorption was "complete" as defined in the EFSA Scientific Opinion – Guidance on Dermal Absorption 2017; 15(6):4873. The mass balance for [^{14}C]PTZ-desthio was 98.8% (4.20 µg equiv./cm^2) of the applied dose for test preparation 4, and 98.1% (1.09 µg equiv./cm^2) of the applied dose for test preparation 5.

A 2.10.2 Study 2 – Sulphur in Prothioconazole + Sulphur (50 + 625) g/L SC.

Comparative dermal absorption, in vitro using rat and human skin

Comments of zRMS:	The study ([redacted], 2022) was performed according to OECD 428 and is considered acceptable. The dermal absorption values proposed by the applicant are acceptable. The dermal penetration estimates for radiolabeled Sulphur in FHO04, to be used for risk assessment, are based on criteria laid down in the EFSA Journal guidance, 2017. The study is accepted

Reference	KCP 7.3/02
Report	Prothioconazole + Sulphur (50 + 625) g/L SC: The In Vitro Percutaneous Absorption of Radiolabelled Sulphur in a Concentrate Formulation and Two In-Use Dilutions through Human Split-Thickness Skin. [redacted] Study No. 20321446 Sponsor Reference No. UPL/2022/0125
Guideline(s)	• OECD Guideline for Testing of Chemicals, Guideline 428: Skin Absorption: In Vitro Method (2004). • OECD Guidance Notes on Dermal Absorption No. 156, ENV/JM/MONO (2011) 36, 2011. • Council Regulation (EC) No. 440/2008, Method B.45; Skin Absorption: In Vitro Method, Brussels, May 2008. • OECD Environmental Health and Safety Publications Series on Testing and Assessment No. 28. Guidance Document for the Conduct of Skin Absorption Studies (2004). • European Commission Guidance Document on Dermal Absorption – Sanco/222/2000/Rev. 7 (19 March 2004). • EFSA Panel on Plant Protection Products and their Residues (PPR); Guidance on Dermal Absorption (EFSA Journal, 2017, 15(6): 4873).
Deviations	No
GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	N/A

Materials and methods

Test material	Name (Lot/Batch No.)	Sulphur techniccal (001 RDC)
	Test preparation	radioformulation
	Specific activity	n/a
	Radiochemical purity	n/a
	Name (Lot/Batch No.)	Elemental Sulphur, -[^{35}S] (2965174)
	Test preparation	radioformulation
	Specific activity	40 mCi/mmol
	Radiochemical purity	N.D (Chemical Purity >71.94%)
Product	Name (Lot/Batch No.)	FHO04
	Company code	FHO04
	Concentration a.s.	Prothioconazole/Sulphur (50+625) g/L
	Formulation type	SC
Blank product	Name (Lot/Batch No.)	Prothioconazole/Sulphur (50+625) g/L SC Blank (no Sulphur) (028521)
	Concentration a.s.	0 g/L (sulphur), 50 g/L (prothioconazole)

Test system		
Diffusion cell	Cell type	Dynamic
	(if dynamic) Flow rate	1.5 ml/h
	Exposed skin area	0.64 cm²
	Cover	Open
Membrane	Skin type	Dermatomed
	Skin thickness range	200-400 µm
	Skin donors age	33-53
	Skin donors sex	f
	Location	Abdomen / breast
	Source	ex vivo
	Integrity test	Yes - Saline (0.9% (w/v) NaCl in water)
Receptor	Receptor medium	Phosohate buffered saline (PBS) containing polyoxyethylene 20 oleyl ether (PEG; 6%, w/v), sodium azide (0.01%, w/v), streptomycin (0.1 mg/mL) and penicillin G (100 units/mL)
	Solubility in receptor medium	y
Sample Time	Exposure time	8 hours
	Observation time	24 hours
Sampling	Sample intervals	0-1 h, 1-2 h, 2-4 h, 4-6 h, 6-8 h, 8-10 h, 10-12 h, 12-16 h, 16-20 h and 20-24 h
Washing		Post exposure and post observation
Final Procedure	Tape stripping	y
	TS1-2 analysed separately	y
Remarks:		

