FINAL REGISTRATION REPORT

Part B

Section 6

Mammalian Toxicology

Detailed summary of the risk assessment

Product code: BAS 758 00 F

Product name(s): Revyflex Plus

Chemical active substance(s):

Mefentrifluconazole, 66.6 g/L

Metrafenone, 100 g/L

Pyraclostrobin, 80 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: BASF

Submission date: March 2022

MS Finalisation date: 27/01/2023

Version history

When	What
03/2022	Initial dRR – BASF DocID 2021/2053450
04/2022	Dossier sent for evaluation
10/2022	zRMS evaluation of dRR
January 2023	Final version prepared by zRMS after Commenting period

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Evaluator comments:
The text highlighted in grey was provided by the evaluator.

During the Commenting period, the final content of mefentrifluconazole was corrected to 66.6 g/L instead of 66.7 g/L due to a density correction (1.092 g/cm³ instead of 1.091 g/cm³). This change does not affect the toxicological assessment of the product conducted for the content of 66.7 g/L.

6 Mammalian Toxicology (KCP 7)

6.1 Summary

Table 6.1-1: Information on BAS 758 00 F*

Product name and code	BAS 758 00 F
Formulation type	Emulsion concentrate [EC]
Active substance(s) (incl. content)	Mefentrifluconazole, 66.~~67~~ g/L Metrafenone, 100 g/L Pyraclostrobin, 80 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 BAS 758 00 F 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 BAS 758 00 F according to Regulation (EC) No 1272/2008

Hazard class(es), categories:	Acute Tox. 4 (oral) Acute Tox. 4 (inhalation – mist) Skin ~~Corr./~~Irrit. 2 Eye Dam./~~Irrit.~~ 1 Skin Sens. 1 STOT SE 3 Aquatic Acute 1 Aquatic Chronic 1
Hazard pictograms or Code(s) for hazard pictogram(s):	 **GHS05**, **GHS07**, **GHS09**
Signal word:	Danger
Hazard statement(s):	**H318: Causes serious eye damage** **H315: Causes skin irritation** **H317: May cause an allergic skin reaction** **H335: May cause respiratory irritation** **H302 + H332: Harmful if swallowed or inhaled** **H400: Very toxic to aquatic life** **H410: Very toxic to aquatic life with long lasting effects**
Precautionary statement(s): - Prevention: - Response: - Storage - Disposal	P101: If medical advice is needed, have product container or label at hand P102: Keep out of reach of children P103: Read carefully and follow all instructions P260: Do not breathe mist or vapour P264: Wash contaminated body parts thoroughly after handling P270: Do not eat, drink or smoke when using this product **P271: Use only outdoors or in a well-ventilated area** P272: Contaminated work clothing should not be allowed out of the workplace **P280: Wear protective gloves and eye protection or face protection** **P310: Immediately call a POISON CENTER or physician** **P305 + P351 + P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.** P304 + P340: IF INHALED: Remove person to fresh air and keep comfortable for breathing P302 + P352: IF ON SKIN: Wash with plenty of soap and water P330: Rinse mouth P391: Collect spillage P362 + P364: Take off contaminated clothing and wash it before reuse **P403 + P233: Store in a well-ventilated place. Keep container tightly closed.** P405: Store locked up **P501: Dispose of contents and container to hazardous or special waste collection point.**
Additional labelling phrases:	To avoid risks to human health and the environment, comply with the instructions for use. [EUH401].

Table 6.1-3: Summary of risk assessment for operators, workers, bystanders and residents for BAS 758 00 F

	Result	PPE / Risk mitigation measures
Operators	Acceptable	~~Gloves and workwear during mixing/loading and application~~ Workwear due to exposure calculations. Protective clothing, protective gloves, face/eye protection during

	Result	PPE / Risk mitigation measures
		handling, mixing and loading due to hazard characterisation.
Workers	Acceptable	Work wear (arms, body and legs covered) ~~Long sleeved shirt, long trousers ("permeable") but no gloves~~
Bystanders	Acceptable	None
Residents	Acceptable	None

No unacceptable risk for operators, workers, bystanders and residents was identified when the product is used as intended and provided that the PPE/ risk mitigation measures stated in Table 6.1-3 are applied.

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, bystander or resident 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) Mefentrifluconazole b) Metrafenone c) Pyraclostrobin**	**Water L/ha min / max**			**Operator**	**Worker**	**Bystander**	**Residents**
1-5	cereals	F	Spraying, LCTM	2; 2 (14d)	a) 0.100 b) 0.150 c) 0.120	100 - 300		critical gap for operator, worker, bystander or resident exposure based on EFSA AOEM	R	A	A	A
6-10	cereals	F	Spraying, LCTM	1; 1	a) ~~0.067 -~~ 0.100 b) ~~0.100 -~~ 0.150 c) ~~0.080 -~~ 0.120	100 - 300			R	A	A	A
11-15	cereals	F	Spraying, LCTM	2; 2 (14d)	a) ~~0.033 -~~ 0.067 b) ~~0.050 -~~ 0.100 c) ~~0.040 -~~ 0.080	100 - 300			R	A	A	A

* 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

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)

	BAS 750 F	**BAS 560 F**	**BAS 500 F**
Common Name	Mefentrifluconazole	Metrafenone	Pyraclostrobin
CAS-No.	1417782-03-6	220899-03-6	175013-18-0
Classification and proposed labelling With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended)			
Hazard classes (s), categories:	Skin Sens. 1	None	Acute Tox. 3 (Inhalation - mist), Skin ~~Corr.~~Irrit. 2, STOT SE 3 (iritating to respiratory system)*
Code(s) for hazard pictogram(s):	(Exclamation mark - GHS07)	–	(Skull&crossbones – GHS 06)
Signal word:	Warning	–	Danger
Hazard statement(s):	H317: May cause an allergic skin reaction	–	H331: Toxic if inhaled. H315: Causes skin irritation. H335: May cause respiratory irritation
Precautionary statement(s):	P261: Avoid breathing dust or fume P272: Contaminated work clothing should not be allowed out of the workplace. P280: Wear protective gloves P302 + P352: IF ON SKIN: Wash with plenty of soap and water. P333 + P313: If skin irritation or rash occurs occurs: Get medical advice/attention. P362 + P364: Take off contaminated clothing and wash it before reuse. P501: Dispose of contents and container to hazardous or special waste collection point.	–	P271: Use only outdoors or in a well-ventilated area P273: Avoid release to the environment P280: Wer protective gloves P260 Do not breathe dust/gas/mist/vapours P264 Wash with plenty of water and soap thoroughly after handling. P311 Call a POISON CENTER or doctor/physician. P304 + P340 IF INHALED: Remove person to fresh air and keep comfortable for breathing. P303 + P352 IF ON SKIN (or hair): Wash with plenty of soap and water. P391 Collect spillage. P362+P364: Take off contaminated clothing and wash before reuse. P403 + P233 Store in a well-ventilated place. Keep container tightly closed. P405 Store locked up. P501 Dispose of contents/container to hazardous or special waste collection point.
Reference:	Com.Del.Reg. (EU) No. 2020/1182	–	Com.Reg. (EC) No. 790/2009
Agreed EU endpoints			
AOEL systemic	0.035 mg/kg bw/d (no correction for oral absorption required)	0.43 mg/kg bwd (correction not required)	0.015 mg/kg bw/d (corrected for 50 % oral absorption)
AAOEL	0.15 mg/kg bw/d	Not allocated	Not allocated
Reference	EFSA Journal 2018; 16(7):5379	EFSA Scientific Report (2006); 58, 1-72	Review report for the active substance pyraclostrobin SANCO/1420/2001-Final, 8. September 2004

	BAS 750 F	BAS 560 F	BAS 500 F
Conditions to take into account/critical areas of concern with regard to toxicology			
Review Report/EFSA Conclusion for active substance	None related to toxicology	None related to toxicology	None related to toxicology

* Based on BASF self-classification

6.3 Toxicological Evaluation of Plant Protection Product

A summary of the toxicological evaluation for BAS 758 00 F 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 BAS 758 00 F

Type of test, species, model system (Guideline)	Result	Acceptability	Classification (acc. to the criteria in Reg. 1272/2008)	Reference (DocID)
Acute oral toxicity, predicted from composition	LD_{50} > 2000 mg/kg bw	Yes	No classification	CLP 1272/2008
LD_{50} oral, rat (OECD 423)	300 < LD_{50} < 2000 mg/kg bw ***1792 mg/kg bw****	Yes	**Acute Tox. 4, H302**	2020/2101764
LD_{50} dermal, rat WoE (Composition + oral-to-dermal extrapolation)	>2000 mg/kg bw	Yes	No classification	CLP 1272/2008
Acute inhalation toxicity, predicted from composition	LC_{50} = 5.05 mg/L	Yes	No classification (borderline)	CLP 1272/2008
LC_{50} inhalation, rat (OECD 436)	**ca. 5 mg/L air**	Yes	**Acute Tox. 4, H332 (+STOT SE 3, H335)**	2021/2021366
Skin corrosion / irritation, predicted from composition)	Irritant	Yes	Skin Irrit. 2, H315	CLP 1272/2008
Skin irritation, *in vitro* (SCT+SIT) (OECD 431 + OECD 439)	Skin irritant in vitro	Yes	**Skin Irrit. 2, H315**	2020/2086972
Eye irritation, *in vitro EpiOcular test* (OECD 492)	Irritant / Eye Damage	Yes	Eye Irrit. 2, H319 or Eye Dam. 1, H318	2020/2086973
Eye irritation, *in vitro Isolated Chicken Eye test* (OECD 438)	Non-irritant	Yes	No classification	2021/2007253
WoE (Composition + i*n-vitro* data)	Eye damage	Yes	**Eye Dam. 1, H318**	CLP 1272/2008
Skin sensitisation (Composition)	Sensitising	Yes	Skin Sens. 1, H317	CLP 1272/2008
Supplementary studies for combinations of plant	No data – not required			–

protection products				

based on Probit analysis according to Finney

Table 6.3-2: Additional toxicolog. information relevant for classification/labelling of BAS 758 00 F

	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)	Mefentrifluconazole (6.1 %)	Skin Sens 1 (≥ 1%)	Reg. 1272/2008	H317
	Pyraclostrobin (7.33 %)	STOT SE 3 (Resp. Irrit) (≥ 20%)		H335*
Toxicological properties of non-active substance(s) (relevant for classification of product)	2-ethyl hexanol (< 2.29 %)	STOT SE 3 (Resp. Irrit) (≥ 20%)	MSDS**	H335*
	N,N dimethyldecan-1-amide, (≤ 3.89%)	STOT SE 3 (Resp. Irrit) (≥ 20%)	MSDS**	H335*
	N,N-dimethyloctan-1 amide; (≤ 4.674 ~~5.057~~%)	Eye Dam. 1; (≥ 3%) STOT SE 3 (Resp. Irrit) (≥ 20%)	MSDS**	H318 H335*
	Benzenesulfonic acid, 4-C10-13-sec-alkyl derivs., calcium salts; (< 3.206 %)	Eye Dam. 1; (≥ 3%)	MSDS**	H318
Further toxicological information	No data – not required			

* Max total concentration of ingredients with STOT SE 3 is 18.6%, thus slighlty below the 20% classification trigger. Classification with H335 is justified based on additional evidence for relevant respiratory irritation potential observed in acute inhalation toxicity study with the product.

** Material safety data sheet by the applicant

6.4 Toxicological Evaluation of Groundwater Metabolites

Comments of zRMS:	Acceptable. Details in the dRR Part B10.

All concentrations for mefentrifluconazole and pyraclostrobin and metrafenone metabolites are predicted to stay below 0.1 µg/L – no groundwater assessment is required (see Section 8.8 of this dossier).

6.5 Dermal Absorption (KCP 7.3)

A summary of the dermal absorption rates for the active substances in BAS 758 00 F is presented in the following table.

Table 6.5-1: Dermal absorption rates for active substances in BAS 758 00 F

	Mefentrifluconazole		Metrafenone		Pyraclostrobin	
	Value	Reference	Value	Reference	Value	Reference
Concentrate	0.2 %	New study reported in	25 % (default)	EFSA Journal 2017;	0.0078 %	New study reported in

	Mefentrifluconazole		Metrafenone		Pyraclostrobin	
	Value	**Reference**	**Value**	**Reference**	**Value**	**Reference**
		Appendix 2		15(6):4873 Table 2 (p. 19)		Appendix 2
Dilution (1:200)	6.3 %	New study reported in Appendix 2	70 % (default)	EFSA Journal 2017; 15(6):4873 Table 2 (p. 19)	2.6 %	New study reported in Appendix 2
Dilution (1:400)	Not tested				2.2 %	New study reported in Appendix 2
Dilution (1:600)	7.8 %	New study reported in Appendix 2				Not tested

6.5.1 Justification for proposed values - mefentrifluconazole

Proposed dermal absorption rates for mefentrifluconazole (BAS 750 F) are based on dermal absorption studies with BAS 758 00 F (identical to the product applied for registration). The estimates were derived in accordance to latest EFSA Guidance (2017). The study has not previously been evaluated within an EU peer review process, therefore a full summary of the study on the dermal absorption of BAS 750 F/BAS 758 00 F is described in detail in Appendix 2. A corresponding excel evaluation file (EFSA Version 3) is provided separately with this dossier submission. The study results are summarized in the following table.

Table 6.5-2: Summary of the results of submitted dermal absorption studies for BAS 750 F

Test	Dermal absorption Concentrate [g/L]	Dermal absorption Spray dilution (dilution factor)	Formulation in study	Acceptability of study	Justification provided on representativity of study formulation for current product	Acceptability of justification	Reference*
In vitro (human)	0.2 % [66.7 g/L]	6.3 % (1:200) 7.8 % (1:600)	BAS 758 00 F	Yes	Yes (see Appendix 2)	Yes	Rieken et al., 2020~~a~~

* indicates that a study was reviewed at EU level

6.5.2 Justification for proposed values – metrafenone

No data on dermal absorption for metrafenone in BAS 758 00 F is available. Justifications for default values according to Guidance on Dermal Absorption (EFSA Journal 2017; 15(6):4873) are presented in the following table.

Table 6.5-3: Default dermal absorption rates for metrafenone

	Value	Justification for value	Acceptability of justification
Concentrate	~~10 %~~ 25 %	BAS 758 00 F is an emulsion concentrate (EC). Therefore, the default value for organic solvent-based formulation types such as emulsion	Yes

	Value	Justification for value	Acceptability of justification
		concentrates, was selected.	
Dilution	~~50 %~~ 70%	See justification above.	Yes

6.5.3 Justification for proposed values - pyraclostrobin

Proposed dermal absorption rates for pyraclostrobin (BAS 500 F) are based on dermal absorption studies with BAS 758 00 F (identical to the product applied for registration). The estimates were derived in accordance to latest EFSA Guidance (2017). The study has not previously been evaluated within an EU peer review process, therefore a full summary of the study on the dermal absorption of BAS ~~7~~500 F/BAS 758 00 F is described in detail in Appendix 2. A corresponding excel evaluation file (EFSA Version 3) is provided separately with this dossier submission. The study results are summarized in the following table.

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

Test	Dermal absorption Concentrate [g/L]	Dermal absorption Spray dilution (dilution factor)	Formulation in study	Acceptability of study	Justification provided on representativity of study formulation for current product	Acceptability of justification	Reference*
In vitro (human)	0.00~~7~~8 % [80 g/L]	2.6 % (1:200) 2.2 % (1:400)	BAS 758 00 F	Yes	Yes (see Appendix 2)	Yes	Rieken et al., 2021~~0b~~

* indicates that a study was reviewed at EU level

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	BAS 758 00 F		
Formulation type	EC		
Category	Fungicide		
Container size(s), short description	Commercialization is intended in various container sizes (0.25 L to 50 L containers with openings of either 42 mm or 54 mm inner diameter).		
Active substance(s) (incl. content)	**Active substance 1** Mefentrifluconazole 66.~~7~~ g/L	**Active substance 2** Pyraclostrobin 80 g/L	**Active substance ~~2~~3** Metrafenone 100 g/L
AOEL systemic	0.035 mg/kg bw/d	0.015 mg/kg bw/d	0.43 mg/kg bw/d
Acute AOEL systemic	0.15 mg/kg bw/d	Not allocated	Not allocated
Inhalation absorption	100 %	100 %	100 %
Oral absorption	>80 %	50 %	>80 %
Dermal absorption	Concentrate: 0.2 %	Concentrate: 0.00~~7~~8 %	Concentrate: 25 %

	Dilution 1: 6.3 % (Dilution rate: 1:200) Dilution 2: 7.8 % (Dilution rate: 1:600)	Dilution 1: 2.6 % (Dilution rate: 1:200) Dilution 2: 2.2 % (Dilution rate: 1:400)	Dilution: 705 % (Default assumptions following EFSA Journal 2017; 15(6):4873 Table 2 (p. 19)

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 of Section 6, Chapter 6.1. A list of all intended uses within the central zone/ EU is given in Part B, Section 0. The critical GAP has been summarized as below:

Crop	**Application rate**		**Spray dilution**	**Application equipment**	**Maximum number of applications**
	(g a.s./ha)		(L/ha)		
Cereal crops (field application only)	Mefentrifluconazole Pyraclostrobin Metrafenone	100 120 150	100 - 300	Tractor mounted boom sprayers (LCTM*)	2 (14 day spray interval)

*Low Crop Tractor Mounted

Justification

Cereals are the crops intended for the preparation BAS 758 00 F. The product is applied by professional applicators. The maximum single application rate investigated is 1.5 L/ha BAS 758 00 F. The minimum intended water volume of 100 L/ha is considered for drift estimates. The maximum intended number of 2 applications is considered for re-entry estimates with the recommended spray interval of 14 days.

6.6.2 Operator exposure (KCP 7.2.1)

Comments of zRMS:	The operator exposure calculations for the proposed uses of BAS 758 00 F conducted by the Applicant using the EFSA calculator are acceptable. Evaluator re-calculated the operator exposure for metrafenone using correct default value of dermal absorption – 70% for dilution according to the EFSA guidance (2017). The corrected spreadsheets were added into Appendix 3. The predicted longer term systemic operator exposure for application via tractor mounted boom sprayer is within acceptable limit. The values were calculated as 4.34% of the AOEL for mefentrifluconazole, 3.84% of the AOEL for pyraclostrobin and 25.89% of the AOEL for metrafenon for an operator wearing work wear (arms, body and legs covered). For mefentrifluconazole the AAOEL value is determined, therefore the predicted acute operator exposure for mefentrifluconazole was calculated as 7.12% of the AAOEL for an operator wearing work wear. Taking into consideration the classification of the BAS 758 00 F regarding human health, the following operator protection phrase is needed: *Protective clothing, protective gloves, face/eye protection during handling, mixing and loading due to hazard characterisation.*

6.6.2.1 Estimation of operator exposure

A summary of the exposure models used for estimation of operator exposure to the active substances during application of BAS 758 00 F according to the critical use is presented in Table 6.6-2. Outcome of the estimation is presented in Table 6.6-3. Detailed calculations are in Appendix 03.

Table 6.6-2: Exposure models for intended uses

Critical use(s)	Cereal crops (max. 1.5 L product/ha)
Model(s)	EFSA guidance AOEM [European Food Safety Authority (2014) Guidance on the Assessment of Exposure for

	Operators, Workers, Residents and Bystanders in Risk Assessment for Plant Protection Products. EFSA Journal 2014;12(10):3874 [55 pp.]. doi:10.2903/j.efsa.2014.3874 .]

Table 6.6-3: Estimated operator exposure

Longer term exposure predictions					
		Mefentrifluconazole		**Pyraclostrobin**	
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, outdoor downward spraying (LCTM) Application rate: 1.5 L product/ha					
EFSA guidance AOEM (75th percentile estimate) Body weight: 60 kg	Potential exposure	0.0023	6.60	0.0008	5.35
	no PPE*	0,.015	4.34	0.00057	3.84
	+ gloves and work wear (arms, body and legs covered) during mixing/loading and during application.	0.00029	0.84	0.00021	1.42
		Metrafenone			
	Potential exposure	~~0.1805~~ 0.1791	~~41.99~~ 41.65		
	no PPE*	~~0.1123~~ 0.1114	~~26.12~~ 25.89		
	+ gloves and work wear (arms, body and legs covered) during mixing/loading and gloves and during application.	~~0.0051~~ 0.0049	~~1.18~~ 1.14		
Acute exposure predictions (only applicable to mefentrifluconazole)					
		Mefentrifluconazole			
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**% of systemic acute AAOEL**		
Vehicle-mounted, outdoor downward spraying (LCTM) Application rate: 1.5 L product/ha					
EFSA guidance AOEM (95th percentile estimate) Body weight: 60 kg	Potential exposure	0.0167	11.14		
	no PPE*	0.01068	7.12		
	+ gloves and work wear (arms, body and legs covered) during mixing/loading and gloves and during	0.0050	3.36		

	application.			

* no PPE: Operator wearing long sleeved shirt, long trousers (“permeable”) but no gloves

6.6.3 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 considering above mentioned personal protective equipment (PPE), a study to provide measurements of operator exposure was not necessary and was therefore not performed.

6.6.4 Worker exposure (KCP 7.2.3)

Comments of zRMS:	The worker exposure calculations for the proposed uses of BAS 758 00 F conducted by the Applicant using the EFSA calculator are acceptable. Evaluator re-calculated the worker exposure for metrafenone using correct default value of dermal absorption – 70% for dilution according to the EFSA guidance (2017). The corrected spreadsheets were added into Appendix 3. The potential worker exposure undertaking crop inspection activity is within acceptable limit assuming workers are wearing workwear (arms, body and legs covered). The values were calculated as 4.34% of the AOEL for mefentrifluconazole, 5.02% of the AOEL for pyraclostrobin and 5.89% of the AOEL for metrafenone. As a standard rule, crops treated by BAS 758 00 F should not be re-entered before spray deposit on leaf surfaces has completely dried.