Tested doses	Concentrate	Spray dilution 1	Spray dilution 2
Target concentration [mg/ml]	625	6.25	1.56
Area dose [µg/cm²]	6102	60.2	15.2
Total dose [µg/cell]	6010	57.2	14.5
Specific activity [MBq/ml]	7.8	12.3	1.59
No. of donors	4	4	4
No of cells used/valid cells	6/7*	6/7**	6/7***

* One replicate showed a pronounced washing-in effect, resulting in a more than 10-fold higher absorption into the receptor fluid (outlier according to Dixon's Q-test at 99% confidence level). Data obtained for this replicate was therefore excluded from the calculations of the mean values.

** One replicate showed a notably deviating amount of radioactivity associated with the stratum corneum when compared to its partner cell and all other replicates (outlier according to Dixon's Q test at 95% confidence level). Data obtained for this replicate was therefore excluded from the calculations of the mean values.

*** Data obtained for one replicate was excluded from the calculations of the mean values. From the high amount recovered in the donor wash and the unexposed skin it was concluded that the unexposed skin was contaminated during washing

Results and discussions

In-vitro dermal penetration of active substance 1 formulated as product code/name through human skin - Recovery data

Summary of the Mean Dermal Absorption Results for $^{35}S_8$

Test preparation:	1: Formulation Concentrate	2: Spray Dilution I	3: Spray Dilution II
Target Sulphur Concentration	625 g/L	6.25 g/L	1.56 g/L
Actual Sulphur Concentration	621 g/L	6.20 g/L	1.55 g/L
Number of replicates	7 1	7 2	7 3
Percentage Absorption into Receptor Fluid Occurring in First Half of the Study	65.5 ± 3.6%	69.1 ± 6.2%	66.6 ± 5.0%

	(% Applied Dose, mean ± SD)		
Dislodgeable Dose 8 h	98.3 ± 1.1	92.3 ± 6.0	94.3 ± 1.0
Dislodgeable Dose 24 h	0.024 ± 0.010	1.35 ± 2.01	0.57 ± 0.28
Total Dislodgeable Dose	98.4 ± 1.1	95.1 ± 1.7	95.2 ± 0.8
Stratum Corneum 1-2	0.035 ± 0.057	0.73 ± 0.78	0.28 ± 0.18
Stratum Corneum 3-last	0.041 ± 0.028	0.66 ± 0.27	0.94 ± 0.18
Total Unabsorbed dose	98.6 ± 1.1	96.5 ± 1.1	96.5 ± 0.9
Total Absorbed Dose	0.032 ± 0.018	0.20 ± 0.08	0.38 ± 0.15
Dermal Delivery	0.065 ± 0.037	0.67 ± 0.30	1.00 ± 0.31
Potentially Absorbable Dose	0.11 ± 0.06	1.33 ± 0.38	1.94 ± 0.45
Mass Balance	98.6 ± 1.1	97.2 ± 1.0	97.5 ± 1.0
	(µg equiv./cm^2, mean ± SD)		
Dislodgeable Dose 8 h	6005 ± 87	55.5 ± 3.6	14.4 ± 0.2
Dislodgeable Dose 24 h	1.49 ± 0.61	0.82 ± 1.24	0.087 ± 0.044
Total Dislodgeable Dose	6010 ± 86	57.2 ± 2.0	14.5 ± 0.2
Stratum Corneum 1-2	2.14 ± 3.44	0.44 ± 0.48	0.042 ± 0.028
Stratum Corneum 3-last	2.52 ± 1.69	0.40 ± 0.16	0.14 ± 0.03
Total Unabsorbed dose	6019 ± 82	58.0 ± 1.8	14.7 ± 0.3
Total Absorbed Dose	1.93 ± 1.11	0.12 ± 0.05	0.058 ± 0.024
Dermal Delivery	3.98 ± 2.20	0.40 ± 0.19	0.15 ± 0.05
Potentially Absorbable Dose	6.50 ± 3.74	0.80 ± 0.23	0.30 ± 0.07
Mass Balance	6023 ± 82	58.4 ± 1.9	14.8 ± 0.3