6.6.4.1 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 BAS 758 00 F according to the critical use(s). Outcome of the estimation is presented in

Table 6.6-5. Detailed calculations are in Appendix 03.

Table 6.6-4: Exposure models for intended uses

Critical use(s)	Cereal crops (max. 2 x 1.5 L product/ha with 14-day spray interval)
Model	EFSA guidance AOEM [European Food Safety Authority (2014) Guidance on the Assessment of Exposure for Operators, Workers, Residents and Bystanders in Risk Assessment for Plant Protection Products. EFSA Journal 2014;12(10):3874 [55 pp.]. doi:10.2903/j.efsa.2014.3874 .]

Table 6.6-5: Estimated worker exposure

		Mefentrifluconazole	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
Number of applications and application rate:		2 x 0.1 kg a.s./ha	
2 hours/day (1), TC: 12500 cm^2/person/h(2) (potential exposure) TC: 1400 cm^2/person/h (2) (workwear)3 Body weight: 60 kg	Potential exposure	0.01357	38.78
	no PPE (3)	0.00152	4.34
	with PPE ~~(4)~~	no TC available for this assessment	-

		Pyraclostrobin		Metrafenone	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
Number of applications and application rate:		2 x 0.12 kg a.s./ha		2 x 0.15 kg a.s./ha	
2 hours/day (1), TC: 12500 cm^2/person/h(2) (potential exposure) TC: 1400 cm^2/person/h (2) (workwear)3 Body weight: 60 kg	Potential exposure	0.00672	44.81	~~0.24238~~ 0.2262	~~56.37~~ 52.61
	no PPE(3)	0.00075	5.02	~~0.02714~~ 0.02533	~~6.31~~ 5.89
	with PPE	no TC available for this assessment	-	no TC available for this assessment	-

(1) 2 h/day for maintenance, inspection or irrigation activities etc.

(2) e.g. EUROPOEM II, 2002, Post-Application Exposure of Workers to Pesticides in Agriculture or US-EPA policy paper [EPA, Science Advisory Council for Exposure; Agricultural Transfer Coefficients, Policy # 3.]. TC: Transfer coefficient

(3) no PPE: Worker wearing long sleeved shirt, long trousers (“permeable”) but no gloves

6.6.4.2 Refinement of generic DFR value (KCP 7.2)

Since model estimates based on default assumptions for DFR values have shown a safe use, further refinement has not been considered necessary and has thus not been performed.

6.6.4.3 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 work clothing, a study to provide measurements of worker exposure was not necessary and was therefore not performed.

6.6.5 Bystander and resident exposure (KCP 7.2.2)

Comments of zRMS:	The bystander and resident exposure calculations for the proposed uses of BAS 758 00 F conducted by the Applicant using the EFSA calculator are acceptable. Evaluator re-calculated the bystander and resident exposure for metrafenone using correct default value of dermal absorption – 70% for dilution according to the EFSA guidance (2017). The corrected spreadsheets were added into Appendix 3. <u>Resident exposure:</u> The predicted exposure for the child and adult residents resulted from spray drift, vapour, surface deposits, entry into treated crops and sum of all pathways calculated for mefentrifluconazole, pyraclostrobin and metrafenone is within acceptable limits, therefore the use of BAS 758 00 F does not cause unacceptable health risk. <u>Bystander exposure:</u> For mefentrifluconazole the AAOEL value is determined, therefore the bystander exposure for mefentrifluconazole was calculated. The estimated bystander exposure for a child and adult resulted from spray drift, vapour, surface deposits and entry into treated crops for mefentrifluconazole is within acceptable limits. For pyraclostrobin and metrafenon the AAOEL values are not determined, therefore it is assumed that bystander exposure is covered by the resident exposure assessment for pyraclostrobin and metrafenon.

6.6.5.1 Estimation of bystander and resident exposure

Table 6.6-6 shows the exposure model(s) used for estimation of bystander and resident exposure to the active substances mefentrifluconazole, pyraclostrobin and metrafenone. Outcome of the estimation is presented in Table 6.6-7 and Table 6.6-8.

Table 6.6-7: Estimated bystander exposure to mefentrifluconazole

		Mefentrifluconazole		Pyraclostrobin and Metrafenone	
Model data		**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
AOEM: Tractor mounted boom spray application outdoors to low crops Application rate: 2 x 1.5 L product/ha corresponding to 2x0.1 kg mefentrifluconazole /ha, 2x0.12 kg pyraclostrobin/ha, 2x0.15 kg metrafenone/ha					
Bystanders (adult)	Spray drift	0.00105	0.70	**Note:** **Pyraclostrobin**: In the absence of an acute AOEL (AAOEL) proposed in the current review process (AIR3, RMS Germany), only the respective resident exposure assessment was calculated with the EFSA model and is presented here. **Metrafenone: No** acute AOEL (AAOEL) has been set, thus no bystander exposure assessment and risk evaluation is presented here.	
	Vapour	0.00023	0.15		
	Surface deposits	0.00022	0.15		
	Entry treated crops	0.00102	0.68		
Bystanders (children)	Spray drift	0.00393	2.62		
	Vapour	0.00107	0.71		
	Surface deposits	0.00084	0.56		
	Entry treated crops	0.00183	1.22		

Table 6.6-8: Estimated resident exposure to mefentrifluconazole, pyraclostrobin and metrafenone

		Mefentrifluconazole		Pyraclostrobin		
Model data		**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg/day)**		**% of systemic AOEL**
AOEM: Tractor mounted boom spray application outdoors to low crops Application rate: 2 x 1.5 L product/ha corresponding to 2x0.1 kg mefentrifluconazole /ha, 2x0.12 kg pyraclostrobin/ha, 2x0.15 kg metrafenone/ha						
Residents (adult) Drift rate: 5.6 % (2-3 m drift) Body weight: 60 kg	Spray drift	0.00041	1.16	Spray drift	0.00020	1.35
	Vapour	0.00023	0.66	Vapour	0.00023	1.53
	Surface deposits	0.00007	0.21	Surface deposits	0.00004	0.24
	Entry treated crops	0.00102	2.91	Entry treated crops	0.00050	3.36
	All pathways (mean)	0.00129	3.68	All pathways (mean)	0.00075	5.04
Residents (children) Drift rate: 5.6 % (2-3 m drift) Body weight: 10 kg	Spray drift	0.00171	4.89	Spray drift	0.00086	5.75
	Vapour	0.00107	3.06	Vapour	0.00107	7.13
	Surface deposits	0.00029	0.85	Surface deposits	0.00016	1.08
	Entry treated crops	0.00183	5.24	Entry treated crops	0.00091	6.05
	All pathways (mean)	0.00369	10.56	All pathways (mean)	0.00239	15.96
	Metrafenone					

	~~Mefentrifluconazole~~			~~Pyraclostrobin~~	
~~Model data~~	~~Total absorbed dose (mg/kg/day)~~		~~% of systemic AOEL~~	~~Total absorbed dose (mg/kg/day)~~	~~% of systemic AOEL~~
	~~Total absorbed dose (mg/kg/day)~~		~~% of systemic AOEL~~		
~~Residents (adult) Drift rate: 5.6 % (2-3 m drift) Body weight: 60 kg~~	~~Spray drift~~	~~0.00723~~	~~1.68~~		
	~~Vapour~~	~~0.00023~~	~~0.05~~		
	~~Surface deposits~~	~~0.00132~~	~~0.31~~		
	~~Entry treated crops~~	~~0.01818~~	~~4.23~~		
	~~All pathways (mean)~~	~~0.01913~~	~~4.45~~		
~~Residents (children) Drift rate: 5.6 % (2-3 m drift) Body weight: 10 kg~~	~~Spray drift~~	~~0.03019~~	~~7.02~~		
	~~Vapour~~	~~0.00107~~	~~0.25~~		
	~~Surface deposits~~	~~0.00303~~	~~0.71~~		
	~~Entry treated crops~~	~~0.03272~~	~~7.61~~		
	~~All pathways (mean)~~	~~0.04601~~	~~10.70~~		

. Detailed calculations are in Appendix 03.

Table 6.6-6: Exposure models for intended uses

Critical use(s)	Cereal crops (max. 2 x 1.5 L product/ha)
Model	- European Food Safety Authority (2014) Guidance on the Assessment of Exposure for Operators, Workers, Residents and Bystanders in Risk Assessment for Plant Protection Products EFSA Journal 2014;12(10):3874 [55 pp.]. doi:10.2903/j.efsa.2014.3874 .

Table 6.6-7: Estimated bystander exposure to mefentrifluconazole

	Mefentrifluconazole			**Pyraclostrobin and Metrafenone**	
Model data	**Total absorbed dose (mg/kg/day)**		**% of systemic AAOEL**	**Total absorbed dose (mg/kg/day)**	**% of systemic AAOEL**
AOEM: Tractor mounted boom spray application outdoors to low crops Application rate: 2 x 1.5 L product/ha corresponding to 2x0.1 kg mefentrifluconazole /ha, 2x0.12 kg pyraclostrobin/ha, 2x0.15 kg metrafenone/ha					
Bystanders (adult)	Spray drift	0.00105	0.70	**Note:** **Pyraclostrobin**: In the absence of an acute AOEL (AAOEL) proposed in the current review process (AIR3, RMS Germany), only the respective resident exposure assessment was calculated with the EFSA model and is presented here**.** **Metrafenone:** No acute AOEL (AAOEL) has been set, thus no	
	Vapour	0.00023	0.15		
	Surface deposits	0.00022	0.15		
	Entry treated crops	0.00102	0.68		
Bystanders (children)	Spray drift	0.00393	2.62		
	Vapour	0.00107	0.71		
	Surface deposits	0.00084	0.56		

	Mefentrifluconazole			Pyraclostrobin and Metrafenone	
Model data	**Total absorbed dose (mg/kg/day)**		**% of systemic AAOEL**	**Total absorbed dose (mg/kg/day)**	**% of systemic AAOEL**
	Entry treated crops	0.00183	1.22	bystander exposure assessment and risk evaluation is presented here.	

Table 6.6-8: Estimated resident exposure to mefentrifluconazole, pyraclostrobin and metrafenone

	Mefentrifluconazole			Pyraclostrobin		
Model data	**Total absorbed dose (mg/kg/day)**		**% of systemic AOEL**	**Total absorbed dose (mg/kg/day)**		**% of systemic AOEL**
AOEM: Tractor mounted boom spray application outdoors to low crops Application rate: 2 x 1.5 L product/ha corresponding to 2x0.1 kg mefentrifluconazole /ha, 2x0.12 kg pyraclostrobin/ha, 2x0.15 kg metrafenone/ha						
Residents (adult) Drift rate: 5.6 % (2-3 m drift) Body weight: 60 kg	Spray drift	0.00041	1.16	Spray drift	0.00020	1.35
	Vapour	0.00023	0.66	Vapour	0.00023	1.53
	Surface deposits	0.00007	0.21	Surface deposits	0.00004	0.24
	Entry treated crops	0.00102	2.91	Entry treated crops	0.00050	3.36
	All pathways (mean)	0.00129	3.68	All pathways (mean)	0.00075	5.04
Residents (children) Drift rate: 5.6 % (2-3 m drift) Body weight: 10 kg	Spray drift	0.00171	4.89	Spray drift	0.00086	5.75
	Vapour	0.00107	3.06	Vapour	0.00107	7.13
	Surface deposits	0.00029	0.85	Surface deposits	0.00016	1.08
	Entry treated crops	0.00183	5.24	Entry treated crops	0.00091	6.05
	All pathways (mean)	0.00369	10.56	All pathways (mean)	0.00239	15.96
	Metrafenone					
	Total absorbed dose (mg/kg/day)		**% of systemic AOEL**			
Residents (adult) Drift rate: 5.6 % (2-3 m drift) Body weight: 60 kg	Spray drift	~~0.00723~~ 0.00674	~~1.68~~ 1.57			
	Vapour	0.00023	0.05			
	Surface deposits	~~0.00132~~ 0.00123	~~0.31~~ 0.29			
	Entry treated crops	~~0.01818~~ 0.01697	~~4.23~~ 3.95			
	All pathways (mean)	~~0.01913~~ 0.01787	~~4.45~~ 4.15			
Residents (children) Drift rate: 5.6 % (2-3 m drift)	Spray drift	~~0.03019~~ 0.02819	~~7.02~~ 6.56			
	Vapour	0.00107	0.25			

	Mefentrifluconazole			Pyraclostrobin	
Model data	**Total absorbed dose (mg/kg/day)**		**% of systemic AOEL**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
Body weight: 10 kg	Surface deposits	~~0.00303~~ 0.00285	~~0.71~~ 0.66		
	Entry treated crops	~~0.03272~~ 0.03054	~~7.61~~ 7.10		
	All pathways (mean)	~~0.04601~~ 0.04303	~~10.70~~ 10.01		

6.6.5.2 Measurement of bystander and/or resident exposure

Since the bystander and/or resident exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) for mefentrifluconazole, pyraclostrobin and metrafenone will not be exceeded under conditions of intended uses a study to provide measurements of bystander/resident exposure was not necessary and was therefore not performed.

6.6.6 Combined exposure

Comments of zRMS:	The combined exposure calculations for operator, workers and residents conducted by the Applicant are acceptable. Evaluator re-calculated exposure for metrafenone using correct default value of dermal absorption – 70% for dilution according to the EFSA guidance (2017 The Hazard Index is < 1, therefore combined exposure to all active substances in BAS 758 00 F is not expected to present a risk for operators, workers and residents. The exposure assessment for residents also covers bystander exposure, therefore combined exposure is also not expected for bystanders.

The product is a mixture of three active substances.

From a scientific point of view, it is regarded necessary to take into account potential combination effects. However, the evaluation of cumulative or synergistic effects as requested by Art. 4 (3b) of Regulation (EC) No. 1107/2009 should only be performed when harmonized “scientific methods accepted by the Authority to assess such effects are available.”

6.6.6.1 Exposure Assessment of mefentrifluconazole, pyraclostrobin and metrafenone in the product BAS 758 00 F

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

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

Table 6.6-8: Longer term risk assessment from combined exposure

Application scenario	Active Ingredient	Estimated exposure / AOEL (HQ)
Longer term exposure assessment Operators – LCTM Working clothing and gloves	Mefentrifluconazole	0.0084
	Pyraclostrobin	0.0142
	Metrafenone	~~0.0118~~ 0.0114
	Cumulative risk Operators (HI)	**0.0344**
Acute exposure assessment Operators – LCTM Working clothing and gloves	Mefentrifluconazole	Not applicable as the acute AOEL was only allocated to mefentrifluconazole
	Pyraclostrobin	
	Metrafenone	
	Cumulative risk Operators (HI)	
Workers crop inspection Working clothing	Mefentrifluconazole	0.0434
	Pyraclostrobin	0.0502
	Metrafenone	~~0.0631~~ 0.0589
	Cumulative risk Workers (HI)	**~~0.1567~~ 0.1525**
Bystander - Adult	Mefentrifluconazole	Covered by resident exposure assessment Acute bystander exposure calculated for mefentrifluconazole only
	Pyraclostrobin	
	Metrafenone	
	Cumulative risk Bystander – Adult (HI)	
Bystander - Child	Mefentrifluconazole	Covered by resident exposure assessment Acute bystander exposure calculated for mefentrifluconazole only
	Pyraclostrobin	
	Metrafenone	
	Cumulative risk Bystander – Adult (HI)	
Resident – Adult All pathways	Mefentrifluconazole	0.0368
	Pyraclostrobin	0.0504
	Metrafenone	~~0.0445~~ 0.0416
	Cumulative risk resident – Adult (HI)	**~~0.1317~~ 0.1288**
Resident – Child All pathways	Mefentrifluconazole	0.1056
	Pyraclostrobin	0.1596
	Metrafenone	~~0.1070~~ 0.1001
	Cumulative risk Resident – Child (HI)	**~~0.3722~~ 0.3653**

The Hazard Index is < 1. Thus, combined exposure to all active substances in the preparation BAS 758 00 F is not expected to present a risk for operators, workers, bystanders and residents. 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 7.1.1/1	xxxxxxxxxxx	2020	BAS 758 00 F - Acute oral toxicity study in rats 2020/2101764 xxxxxxxxxxxxxxxxxxxxxxx yes Unpublished	Yes	BASF
KCP 7.1.3/1	xxxxxxxxxxx	2021	BAS 758 00 F - Acute inhalation toxicity study in Wistar rats 4-hour liquid aerosol exposure (nose only) 2021/2021366 xxxxxxxxxxxxxxxxxxxxxxxxx yes Unpublished	Yes	BASF
KCP 7.1.4/1	Remmele, M.	2020	BAS 758 00 F - In vitro Skin Irritation and Corrosion Turnkey Testing Strategy 2020/2086972 BASF SE, Ludwigshafen, Germany Fed.Rep. yes Unpublished	No	BASF
KCP 7.1.5/1	Remmele, M.	2020	BAS 758 00 F - In Vitro Eye Irritation Test (EIT) in Reconstructed Human Cornea 2020/2086973 BASF SE, Ludwigshafen, Germany Fed.Rep. yes Unpublished	No	BASF
KCP 7.1.5/2	Barre T.	2021	BAS 758 00 F - Isolated Chicken Eye Test Method for Identifying - (i) Chemicals Inducing Serious Eye Damage and - (ii) Chemicals Not Requiring Classification for Eye Irritation or Serious Eye Damage 2021/2007253 Laboratoire ICARE, Martillac, France yes Unpublished	No	BASF

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 7.3/1	Rieken, C.	2020	14C-BAS 750 F in BAS 758 00 F - Study of penetration through human skin in vitro 2020/2097877 BASF SE, Ludwigshafen, Germany Fed.Rep. yes Unpublished	No	BASF
KCP 7.3/2	Stinchcombe, S.	2021	Excel file using "efs24873-sup-0001-supinfo_1.xlsx" (version 3) to support dermal absorption calculations according to EFSA Guidance on Dermal Absorption [EFSA Journal 2017;15(6):4873)] for study 14C-BAS 750 F in BAS 758 00 F - Study of penetration through human skin in vitro (BASF DocID 2020/2097877) 2021/2040395 BASF SE no Unpublished	No	BASF
KCP 7.3/3	Rieken, C.	2021	14C-BAS 500 F in BAS 758 00 F - Study of penetration through human skin in vitro 2020/2093957 BASF SE, Ludwigshafen, Germany Fed.Rep. yes Unpublished	No	BASF
KCP 7.3/4	Stinchcombe, S.	2021	Excel file using "efs24873-sup-0001-supinfo_1.xlsx" (version 3) to support dermal absorption calculations according to EFSA Guidance on Dermal Absorption [EFSA Journal 2017;15(6):4873)] for study 14C-BAS 500 F in BAS 758 00 F - Study of penetration through human skin in vitro (BASF DocID 2020/2093957) 2021/2040396 BASF SE no Unpublished	No	BASF

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

There are no already data/studies submitted in this Section

Appendix 2 Detailed evaluation of the studies relied upon

BAS 758 00 F is an organic-solvent based EC-type product (emulsifiable suspension concentrate) that contains the active substances mefentrifluconazole (66.7 g/L) , metrafenone (100 g/L) and pyraclostrobin (80 g/L).

For toxicological evaluation of this product, alternatives to vertebrate animal testing were taken into consideration as far as could be scientifically justified. A weight-of-evidence approach was pursued to provide a sufficiently reliable assessment of the product's acute toxicity by oral, dermal and inhalation routes of exposure, and of its potential to cause skin irritation, eye irritation and skin sensitization:

a) Prediction of toxicity, based on toxicity data from active ingredient and co-formulants, as far as available
b) results of in-vitro studies, and
c) in the absence of available similar EC-type products containing all three active substances, limited (acute oral toxicity) testing of the product in vertebrate animals to verify if the additivity assumption for predicting the health hazards from the product's composition according to CLP Regulation 1272/2008 (GHS approaches) – and as prerequisite for potentially waiving acute dermal and acute inhalation toxicity studies.

Availability of acute toxicity data of BAS 758 00 F components

An overview of the available safety data sheet information on acute toxicity classification of the individual components contained in BAS 758 00 F is given in the following table (co-formulants are number-coded corresponding to the numbering of co-formulants listed in Appendix 2 of Confidential Document Part C.

Table A 1: Overview of BAS 758 00 F ingredient MSDS information concerning acute toxicity C&L (CLP)

Ingredient	Conc [% w/w] (rounded)	Acute tox. C&L (MSDS)	Acute oral toxicity	Acute dermal toxicity	Acute inhalation toxicity	Skin Corr / Irrit	Eye Dam / Irrit	Skin Sens
BAS 750 F	6.10	H317	No	No	No	No	No	H317
BAS 500 F	7.33	H331; H315; H335	No	No	H331 (0.58 mg/L)	H315	No	No
BAS 560 F	9.17	–	No	No	No	No	No	No
#4	8.25	–	No	No	No data	No	No	No
#5	4.58	H332; H315; H318; H335	No	No	H332 (3.75 mg/L)	H315	H318	No
#6	9.17	–	No	No (od)	No	No	No	No
#7	12.83	H319	No	No	No	No	H319	No
#8	4.58	–	No	No	No	No	No	No
#9	4.58	H315; H319	No	No	No	H315	H319	No
#10	4.58	–	No	No	No	No	No	No
#11	7.79	H315; H318; H335	No	No	No data	H315	H318	No
#12	4.58	H319	No	No (od)	No data	No	H319	No data
#13	9.17	–	No	No (od)	No data	No	No	No data
#14	6.71	–	No	No	No	No	No	No
% of product with acute toxicity data			100	77 (100)	70	100	100	86

(1) No (od) =No data but classification not required based on oral-to-dermal extrapolation

(2) no (r-a) = classification not required based on read-across

The weight-of-evidence approach used to predict the classification of BAS 758 00 F for a certain acute toxicity endpoint is described at the beginning of the corresponding sub-sections of this Appendix.