[1] One replicate showed a pronounced washing-in effect, resulting in a more than 10-fold higher absorption into the receptor fluid (outlier according to Dixon's Q-test at 99% confidence level). Data obtained for this replicate was therefore excluded from the calculations of the mean values.

[2] One replicate showed a notably deviating amount of radioactivity associated with the stratum corneum when compared to its partner cell and all other replicates (outlier according to Dixon's Q test at 95% confidence level). Data obtained for this replicate was therefore excluded from the calculations of the mean values. (See 8.5 for discussion).

[3] Data obtained for one replicate was excluded from the calculations of the mean values. From the high amount recovered in the donor wash and the unexposed skin it was concluded that the unexposed skin was contaminated during washing. (See 8.6 for discussion).

Dislodgeable Dose 8 h = Skin Wash 8 h + Cotton Swab 8 h + Dry Cotton Swab 8 h
Dislodgeable Dose 24 h = Skin Wash 24 h + Cotton Swab 24 h + Dry Cotton Swab 24 h
Total Dislodgeable Dose = Donor Wash + Dislodgeable Dose 8 h + Dislodgeable Dose 24 h
Stratum Corneum 1-2 = Tape Strips 1 and 2
Stratum Corneum 3-last = Tape Strips 3 until the last strip collected
Total Unabsorbed dose = Total Dislodgeable Dose + *Stratum Corneum* + Unexposed Skin
Total absorbed dose = Cumulative Receptor fluid + Receptor Chamber Wash
Dermal Delivery = Total absorbed dose + Exposed Skin
Potentially Absorbable Dose = Dermal Delivery + *Stratum Corneum* 3-last Mass
Balance = Total Unabsorbed dose + Dermal Delivery

Conclusion/endpoint:

In conclusion, following topical application of 35S8 in test preparation 1 (actual concentration 621 g/L), test preparation 2 (actual concentration 6.20 g/L) and test preparation 3 (actual concentration 1.55 g/L) to

human skin in vitro, the total absorbed dose of 35S8 was 0.032% (1.93 µg equiv./cm^2), 0.20% (0.12 µg equiv./cm^2) and 0.38% (0.058 µg equiv./cm^2) of the applied dose, respectively.

The 8 h dislodgeable dose was 98.3%, 92.3% and 94.3% of the applied dose for test preparations 1, 2 and 3, respectively. The 24 h dislodgeable dose was 0.024%, 1.35% and 0.57% of the applied dose for test preparations 1, 2 and 3, respectively. The dermal delivery of 35S8 was 0.065% (3.98 µg equiv./cm^2) of the applied dose for test preparation 1, 0.67% (0.40 µg equiv./cm^2) of the applied dose for test preparation 2 and 1.00% (0.15 µg equiv./cm2) of the applied dose for test preparation 3. The potentially absorbable dose of 35S8 was 0.11% (6.50 µg equiv./cm^2) of the applied dose for test preparation 1, 1.33 (0.80 µg equiv./cm^2) of the applied dose for test preparation 2 and 1.94% (0.30 µg equiv./cm^2) of the applied dose for test preparation 3.

The mass balance for 35S8 was 98.6% (6023 µg equiv./cm^2) of the applied dose for test preparation 1, 97.2% (58.4 µg equiv./cm^2) of the applied dose for test preparation 2 and 97.5% (14.8 µg equiv./cm^2) of the applied dose for test preparation 3.

A 2.11 Other/Special Studies

No other studies required.