A 2.1 Statement on bridging possibilities

For the organic-solvent-based BAS 758 00 F (EC), products of similar composition were not identified that appeared sufficiently useful for bridging. BAS 758 00 F is currently the only product developed that

contains all three active ingredients mefentrifluconazole, pyraclostrobin and metrafenone.

Limited evidence for increased acute oral and acute inhalation toxicity is suggested for EC-type products containing mefentrifluconazole and/or pyraclostrobin at concentrations comparable to or higher than in BAS 758 00 F. Moreover, since the combination of mefentrifluconazole with metrafenone and pyraclostrobin is unique, bridging to other organic solvent-based mefentrifluconazole or pyraclostrobin formulations was not considered useful.

In order to assess the likelihood for non-additive toxicity phenomena, limited vertebrate testing was considered necessary, and an acute oral toxicity study in rats was therefore performed with the product as a first step. In view of the results obtained and considering the presence of ingredients with an acute inhalation toxicity hazard, testing of the product was followed up by an acute inhalation toxicity study with BAS 758 00 F in rats.

Comments of zRMS:	Acceptable

A 2.2 Acute oral toxicity (KCP 7.1.1)

Comments of zRMS:	The approach and study are acceptable. Acute oral toxicity was examined according to the guideline OECD Test Guideline 423 (2001); Comm. Reg. (EC) No 440/2008, Japan MAFF 8147 (2000) and US EPA OPPTS 870.1100 (2002). The Guideline 423 is also included to the OECD Series on Testing and Assessment (Number 24) - Guidance Document on Acute Oral Toxicity Testing. The study was performed on female rats (4 groups of 3 rats) in compliance with Principles of Good Laboratory Practice (GLP). No deviations during the study were noticed. The median lethal dose of BAS 758 00 F after oral administration was assessed to be greater than 300 mg/kg bw and less than 2000 mg/kg bw in rats, which corresponds to the Acute Tox. Cat. 4. Therefore, it is accepted that the formulation BAS 758 00 F should be classified as Acute Tox. 4 with the hazard statement H302 (Harmful if swallowed) according to Regulation (EC) No. 1272/2008.

Data for assessment of acute oral toxicity is available for all ingredients of the product. None of the active ingredients or co-formulants are classified for acute oral toxicity (see **Table A 1**).

Co-formulant #9 (4.58% in BAS 758 00 F) contains < 25% acetophenone (Acute Tox 4; H302), therefore its presence neither triggers classification of co-formulant #9 (see MSDS) nor classification of BAS 758 00 F. At the end concentration of 1% in BAS 758 00 F, acetophenone is a relevant ingredient according the CLP Regulation, the concentration corresponding to the generic cut-off value of 1%; thus the ingredient needs to be taken into account for classification of the mixture. Using the default ATE value of 500 mg/kg bw for Acute Tox Cat. 4, and applying the calculation algorithm:

$$\frac{100}{ATE_{mix}} = \sum_n \frac{C_i}{ATE_i} = \frac{1}{500}; \qquad ATE_{mix} = 100 \times \frac{500}{1} = 50{,}000 \text{ mg/kg bw}$$

Based on the calculated acute oral toxicity ATE_{mix} (LD_{50}) of 50,000 mg/kg bw, a classification for acute oral toxicity is not indicated for BAS 758 00 F on the basis of its composition.

Limited evidence for increased acute oral and acute inhalation toxicity is suggested for EC-type products containing mefentrifluconazole and/or pyraclostrobin at concentrations comparable to or higher than in BAS 758 00 F. Moreover, since BAS 758 00 F represents a currently unique combination of active ingredients, an acute oral toxicity study in rats was performed to check if higher-than-expected toxicity occurs.

In the study, 4 of 6 rats administered a dose of 2000 mg/kg bw died. No deaths occurred in two groups of three rats at a dose of 300 mg/kg bw. By Probit analysis according to Finney, an oral LD50 of 1792 mg/kg bw could be calculated. A study summary is provided at the end of this chapter.

In conclusion, based on the available data, BAS 758 00 F is classified in Acute Tox. Cat. 4; H302 (harmful if swallowed) according to Regulation (EC) No. 1272/2008, with an ATE = 1792 mg/kg bw.

A 2.2.1 Study 1

Reference:	CP 7.1.1/1
Report	BAS 758 00 F - Acute oral toxicity study in rats xxxxxxxxxxxxxxxx, 2020 Report No 10A0152/14X204 BASF DocID 2020/2101764
Guideline(s):	OECD 423 (2001), Comm. Reg. (EC) No 440/2008, JMAFF 8147, EPA 870.1100
Deviations:	No
GLP:	Yes (certified by Landesanstalt fuer Umwelt, Messungen und Naturschutz Baden-Wuerttemberg, Karlsruhe, Germany)
Acceptability:	Yes
Duplication (if vertebrate study)	No

Materials and methods

Test material (Lot/Batch No.)	BAS 758 00 F Batch No. FD-200124-0004 Purity/Content: - Metrafenone (BAS 560 F): 94.8 g/L - Mefentrifluconazole (BAS 750 F): 66.7 g/L - Pyraclostrobin (BAS 500 F): 81.0 g/L
Species	Wistar rat (Crl:WI (Han) SPF)
No. of animals (group size)	3 female rats/group
Dose(s)	2000 mg/kg bw (two groups) 300 mg/kg bw (two groups)
Exposure	Once by oral gavage
Vehicle/Dilution	2000 mg/kg bw: undiluted 300 mg/kg bw: 15 g/100 mL deionized water
Post exposure observation period	14 days
Remarks	None

Results and discussions

Table A 2: Results of acute oral toxicity study in rats of BAS 758 00 F

Dose (mg/kg bw)	Toxicological results *	Duration of signs	Time of death	LD_{50} (mg/kg bw) (14 days)
Female rats				
2000	1 / 3 / 3	h1 – h5	h3	1792**
2000	3 / 3 / 3	h0 – h2	h1 or h3	
300	0 / 0/ 3	No signs	No deaths	
300	0 / 0 / 3	No signs	No deaths	

***** Number of animals which died/number of animals with clinical signs/number of animals used
hx: hours after administration at day 0; dx: days after administration
** LD_{50} 1791.762 mg/kg bw calculated by Probit Analysis according to Finney (SAS v9.4; intercept: -29.35, slope: 3.918).

- Mortality was observed in one of three animals in the first test group receiving 2000 mg/kg bw of the formulation; the animal died at hour 3 after treatment. In the second 2000 mg/kg bw test group all animals died within 1 or 3 hours after administration. No mortality occurred in both 300 mg/kg bw test groups [see
- **Table A 2**]. An ATE of 1792 mg/kg bw was calculated by Probit analysis (according to Finney) on account of 6/6 survivors at 300 mg/kg bw and 2/6 survivors at 2000 mg/kg bw.
- In the first 2000 mg/kg bw test group, impaired general state and piloerection were noted in two animals from hour 1 until hour 5 after administration. In addition, one of these animals showed dyspnoea from hour 1 until hour 5 and staggering from hour 1 until hour 4 after administration. The third animal of this test group showed poor general state, dyspnoea, apathy and abdominal position from hour 1 until hour 2 and died at hour 3.
- In the second 2000 mg/kg bw test group, impaired general state, piloerection and dyspnoea were seen in all animals at hour 0. In one of these animals, impaired general state persisted until hour 1, while dyspnoea and piloerection persisted until hour 2. Furthermore, poor general state and abdominal position were noticed in this animal at hour 2, while diarrhea was seen from hour 1 until hour 2.
- In both 300 mg/kg bw test groups no clinical signs were observed during clinical examination.
- All surviving animals gained weight in a normal range throughout the study period.
- In the single animal that died in the first 2000 mg/kg bw group, dark, red spotted discoloration of the liver and congestion in the kidneys was observed. In three animals of the second 2000 mg/kg bw group that died, dark discoloration of the liver, whitish discoloration of the stomach contents and red discoloration of the small intestines in all animals and dark spotted discoloration of all lung lobes in one animal were noted. There were no macroscopic pathological findings in the surviving animals sacrificed at the end of the observation period.

Conclusion

Under the study conditions, the acute oral LD_{50} of BAS 758 00 F in rats was approx. 1792 mg/kg bw.

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

Comments of zRMS:	The approach is acceptable. The formulation BAS 758 00 F does not require to be classified for acute dermal toxicity according to Regulation (EC) No. 1272/2008.

Data for assessment of acute dermal toxicity is available for 77% of the product's composition (for 11 out of 14 ingredients, see **Table A 1**). Since oral toxicity data is available for all ingredients, oral-to-dermal extrapolation could be applied either at product or ingredient level to finally predict the acute dermal toxicity of the product thereby considering data from all ingredients. At ingredient level, in the absence of concern for acute oral toxicity, classification of BAS 758 00 F for acute dermal toxicity is not triggered. Also applying oral-to-dermal extrapolation from the available acute oral toxicity test with BAS 758 00 F (oral LD_{50} 1792 mg/kg bw, no deaths at 300 mg/kg bw) does not give rise to any relevant concern for acute dermal toxicity (even if unrealistic systemic bioavailability is assumed), due to the predicted low acute oral toxicity of the product.

Thus, based on weight-of-evidence (composition and oral-to-dermal extrapolation), it is concluded BAS 758 00 F does not require classification for acute dermal toxicity according to Regulation (EC) No. 1272/2008.

A 2.4 Acute inhalation toxicity (KCP 7.1.3)

Comments of zRMS:	The approach and study are acceptable. Acute inhalation toxicity was examined according to the guideline OECD Test Guideline 436 (2009). The study was performed on male and female rats (two groups of each 3 male and 3 female) in compliance with Principles of Good Laboratory Practice (GLP). No deviations were noticed, which could influence the study results. An LC_{50} value obtained after 4-hour inhalation exposure to the BAS 758 00 F corresponds to the LC_{50} cut-off value of 5 mg/L. Therefore the formulation BAS 758 00 F is classified as Acute Tox. 4 with the hazard statement H332 (Harmful if inhaled) according to Regulation (EC) No. 1272/2008. Additionally, taking into consideration the classifications of components of the formulation BAS 758 00 F the Applicant proposed the classification of the product as STOT SE 3 with the hazard statement H335 (May cause respiratory irritation) – acceptable.

Data for assessment of acute inhalation toxicity is available for 10 out of 14 co-formulants comprising approximately 70% of the total composition (see Table A 1). One ~~co-formulant~~ active substance (7.33% w/w) is classified as toxic by inhalation (H331, Cat. 3 with an ATE of 0.58 mg/L) and another co-formulant (#5, 4.58% w/w) is classified as harmful by inhalation (H332, Cat.4 with an ATE of 3.75 mg/L). None of the other co-formulants with data indicate a concern for acute inhalation toxicity.

A calculation approach using the modified GHS algorithm for mixtures containing >10% relevant ingredients with unknown acute inhalation toxicity …

$$\frac{100-\left(\sum C_{unknown\ if\ >10\%}\right)}{ATE_{mix}}=\sum_{n}\frac{C_i}{ATE_i} \qquad \frac{70}{ATE_{mix}}=\sum_{n}\frac{C_i}{ATE_i}=\frac{7.33}{0.58}+\frac{4.58}{3.75}$$

$$ATE_{mix}=\frac{70}{13.86}=5.05\ \text{mg/L}$$

... predicts the product BAS 758 00 F to be of low acute toxicity by the inhalation route, with no need for acute toxicity classification (because LC_{50} > 5 mg/L).