Appendix 3 Exposure calculations

A 3.1 Exposure calculations (KCP 7.2.1.1)

A 3.1.1 Calculations for prothioconazole

Information on the product and active substances:

Product name	FHO04 prothioconazole only (2 x 4 L)
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.
Product category	Other
Name of active substance	Prothioconazole
Concentration of active substance [g a.s./l or kg]	50
AOEL [mg/kg bw/day]	0.2
AAOEL [mg/kg bw]	
Inhalation absorption [%]	100
Oral absorption [%]	100
Dermal absorption [%] (concentrate)	0.1
Dermal absorption [%] (dilution) 0.5 [g a.s./l or kg]	3.3

Assessed Uses:

Use	Crops	Max. application rate of the product [l or kg/ha]	Unit	Max. no. of applications	Interval between multiple applications [days]	Min. volume water [l/ha]	Max. volume water [l/ha]	In-door/out-door	Application method	Type of cultivation	Application technique	Buffer strip [m]	Drift reduction [%]
Use 1	Field crops	4	l/ha	2	14	100	400	Outdoor	Downward spraying	Normal	Vehicle-mounted	2-3	0

Operator – short term exposure:

Model data		Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL
	Field crops/Outdoor/Downward spraying/Vehicle-mounted/Drift reduction: 0 %/75th percentile Crop density: Normal			
Prothioconazole	Number of applications and application rate: 2 x 0.2 kg a.s./ha Dermal absorption (concentrate): 0.1 % Dermal absorption (in-use dilution): 3.3 %			
		M/L: Workwear App: Workwear	0.002	0.8

Worker:

	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL	Re-entry restriction [days]
				Inspection, irrigation / Outdoor Work rate: 2 hours/day Interval: 14 days Body weight: 60 kg TC (potential): 12500 cm²/h TC (workwear (arms, body and legs covered)): 1400 cm²/h TC (workwear (arms, body and legs covered) and gloves): 1250 cm²/h TC (gloves): NA cm²/h
	Prothioconazole			Number of applications & application rate: 2 x 0.2 kg a.s./ha Dermal absorption: 3.3 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days
	Potential	0.01	7.1	0
	Workwear	0.002	0.8	0
	Workwear and gloves	0.001	0.7	0
	Hands covered, no workwear			

Resident:

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL
			Season: Not relevant Buffer zone: 2-3 m Drift reduction technology: 0 % Interval between treatments: 14 days Minimum volume of water: 100 l
Prothioconazole			Number of applications and application rate: 2 x 0.2 kg a.s./ha Dermal absorption: 3.3 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days
Resident child Body weight: 10 kg	Drift (75th perc.)	0.002	0.9
	Vapour (75th perc.)	0.0008	0.4
	Deposits (75th perc.)	0.0004	0.2
	Re-entry (75th perc.)	0.002	1
	Sum (mean)	0.004	1.8
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0004	0.2
	Vapour (75th perc.)	0.0003	0.1
	Deposits (75th perc.)	8e-05	0.04
	Re-entry (75th perc.)	0.001	0.5
	Sum (mean)	0.001	0.7

A 3.1.2 Calculations for sulphur

Information on product and active substance:

Product name	FHO04 (2 x 4 L)
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.
Product category	Other
Name of active substance	Sulphur
Concentration of active substance [g a.s./l or kg]	625
AOEL [mg/kg bw/day]	26
AAOEL [mg/kg bw]	
Inhalation absorption [%]	100

Oral absorption [%]	100
Dermal absorption [%] (concentrate)	0.16
Dermal absorption [%] (dilution) 6.25 [g a.s./l or kg]	1.7

Assessed uses:

Use	Crops	Max. application rate of the product [l or kg/ha]	Unit	Max. no. of applications	Interval between multiple applications [days]	Min. volume water [l/ha]	Max. volume water [l/ha]	Indoor/outdoor	Application method	Type of cultivation	Application technique	Buffer strip [m]	Drift reduction [%]
Use 1	Field crops	4	l/ha	2	14	100	400	Outdoor	Downward spraying	Normal	Vehicle-mounted	2-3	0