However, there is some doubt whether the additivity prerequisite for using the GHS calculation approach applies in the case of BAS 758 00 F, since it under-predicted the acute oral toxicity of the product, when compared to results of the acute oral toxicity study in rats. Behind this background and for reasons of

caution, it was considered necessary to perform an acute inhalation toxicity test with BAS 758 00 F in rats.

In the acute inhalation toxicity study performed using the acute toxic class method, mortality occurred at the tested concentration of 5.072 mg/L in 1/3 males and 2/3 females; no mortality occurred at 1.1 mg/L. An LC50 value derived according to OECD Guideline 436 Annex 3c~~x~~ corresponded to the LC50 cut-off value of 5 mg/L. In the study, the animals showed clear signs of respiratory irritation, which were mostly reversible within the study period.

Thus, BAS 758 00 F is to be classified as 'Harmful if inhaled', Cat 4, H332 according to Regulation (EC) No. 1272/2008. In addition, based on weight-of-evidence additional classification with STOT SE 3 for respiratory irritation (H335~~6~~) is proposed, taking into account the total concentration of respiratory irritants in the product (ca. 18.6%)

A 2.4.1 Study 1

Reference:	CP 7.1.3/1
Report	BAS 758 00 F - Acute inhalation toxicity study in Wistar rats - 4-hour liquid aerosol exposure (nose-only) xxxxxxxxxxxxxxx, 2021 Report No 14I0152/14I163 BASF DocID: 2021/2021366
Guideline(s):	OECD 436 (2009), (EC) No 440/2008 of 30 May 2008 laying down test methods pursuant to (EC) No 1907/2006 of European Parliament and of Council on the REACH - Part B No. L 142
Deviations:	No
GLP:	Yes (certified by Landesamt fuer Umwelt, Wasserwirtschaft und Gewerbe-aufsicht, Mainz, Germany)
Acceptability:	Yes
Duplication (if vertebrate study)	No

Materials and methods

Test material (Lot/Batch No.)	BAS 758 00 F Batch No. FD-200124-0004 Purity/Content: - Metrafenone (BAS 560 F): 94.8 g/L - Mefentrifluconazole (BAS 750 F): 66.7 g/L - Pyraclostrobin (BAS 500 F): 81.0 g/L
Species	Rat, Wistar (Crl:WI (Han) SPF)
No. of animals (group size)	3 male and 3 female rats per dose
Concentration(s)	1.110 and 5.072 mg/L air
Exposure	4 hours (nose only)
Vehicle/Dilution	None
Post exposure observation period	14 days

Remarks	None

Results and discussions

Table A 3: Concentration(s) and exposure conditions

Nominal conc. (mg/L air)	Actual conc. (mg/L air)	MMAD * (µm)	GSD ** (µm)
3.1	1.110	0.65 – 0.72	3.82 – 3.93
29.7	5.072	0.88 – 0.89	3.53 – 3.66

* MMAD = Mass Median Aerodynamic Diameter; ** GSD = Geometric Standard Deviation

Table A 4: Results of acute inhalation toxicity study in rats of BAS 758 00 F

Concentration (mg/L air)	Toxicological results *	Duration of signs	Time of death	LC_{50} (mg/L air) (14 days)
Male rats				ca. 5 mg/L
1.132	0 / 3 / 3	d0 – d14	No deaths	
5.622	1 / 3 / 3	d0 – d14		
Female rats				
1.132	0 / 3 / 3	d0 – d14	No deaths	
5.622	2 / 3 / 3	d0 – d14		

* Number of animals which died/number of animals with clinical signs/number of animals used
h(x): hours after start of exposure; d(y): day of observation; d1 = day of application

Table A 5: Summary of findings of acute inhalation toxicity study in rats of BAS 758 00 F.

Mortality:	None of the animals died at 1.132 mg/L. At the high dose of 5.622 mg/L, ~~2~~ 1 males and ~~3~~ 2 females died after exposure on Day 0~~. and one male died on Day 1~~.
Clinical signs:	Clinical signs of toxicity in animals exposed to 1.110 mg/L comprised accelerated respiration, intermittent respiration, labored respiration, abdominal respiration, gasping, respiration sounds, eyelids semiclosed, red crusts and colorless discharge of the nose, poor general condition, no feces, reduced fur care, piloerection and substance-contaminated fur. At the end of the 14-day study period, some animals still showed piloerection (1 male and 3 females), either slightly accelerated respiration (3 males) or intermittent respiration (3 females), and respiration sounds (1 male). Clinical signs of toxicity in animals exposed to 5.072 mg/L were similar to those described at lower concentrations. Some more unspecific symptoms (e.g. hunched posture or eyelid closed) were seen. Accelerated respiration and colorless discharge of the nose were not seen. At the end of the 14-day study period, there were two surviving males, one without clinical signs, the other with piloerection, abdominal respiration and sounds; the surviving female rat was without symptoms.
Body weight:	At both dose levels of 1.1 mg/L and 5.072 mg/L, the mean body weights of the surviving animals decreased on the first post-exposure day but increased thereafter.
Macroscopic examination:	Gross pathological findings were not noted during the necropsy of the animals that died or that were sacrificed in a moribund state during exposure (one male and two females), nor during the necropsy of the surviving animals at the termination of the study.

Conclusion

Under the experimental conditions, the calculated inhalation LC_{50} of BAS 758 00 F was approx. 5 mg/L (cut-off value derived in accordance with OECD test guideline 436, Annex 3ce) in male and female Wistar rats after 4-hour inhalation exposure to liquid aerosol of BAS 758 00 F. Thus, BAS 758 00 F is to be classified as 'Harmful if inhaled', Cat 4, H332 according to Regulation (EC) No. 1272/2008.

A 2.5 Skin irritation (KCP 7.1.4)

Comments of zRMS:	The approach and study acceptable. In vitro Skin Irritation and Corrosion study was performed according to the guidelines OECD 431 and 439, Commission Regulation (EU) 2019/1390 (B.40 bis and B.46) and New guidance document on an integrated approach on testing and assessment (IATA) for skin corrosion and irritation, Series on Testing and Assessment No. 203 (11 July 2014). The study was performed in compliance with Principles of Good Laboratory Practice (GLP), no deviations were noticed. The study results revealed that the formulation BAS 758 00 F shows a skin irritation potential. Taking also into consideration the classifications of components of the formulation BAS 758 00 F the product should be classified as Skin Irrit. 2 with the hazard statement H315 (Causes skin irritation) according to Regulation (EC) No. 1272/2008.

Safety Data sheet information for assessment of skin irritation is available for all ingredients of the product. Pyraclostrobin (7.33%), and co-formulants #5 (4.58%), #9 (4.58%) and #11 (7.79%) are classified as skin irritants. The total product concentration of skin irritating ingredients is above the 10% trigger for classification. Thus, based on skin irritation data available for the components, product classification as skin irritant would be triggered for BAS 758 00 F according to GHS/CLP criteria.

When the skin corrosive and irritant potential of the product was tested in-vitro in the EpiDerm™ test (OECD 431 and OECD 439), BAS 758 00 F showed evidence for a relevant skin irritation potential (viability 4.4 ~~20.2~~% after 1-h exposure followed by 42-h incubation period, compared to the negative control). However, based on published literature, a false-positive rate of 40% was identified for agrochemical formulations in this in-vitro skin irritation test (Kolle et al. (Regul. Toxicol. Pharmacol. 89, 125-130, 2017). Therefore, some doubt remains regarding the reliability of the study result.

In absence of bridging opportunities for read-across to similar products, the overall data available points to a borderline situation. For reasons of precaution, and to avoid vertebrate testing, it is proposed to classify BAS 758 00 F on the basis of the in-vitro study results as skin irritant.

A 2.5.1 In-vitro skin corrosion and skin irritation study

Reference:	CP 7.1.4/1
Report	BAS 758 00 F - In vitro skin irritation and corrosion Turnkey Testing Strategy Remmele M., 2020 Report No: 69V0152/14B027 BASF DocID 2020/2086972
Guideline(s):	OECD 431, OECD 439, Commission Regulation (EC) No 440/2008 - Part B No. B.40 bis, Commission Regulation EU No. 640/2012 of 06 July 2012 - B.46

Deviations:	No
GLP:	Yes (certified by Landesamt fuer Umwelt, Wasserwirtschaft und Gewerbeaufsicht, Mainz, Germany)
Acceptability:	Yes
Duplication (if vertebrate study)	No

Materials and methods

Test material (Lot/Batch No.)	BAS 758 00 F Batch No. FD-200124-0004 Purity/Content: - Metrafenone (BAS 560 F): 94.8 g/L - Mefentrifluconazole (BAS 750 F): 66.7 g/L - Pyraclostrobin (BAS 500 F): 81.0 g/L pH value: ca. 5.0 (undiluted, determined in test facility)	
Test system	Reconstructed in vitro human skin model, EpiDerm™	
Principle of the method	Induced cytotoxicity (loss of viability) is expressed as the reduction of mitochondrial dehydrogenase activity measured by reduction of MTT conversion to blue-colored formazan, in comparison to a negative control. The test substance was not able to reduce MTT directly. Therefore and addition MTT reduction control "KC" (freeze-killed control tissues) was not introduced.	
	Skin Corrosivity test (SCT) OECD 431	***Skin Irritation test (SIT) OECD 439***
No. of tissues per exposure and group	2	3
Exposure	50 µL (3 min), 50 µL (1 h)	30 µL (1 h)
Vehicle / dilution	Tested undiluted	Tested undiluted
Post-exposure incubation period	Not applicable	42 h
Positive control	8 N potassium hydroxide	5% (w/v) sodium dodecyl sulfate (SDS)
Negative control	De-ionized water	Phosphate-buffered saline (PBS)
Assessment	***Mean tissue viability (% of negative control)***	
Corrosive (optional subcategory 1A) [a]	3 min: < 50	–
Corrosive (opt. subcategory 1B and 1C) [a]	3 min: ≥ 50 and 1 hour: < 15	–
Non-corrosive	3 min: ≥ 50 and 1 hour: ≥ 15	–
Irritant	–	1 +42 hours: ≤ 50
Non-Irritant	–	1 +42 hours: > 50

[a] According to the current OECD Guideline 431 a sub-categorization is possible based on the results. However, the sub-categorization into 1A is highly over-predictive as stated in the guideline and differentiation into sub-category 1B or 1C is not

possible. If the test substance is identified to be corrosive by SCT and a transport classification is needed, the Corrositex® test (OECD 435) should be performed, if applicable, to confirm classification as 1A or to differentiate between 1B and 1C.

Results and discussions

Results of the skin corrosion and skin irritation tests are summarized in the table below.