Operator – short term exposure:

Model data		Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL
Field crops/Outdoor/Downward spraying/Vehicle-mounted/Drift reduction: 0 %/75th percentile Crop density: Normal				
	Sulphur	Number of applications and application rate: 2 x 2.5 kg a.s./ha Dermal absorption (concentrate): 0.16 % Dermal absorption (in-use dilution): 1.7 %		
		M/L: Workwear App: Workwear	0.01	0.04

Worker:

	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL	Re-entry restriction [days]
Inspection, irrigation / Outdoor Work rate: 2 hours/day Interval: 14 days Body weight: 60 kg TC (potential): 12500 cm²/h TC (workwear (arms, body and legs covered)): 1400 cm²/h TC (workwear (arms, body and legs covered) and gloves): 1250 cm²/h TC (gloves): NA cm²/h				
Sulphur	Number of applications & application rate: 2 x 2.5 kg a.s./ha Dermal absorption: 1.7 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days			
	Potential	0.09	0.4	0
	Workwear	0.01	0.04	0
	Workwear and gloves	0.009	0.04	0
	Hands covered, no workwear			

Resident:

Model data		Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL
				Season: Not relevant Buffer zone: 2-3 m Drift reduction technology: 0 % Interval between treatments: 14 days Minimum volume of water: 100 l
Sulphur				Number of applications and application rate: 2 x 2.5 kg a.s./ha Dermal absorption: 1.7 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days
Resident child Body weight: 10 kg		Drift (75th perc.)	0.01	0.05
		Vapour (75th perc.)	0.0008	0.003
		Deposits (75th perc.)	0.005	0.02
		Re-entry (75th perc.)	0.01	0.05
		Sum (mean)	0.02	0.08
Resident adult Body weight: 60 kg		Drift (75th perc.)	0.003	0.01
		Vapour (75th perc.)	0.0003	0.001
		Deposits (75th perc.)	0.0005	0.002
		Re-entry (75th perc.)	0.007	0.03
		Sum (mean)	0.007	0.03

A 3.1.3 Calculations for prothioconazole-desthio

Information on product and active substance:

Product name	FHO04 (2 x 4 L)
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.
Product category	Other
Name of active substance	Protioconazole-desthio
Concentration of active substance [g a.s./l or kg]	45.34
AOEL [mg/kg bw/day]	0.01
AAOEL [mg/kg bw]	
Inhalation absorption [%]	100
Oral absorption [%]	100
Dermal absorption [%] (concentrate)	0
Dermal absorption [%] (dilution) 0.45 [g a.s./l or kg]	13

Assessed uses:

Use	Crops	Max. application rate of the product [l or kg/ha]	Unit	Max. no. of applications	Interval between multiple applications [days]	Min. volume water [l/ha]	Max. volume water [l/ha]	Indoor/outdoor	Application method	Type of cultivation	Application technique	Buffer strip [m]	Drift reduction [%]
Use 1	Field crops	4	l/ha	2	14	100	400	Outdoor	Downward spraying	Normal	Vehicle-mounted	5	0

Operator – short term exposure:

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL
Field crops/Outdoor/Downward spraying/Vehicle-mounted/Drift reduction: 0 %/75th percentile Crop density: Normal			
Prothioconazole-desthio	Number of applications and application rate: 2 x 0.18136 kg a.s./ha Dermal absorption (concentrate): 0 % Dermal absorption (in-use dilution): 13 %		
	M/L: Workwear App: Workwear	0.003	32

Worker:

Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL	Re-entry restriction [days]
Inspection, irrigation / Outdoor Work rate: 2 hours/day Interval: 14 days Body weight: 60 kg TC (potential): 12500 cm²/h TC (workwear (arms, body and legs covered)): 1400 cm²/h TC (workwear (arms, body and legs covered) and gloves): 1250 cm²/h TC (gloves): NA cm²/h			
Prothioconazole-desthio	Number of applications & application rate: 2 x 0.18136 kg a.s./ha Dermal absorption: 13 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days		
Potential	0.05	507	71
Workwear	0.006	56.8	0
Workwear and gloves	0.005	50.7	0
Hands covered, no workwear			

Resident:

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL
Season: Not relevant Buffer zone: 2-3 m Drift reduction technology: 0 % Interval between treatments: 14 days Minimum volume of water: 100 l			
Protioconazole-desthio	Number of applications and application rate: 2 x 0.18136 kg a.s./ha Dermal absorption: 13 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days		
Resident child Body weight: 10 kg	Drift (75th perc.)	0.006	64.1
	Vapour (75th perc.)	0.0008	8
	Deposits (75th perc.)	0.0008	8.4
	Re-entry (75th perc.)	0.007	68.4
	Sum (mean)	0.01	104
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.002	15.2
	Vapour (75th perc.)	0.0003	2.7
	Deposits (75th perc.)	0.0003	2.8
	Re-entry (75th perc.)	0.004	38
	Sum (mean)	0.004	42.2

A 3.2 Combined exposure calculations for prothioconazole-desthio and sulphur

Field crops (max. 2 x 4 L product/ha) – 5m buffer zone

Information on product and active substances:

Product name	FHO04 (2 x 4 L) 5m BZ
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.
Product category	Other
Name of active substance	Protioconazole-desthio
Concentration of active substance [g a.s./l or kg]	45.34
AOEL [mg/kg bw/day]	0.01
AAOEL [mg/kg bw]	
Inhalation absorption [%]	100
Oral absorption [%]	100
Dermal absorption [%] (concentrate)	0
Dermal absorption [%] (dilution) 0.45 [g a.s./l or kg]	13
Name of active substance	Sulphur
Concentration of active substance [g a.s./l or kg]	625
AOEL [mg/kg bw/day]	26
AAOEL [mg/kg bw]	
Inhalation absorption [%]	100
Oral absorption [%]	100
Dermal absorption [%] (concentrate)	0.16
Dermal absorption [%] (dilution) 6.25 [g a.s./l or kg]	1.7

Assessed uses:

Use	Crops	Max. application rate of the product [l or kg/ha]	Unit	Max. no. of applications	Interval between multiple applications [days]	Min. volume water [l/ha]	Max. volume water [l/ha]	Indoor/outdoor	Application method	Type of cultivation	Application technique	Buffer strip [m]	Drift reduction [%]
Use 1	Field crops	4	l/ha	2	14	100	400	Outdoor	Downward spraying	Normal	Vehicle-mounted	5	0

Operator – short term exposure:

Model data		Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL
Field crops/Outdoor/Downward spraying/Vehicle-mounted/Drift reduction: 0 %/75th percentile Crop density: Normal				
Prothioconazole-desthio	Number of applications and application rate: 2 x 0.18136 kg a.s./ha Dermal absorption (concentrate): 0 % Dermal absorption (in-use dilution): 13 %			
		M/L: Workwear App: Workwear	0.003	32

Model data		Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL
Sulphur		Number of applications and application rate: 2 x 2.5 kg a.s./ha Dermal absorption (concentrate): 0.16 % Dermal absorption (in-use dilution): 1.7 %		
		M/L: Workwear App: Workwear	0.01	0.04
Combined exposure				Hazard index
		M/L: Workwear App: Workwear		0.3

Worker:

Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL	Re-entry restriction [days]
			Inspection, irrigation / Outdoor Work rate: 2 hours/day Interval: 14 days Body weight: 60 kg TC (potential): 12500 cm²/h TC (workwear (arms, body and legs covered)): 1400 cm²/h TC (workwear (arms, body and legs covered) and gloves): 1250 cm²/h TC (gloves): NA cm²/h
Prothioconazole-desthio			Number of applications & application rate: 2 x 0.18136 kg a.s./ha Dermal absorption: 13 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days
Potential	0.05	507	71
Workwear	0.006	56.8	0
Workwear and gloves	0.005	50.7	0
Hands covered, no workwear			
Sulphur			Number of applications & application rate: 2 x 2.5 kg a.s./ha Dermal absorption: 1.7 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days
Potential	0.09	0.4	0
Workwear	0.01	0.04	0
Workwear and gloves	0.009	0.04	0
Hands covered, no workwear			
Combined		Hazard index	
potential		5.1	71
Workwear		0.6	0
Workwear and gloves		0.5	0
Hands covered, no workwear			0

Resident:

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL
			Season: Not relevant Buffer zone: 5 m Drift reduction technology: 0 % Interval between treatments: 14 days Minimum volume of water: 100 l
Prothioconazole-desthio			Number of applications and application rate: 2 x 0.18136 kg a.s./ha Dermal absorption: 13 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days
Resident child Body weight: 10 kg	Drift (75th perc.)	0.004	42.8
	Vapour (75th perc.)	0.0008	8
	Deposits (75th perc.)	0.0003	3.5
	Re-entry (75th perc.)	0.007	68.4
	Sum (mean)	0.009	88.7
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0008	7.8
	Vapour (75th perc.)	0.0003	2.7
	Deposits (75th perc.)	0.0001	1.1
	Re-entry (75th perc.)	0.004	38
	Sum (mean)	0.004	37.8
Sulphur			Number of applications and application rate: 2 x 2.5 kg a.s./ha Dermal absorption: 1.7 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days
Resident child Body weight: 10 kg	Drift (75th perc.)	0.008	0.03
	Vapour (75th perc.)	0.0008	0.003
	Deposits (75th perc.)	0.002	0.007
	Re-entry (75th perc.)	0.01	0.05
	Sum (mean)	0.02	0.06
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.001	0.006
	Vapour (75th perc.)	0.0003	0.001
	Deposits (75th perc.)	0.0002	0.0008
	Re-entry (75th perc.)	0.007	0.03
	Sum (mean)	0.007	0.03
Combined exposure			Hazard index
Resident child Body weight: 10 kg	Drift (75th perc.)		0.4
	Vapour (75th perc.)		0.08
	Deposits (75th perc.)		0.03
	Re-entry (75th perc.)		0.7
	Sum (mean)		0.9
Resident adult Body weight: 60 kg	Drift (75th perc.)		0.08
	Vapour (75th perc.)		0.03
	Deposits (75th perc.)		0.01
	Re-entry (75th perc.)		0.4
	Sum (mean)		0.4

Field crops (max. 2 x 4 L product/ha) – DRT

Information on product and active substances:

Product name	FHO04 (2 x 4 L) DRT
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.
Product category	Other
Name of active substance	Protioconazole-desthio
Concentration of active substance [g a.s./l or kg]	45.34
AOEL [mg/kg bw/day]	0.01
AAOEL [mg/kg bw]	
Inhalation absorption [%]	100
Oral absorption [%]	100
Dermal absorption [%] (concentrate)	0
Dermal absorption [%] (dilution) 0.45 [g a.s./l or kg]	13
Name of active substance	Sulphur
Concentration of active substance [g a.s./l or kg]	625
AOEL [mg/kg bw/day]	26
AAOEL [mg/kg bw]	
Inhalation absorption [%]	100
Oral absorption [%]	100
Dermal absorption [%] (concentrate)	0.16
Dermal absorption [%] (dilution) 6.25 [g a.s./l or kg]	1.7

Assessed uses:

Use	Crops	Max. application rate of the product [l or kg/ha]	Unit	Max. no. of applications	Interval between multiple applications [days]	Min. volume water [l/ha]	Max. volume water [l/ha]	Indoor/outdoor	Application method	Type of cultivation	Application technique	Buffer strip [m]	Drift reduction [%]
Use 1	Field crops	4	l/ha	2	14	100	400	Outdoor	Downward spraying	Normal	Vehicle-mounted	2-3	50