Table A 6: in-vitro skin corrosion / irritation of BAS 758 00 F

Parameter	Negative control (NC) viable tissue	Test item viable tissue	Positive control viable tissue
Exposure: 3 min			
OD_{570} tissue I	2.085	2.175	0.171
OD_{570} tissue II	2.131	2.070	0.192
mean OD_{570}	2.108	2.122	0.181
Viability (% of NC)	**100.0 ± 1.5**	**100.7 ± 3.5**	**8.6 ± 0.7**
Exposure: 1 h			
OD_{570} tissue I	2.083	1.588	0.061
OD_{570} tissue II	1.936	1.983	0.063
mean OD_{570}	2.010	1.786	0.062
Viability (% of NC)	**100.0 ± 5.2**	**88.9 ± 13.9**	**3.1 ± 0.1**
Exposure:1 h + post-exposure incubation: 42 h			
OD_{570} tissue I	1.999	0.087	0.041
OD_{570} tissue II	1.887	0.109	0.037
OD_{570} tissue III	1.933	0.060	0.036
mean OD_{570}	1.940	0.085	0.038
Viability (% of NC)	**100.0 ± 2.9**	**4.4 ± 1.3**	**2.0 ± 0.1**

NC = negative control (deionised water), PC = positive control (8 N KOH); OD_{570} = optical density by λ = 570 nm

BAS 758 00 F was not corrosive to skin under the in-vitro study conditions. The mean relative viability of the tissues treated with the test substance determined after an exposure period of 3 minutes was 100.7%, and it was 88.9% after an 1-hour exposure period.

In the skin irritation test (SIT), the mean relative viability of the tissues treated with the test substance determined after an exposure period of 1 hour with an about 42-hour post-incubation period was 4.4%.

Conclusion

Based on the results obtained BAS 758 00 F was found to be skin irritant in the in vitro test with human reconstituted epidermis (mean tissue viability 4.4% of the negative control, thus below the 50% viability threshold). In the corrosivity assay, mean tissue viability values at 3 minutes of ≥ 50% of the negative control and at one hour of ≥ 15% of the negative control indicated that BAS 758 00 F was not corrosive under the conditions of this assay. On the basis of these results, the product meets the criteria for classification as skin irritant.

A 2.6 Eye irritation (KCP 7.1.5)

Comments of zRMS:	The approach and studies acceptable. In vitro Eye Irritation Test (EIT) in Reconstructed Human Cornea study was performed according to the guidelines OECD 492, Commission Regulation (EU) 2019/1390, B.69 and Guidance document on integrated approaches to testing and assessment (IATA) for serious eye damage and eye irritation, Series on Testing and Assessment No. 263 (25 July 2019). The study was performed in compliance with Principles of Good Laboratory Practice (GLP), no deviations were noticed. The study results revealed that the formulation BAS 758 00 F shows an eye irritation potential, but the result does not exclude a serious eye irritation potential of the test substance. For final assignment of a classification according to CLP criteria, additional data are required. Isolated chicken eye test method for identifying (i) Chemicals including serious eye damage and (ii) Chemicals not requiring classification for eye Irritation or serious eye damage study was performed according to the guidelines OECD 438. The study was performed in compliance with Principles of Good Laboratory Practice (GLP), no deviations were noticed, which could influence the study results. The study results revealed that the formulation BAS 758 00 F does not require classification for eye irritation and serious eye damage according to CLP criteria. Taking into consideration results of above studies and also the classifications of components of the formulation BAS 758 00 F as well as a precautionary approach it is accepted that the product should be classified as Eye Dam. 1 with the hazard statement H318 (Causes serious eye damage) according to Regulation (EC) No. 1272/2008.

Data for assessment of eye irritation is available for all 14 ingredients of the product (see **Table A 1**). Co-formulants #5 (4.~~2~~58%) and #11 (7.79 ~~4.40~~%) are classified with Eye Dam. 1. Three further co-formulants (#7, #9~~,~~ and #12) making up 22% of the product composition are classified as eye irritants (Eye Irrit 2; H319). The remaining nine ingredients are classified as non-irritants (ca. 65%). According to mixture classification algorithms of GHS/CLP, the total concentration of the eye damaging ingredients of 12.4% clearly exceeds the 3% trigger for classification of the mixture with Eye Dam.1; H318.

A pH value of ca. 5.9-6.5 was determined for undiluted BAS 758 00 F, indicating no concern for corrosivity (see KCP 2.4.2; Keller, 2020; DocID 2020/2109344).

When BAS 758 00 F was investigated in-vitro, the EpiOcular™ test (OECD 492) gave evidence for an eye irritating potential. This test method has been shown to be sufficiently reliable for predicting true negative in-vivo study outcomes in tests with agrochemical formulations (Kolle et al. 2017), but the test method cannot specify the Category of a test substance that is positive in the EpiOcular™test.

In the Isolated Chicken Eye test (ICE, OECD 438), treatment with BAS 758 00 F caused slight retention of fluorescein and cornea swelling (each ICE Class II) but only very slight effects on cornea opacity (ICE Class I)); microscopic examination of the corneas did not reveal any morphological changes. Based on the results, the test substance would be categorized as non-irritant to the eye.

Based on the overall weight-of-evidence …

- classification with Eye Dam. 1 predicted from the concentration of eye damaging components in BAS 758 00 F / GHS calculation approach),
- classification with either Eye Dam. 1 or Eye Irrit. 2; H319 on account of results obtained in the EpiOcular™ Test, and

- No classification for eye damage concluded from the Isolated Chicken Eye Test results

… uncertainty remains on the appropriate classification of BAS 758 00 F for eye irritation/ damage.

The results of the ICE appear to be questionable in view of the very clear prediction outcomes obtained with the other two approaches. Under the circumstances, a precautionary approach seems to be prudent. Therefore, BAS 758 00 F should be classified with Eye Dam. 1; H318, based on concern from its composition and supported by results obtained in the EpiOcular test.

A 2.6.1 EpiOcular in-vitro eye irritation test (OECD 492)

Reference:	CP 7.1.5/1
Report	BAS 758 00 F – In Vitro Eye Irritation Test (EIT) in Reconstructed Human Cornea Remmele M., 2020 Report No: 62V0152/14B026 BASF DocID 2020/2086973
Guideline(s):	OECD 492 (2018) IATA for serious eye damage and eye irritation, Series on Testing and Assessment No. 263, 20 July 2017
Deviations:	No
GLP:	Yes (certified by Landesamt fuer Umwelt, Wasserwirtschaft und Gewerbeaufsicht, Mainz, Germany)
Acceptability:	Yes
Duplication (if vertebrate study)	No

Materials and methods

Test material (Lot/Batch No.)	BAS 758 00 F Batch No. FD-200124-0004 Purity/Content: - Metrafenone (BAS 560 F): 94.8 g/L - Mefentrifluconazole (BAS 750 F): 66.7 g/L - Pyraclostrobin (BAS 500 F): 81.0 g/L pH value: ca. 5.0 (undiluted, determined in test facility)

EpiOcular™ Test

Test system	Reconstructed in vitro human ocular model, EpiOcular™
Principle of the method	The test substance is administered to the surface of the EpiOcular™ tissue. Induced cytotoxicity (loss of viability) is expressed as the reduction of mitochondrial dehydrogenase activity measured by reduction of MTT conversion to blue-colored formazan, in comparison to a negative control.
No. of tissues per test group	2
Pretest for detection of direct (= non-enzymatic) MTT reduction	In a pre-test, the test substance is incubated with the substrate MTT and checked for formazan formation, indicating "direct" MTT reduction. In this event, two additional "freeze-

	killed" tissues each for the test substance group and the negative control group are added to the standard test protocol. Based on the result of the pretest, it was judged that application of killed control tissues is not necessary.
Exposure	50 µL: 30 min
Vehicle / dilution	Tested undiluted
Post-exposure wash solution	Phosphate-buffered saline (PBS)
Post-exposure incubation period	2 hours
Positive control	Methyl acetate
Negative control	De-ionized water
Assessment	***Mean tissue viability*** *(% of negative control)*
Irritant	≤ 60
Non-irritant	> 60

Results and discussions

Table A 7: in-vitro eye corrosion / irritation of BAS 758 00 F (EpiOcular™ Assay)

Test substance		Tissue 1	Tissue 2	**Mean**	Inter-tissue variability [%]
Neg. control (NC)	mean OD_{570}	1.950	2.152	2.051	
	Viability [% of NC]	95.1	104.9	**100.0**	9.8
BAS 758 00 F	mean OD_{570}	0.455	0.455	0.455	
	Viability [% of NC]	22.2	22.2	**22.2**	0.0
Positive control (PC)	mean OD_{570}	0.573	0.499	0.536	
	Viability [% of NC]	27.9	24.3	**26.1**	3.6

NC = negative control (de-ionized water), PC = positive control (methyl acetate); OD_{570} = optical density by λ = 570 nm

The viability of reconstructed corneal tissues following exposure to BAS 758 00 F was 22.2% of the negative control value (thus lower than 60%), indicating eye irritating or eye damaging properties of the test substance.

Conclusion

Based on the results observed and the assessment criteria, BAS 758 00 F shows an eye irritation potential in the EpiOcular™ test. For final assignment of a classification according to GHS/CLP criteria, additional data are required.

A 2.6.2 Isolated Chicken Eye test (OECD 438)

Reference:	CP 7.1.5/2
Report	BAS 758 00 F - Isolated chicken eye test method for identifying (i) chemicals including serious eye damage and (ii) chemicals not requiring classification for eye Irritation or serious eye damage Barré T., 2021 Report No: 99A0152/14X366, ICE-PH-20/0789 BASF DocID 2021/2007253
Guideline(s):	OECD 438 (2018)

	Commission Regulation (EU) 1152/2010 – Test method B.48 of 8 December 2008 Council Regulation 440/2008 of 30 May 2008
Deviations:	No
GLP:	Yes (certified by Groupe Interministeriel des Produits Chimiques, Ivry-sur-Seine CEDEX, France)
Acceptability:	Yes
Duplication (if vertebrate study)	No

Materials and methods

Test material (Lot/Batch No.)	BAS 758 00 F Batch No. FD-200124-0004 Purity/Content: - Metrafenone (BAS 560 F): 94.8 g/L - Mefentrifluconazole (BAS 750 F): 66.7 g/L - Pyraclostrobin (BAS 500 F): 81.0 g/L
Test system	Chicken eyes obtained from slaughter animals (ca. 7 wk old male or female chickens) used for human consumption
Principle of the method	The test substance is administered to the surface of the isolated chicken eye, so that the total surface of the cornea is evenly covered. After 10-second exposure, the eye is rinsed with saline. Corneal thickness (expressed as corneal swelling), corneal opacity and fluorescein retention are determined before (t=0) and after exposure, and histopathology of the corneas is performed.
No. of tissues per test group	3
Pre- and post-exposure incubation	The dissected eye ball was placed in a stainless steel clamp and transferred into a chamber kept at 32 °C. The entire cornea was continuously rinsed with physiological saline (ca. 32 °C) supplied by a peristaltic pump at a target rate of 0.1 – 0.15 mL/min. Eyes were removed from the chamber for treatment and post-treatment rinse and subsequently returned to the chamber.
Exposure	30 µL: 10 seconds
Vehicle / dilution	Tested undiluted
Post-exposure rinse	2x 10 mL physiological saline (0.9% aqueous NaCl solution)
Post-exposure assessment time point	0, 30, 75, 120, 180, 240 minutes
Negative control	0.9% aqueous NaCl (physiological saline) – 1 eye
Positive control	5% Benzalkonium chloride in physiological saline (BAC) – 2 eyes

Assessment

The three effect parameters corneal swelling, corneal opacity and fluorescein retention are scored at designated time points using an effect severity classification in one of four categories **I-IV** (not irritating; slightly irritating; moderately irritating; severely irritating). A prediction model assigns a final classification based on the combination of severity scores determined for the different parameters.