Operator – short term exposure:

Model data		Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL
Field crops/Outdoor/Downward spraying/Vehicle-mounted/Drift reduction: 50 %/75th percentile Crop density: Normal				
Prothioconazole-desthio	Number of applications and application rate: 2 x 0.18136 kg a.s./ha Dermal absorption (concentrate): 0 % Dermal absorption (in-use dilution): 13 %			
		M/L: Workwear App: Workwear	0.001	14.3
Sulphur	Number of applications and application rate: 2 x 2.5 kg a.s./ha Dermal absorption (concentrate): 0.16 % Dermal absorption (in-use dilution): 1.7 %			

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL
	M/L: Workwear App: Workwear	0.008	0.03
Combined exposure			Hazard index
	M/L: Workwear App: Workwear		0.1

Worker:

Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL	Re-entry restriction [days]
			Inspection, irrigation / Outdoor Work rate: 2 hours/day Interval: 14 days Body weight: 60 kg TC (potential): 12500 cm²/h TC (workwear (arms, body and legs covered)): 1400 cm²/h TC (workwear (arms, body and legs covered) and gloves): 1250 cm²/h TC (gloves): NA cm²/h
Prothioconazole-desthio			Number of applications & application rate: 2 x 0.18136 kg a.s./ha Dermal absorption: 13 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days
Potential	0.05	507	71
Workwear	0.006	56.8	0
Workwear and gloves	0.005	50.7	0
Hands covered, no workwear			
Sulphur			Number of applications & application rate: 2 x 2.5 kg a.s./ha Dermal absorption: 1.7 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days
Potential	0.09	0.4	0
Workwear	0.01	0.04	0
Workwear and gloves	0.009	0.04	0
Hands covered, no workwear			
Combined		Hazard index	
potential		5.1	71
Workwear		0.6	0
Workwear and gloves		0.5	0
Hands covered, no workwear			0

Resident:

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL
			Season: Not relevant Buffer zone: 2-3 m Drift reduction technology: 50 % Interval between treatments: 14 days Minimum volume of water: 100 l
Prothioconazole-desthio			Number of applications and application rate: 2 x 0.18136 kg a.s./ha Dermal absorption: 13 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days
Resident child Body weight: 10 kg	Drift (75th perc.)	0.003	32
	Vapour (75th perc.)	0.0008	8
	Deposits (75th perc.)	0.0004	4.2
	Re-entry (75th perc.)	0.007	68.4
	Sum (mean)	0.008	83.2
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0008	7.6
	Vapour (75th perc.)	0.0003	2.7
	Deposits (75th perc.)	0.0001	1.4
	Re-entry (75th perc.)	0.004	38
	Sum (mean)	0.004	37.6
Sulphur			Number of applications and application rate: 2 x 2.5 kg a.s./ha Dermal absorption: 1.7 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days
Resident child Body weight: 10 kg	Drift (75th perc.)	0.006	0.02
	Vapour (75th perc.)	0.0008	0.003
	Deposits (75th perc.)	0.002	0.009
	Re-entry (75th perc.)	0.01	0.05
	Sum (mean)	0.02	0.06
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.001	0.005
	Vapour (75th perc.)	0.0003	0.001
	Deposits (75th perc.)	0.0002	0.001
	Re-entry (75th perc.)	0.007	0.03
	Sum (mean)	0.007	0.03
Combined exposure			Hazard index
Resident child Body weight: 10 kg	Drift (75th perc.)		0.3
	Vapour (75th perc.)		0.08
	Deposits (75th perc.)		0.04
	Re-entry (75th perc.)		0.7
	Sum (mean)		0.8
Resident adult Body weight: 60 kg	Drift (75th perc.)		0.08
	Vapour (75th perc.)		0.03
	Deposits (75th perc.)		0.01
	Re-entry (75th perc.)		0.4
	Sum (mean)		0.4

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

Not required.