Endpoint	**Severity Category**
Corneal thickness / swelling Determined at each time-point according to following formula: $\frac{\text{corneal thickness t - corneal thickness } t0}{\text{corneal thickness } t0} \times 100$ The highest mean score determined from different time points taken for assessment.	**I** (0-5%), **II** (>5-12% or >75 minutes after treatment: >12-18%), **III** (≤ 75 minutes after treatment: >12-18% or >75 minutes: 26-32% or >18 to 26%), **IV** (≤ 75 minutes after treatment: >26-32% or >32%)
Corneal opacity score time point with area most densely opacified was taken for scoring. The highest mean score determined from different time points taken for assessment. Scores (comparable to Draize): 0 (no opacity) 0.5 (very faint opacity) 1 (scattered or diffuse area; iris details clearly visible) 2 (easily discernable translucent area, iris details slightly obscured) 3 (severe opacity, iris details not visible, pupil size barely discernable 4 (complete corneal opacity, iris invisible)	**I** (0.0-0.5), **II** (0.6-1.5), **III** (1.6-2.5), **IV** (2.6-4.0)
Fluorescein retention (at 30 min only) Scores: 0 (no fluorescein retention) 0.5 (very minor single cell staining) 1 (single cell staining scattered throughout the cornea area 2 (Focal or confluent dense single cell staining) 3 (Confluent large areas of the cornea retaining fluorescein)	**I** (0.0-0.5), **II** (0.6-1.5), **III** (1.6-2.5), **IV** (2.6-3.0)
Morphological effects (reported but not used for classification due to lack of established criteria)	These include "pitting" of corneal epithelial cells, "loosening" of epithelium, "roughening" of the corneal surface and "sticking" of the test substance to the cornea. These findings can vary in severity and may occur simultaneously. The classification of these findings is subject to the interpretation of the investigator.

Proposed criteria for classification according to UN GHS

Eye Dam. 1 (H318)	3x **IV** 2x **IV,** 1 x **III**
No Category	3x **I** 2x **I** and 1x **II** 2x **II** and 1x **I**
Other combinations	***No prediction can be made***

Results and discussions

Table A 8: Results of slit-lamp examination in in-vitro isolated chicken eye (ICE) test

Test material	Maximum mean score for: Swelling % (Irritation category)	Opacity (Irritation category)	Fluorescein retention (Irritation category)	Classification (CLP)
BAS 758 00 F	6 (**II**)	0.2* (**I**)	0.7 (**II**)	**No category.**
Positive ctrl (5% BAC)	35 (**IV**)	3.0* (**IV**)	3.0 (**IV**)	Eye Dam. 1
Negative ctrl	0 (**I**)	0.0* (**I**)	0.5 (**I**)	No classification

*no morphological effects were noted in exposed corneas of the negative control and of the test substance groups regardless of the examination time point.

BAS 758 00 F caused slight corneal swelling (ICE class II) and very slight corneal opacity (ICE class I) and slight fluorescein retention (max. mean score of 0.7, corresponding to ICE class II). Microscopic examination of the corneas generally did not reveal morphological effects.

The negative control eye did not show any corneal effect and demonstrated that the general conditions during the tests were adequate. Microscopic examination of the cornea did not reveal any abnormalities.

The positive control BAC 5% caused severe corneal effects and demonstrated the validity of the ICE test to detect severe eye irritants.

Conclusion

The results obtained for BAS 758 00 F under the experimental conditions of the Isolated Chicken Eye test – 2x Category II + 1x Category I – lead to the outcome "No category" according to assessment criteria of OECD Guideline 438. Therefore, the results of the study indicate that BAS 758 00 F does not require classification for serious eye irritation and eye damage as defined by the UH GHS..

A 2.7 Skin sensitisation (KCP 7.1.6)

Comments of zRMS:	Acceptable. Taking into consideration the composition of the formulation BAS 758 00 F the whole formulation should be classified as Skin Sens. 1 with the hazard statement H317 (May cause an allergic skin reaction) according to Regulation (EC) No. 1272/2008.

No skin sensitisation test was performed for the product BAS 758 00 F.

Data for assessment of skin sensitization is available for 86% of the product's composition (**Table A 1**). Skin sensitization information is missing for two co-formulants #12 (4.58%), and #13 (#9.17%).

The active ingredient mefentrifluconazole (6.1%) was found to be a skin sensitizer in the GPMT.

On this basis, classification with Skin Sens. 1; H317 is required for BAS 758 00 F according to classification criteria of Commission Reg. No. 1172/2008.

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

No study available.

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 (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 (Registration Report - Part C).

A 2.10 Studies on dermal absorption (KCP 7.3)

In-vitro dermal penetration studies with human skin membranes have been carried out, to investigate the dermal absorption of active ingredients mefentrifluconazole and pyraclostrobin formulated in BAS 758 00 F. The studies have not undergone a previous EU peer-review, therefore full summaries are presented in detail below. Assessments were carried out according to the revised EFSA Guidance (2017) and using the Excel data entry sheets (EFSA template “efs24873-sup-0001-supinfo_1.xlsx" (version 3), released 20 August 2018).

A 2.10.1 ^{14}C-mefentrifluconazole (BAS 750 F) in BAS 758 00 F

Comments of zRMS:	Study acceptable. The *in vitro* study on dermal absorption of mefentrifluconazole in formulation 758 00 F was performed according to the OECD and EFSA guidance in compliance with GLP rules. No deviation was occurred during the study. The formulation was tested at the concentrated formulation (66.7 mg/mL of mefentrifluconazole) and at the 1:200 and 1:600 dilutions which corresponds to the concentrations of 0.333 mg/mL and 0.111 mg/mL of mefentrifluconazole, respectively. The dermal penetration was estimated as 0.2% for the formulation concentrate, 6.3% for the 1:200 spray dilution and 7.8% for the 1:600 spray dilution based on current EFSA guidance criteria (2017).

Reference:	CP 7.3/1
Report	^{14}C-BAS 750 F in BAS 758 00 F - Study of penetration through human skin in vitro Rieken C., 2020 Report No. 10B0704/14B028 BASF DocID 2020/2097877
Guideline(s):	OECD 428, OECD Guidance Document No. 28 for the conduct of skin absorption studies (March 2004)
Deviations:	No
GLP:	yes (certified by Landesamt fuer Umwelt, Wasserwirtschaft und Gewerbeaufsicht, Mainz, Germany, Germany)
Acceptability:	Yes
Duplication (if vertebrate study)	No

Reference:	CP 7.3/2
Report	Excel file using "efs24873-sup-0001-supinfo_1.xlsx" (version 3) to support dermal absorption calculations according to EFSA Guidance on Dermal Absorption [EFSA Journal 2017;15(6):4873)] for study … BASF DocID 2020/2097877
	Stinchcombe, S., 2021
	BASF DocID 2021/2040395

Materials and methods

^{14}C-BAS 750 F formulated as emulsion concentrate (EC) formulation BAS 758 00 F was applied to dermatomed human skin membranes at three nominal dose levels ("concentrate", 1:200 and 1:600 dilutions). The "concentrate" was the undiluted formulation with spiked radiolabel at a nominal concentration of BAS 750 F of 66.7 mg/mL. The 1:200 and 1:600 dilutions were prepared with the radiolabeled test substance in combination with blank formulation, which resulted in nominal concentrations of 0.333 mg/mL and 0.111 mg/mL. For details see Table A 9.

Table A 9: General information on the test system and test material used

	Species	Human		
	Method	In vitro		
Test material				
Active substance	Name (Lot/Batch No.)	^{14}C-BAS 750 F (1075-2301)		
	Test preparation	spiked		
	Radiochemical purity		>98	%
Product	Name (Lot/Batch No.)	BAS 758 00 F (FD-200124-0004)		
	Company code	BAS 758 00 F		
	Concentration a.s.		66.7	g/L
	Type of formulation	EC		
	Vehicle used (if any)	Drinking water		
Blank product	Name (Lot/Batch No.)	BAS 758 BD F (FD-200218-1015)		
	Concentration a.s.		0	g/L
	Type of formulation	EC		

The dermal penetration study used a flow-through system with cells having an exposed skin area of 1 cm². Eight cells were placed in an apparatus connected with a water bath for maintaining a skin temperature of 32 °C. Skin sections of 217 – 400 µm thickness from 4 human donors per dose were used (for details see Table A 10). Prior to the application of the test substance the integrity of the skin samples was investigated via TEER measurements. Measured values above 1 kΩ were expected for intact skin preparations.

Ethanol/tap water (1:9) and physiological saline with 0.01% NaN_3 were used as receptor fluids for the concentrate and the spray dilutions, respectively. The flow rate of the receptor was approx. 2.3 mL/h. The receptor fluid was sampled at hourly intervals during the first 8 hours, bi-hourly thereafter up to 18 hours and after 21 and 24 hours. The solubility of mefentrifluconazole in the receptor fluids was determined to be 46 and 15 mg/L in the receptors used for the concentrate and the spray dilution, respectively. Taking into account the solubility, the actual applied doses and the total receptor volume of approx. 55.2 mL (over 24 hours), no rate limiting effects on the diffusion process by saturation of the receptor fluid was expected as 12, 0.06 and 0.02 mg/L would have been the theoretically maximum achievable concentrations for the concentrate and 1:200 and 1:600 spray dilutions in the receptor fluid, respectively (for more details see Table A 10 and Table A 11).

A volume of 10 µL per chamber was applied to the skin. A first skin wash was performed after the 8-hour exposure. At the end of the study period of 24 hours a second skin wash was performed. Thereafter the diffusion cells were dismantled, and the skin samples removed and consecutively stripped with an adhesive

tape. A total of 20 tape strips were performed. The tapes were pooled into five samples (2, 4, 4, 4 and 6 tape strips for samples 1-5, respectively) for analysis. More details are given in Table A 10.

Table A 10: Details on the test system and test material used (Excerpt from EFSA excel sheet)

Diffusion cell	Type of diffusion cell	Flow-through	
	(If dynamic) Flow rate	2.3	mL/h
	Exposed skin area	1	cm^2
	Cover	Semi-occluded	
Skin sample	Skin type	Dermatomed	
	Skin thickness range	217 – 400	µm
	Skin donor age	35 - 63	years
	Skin donor sex	Female	
	Site	Abdomen	
	Source	Surgery	
	Integrity test	TEER	
Receptor	Receptor medium	undiluted: ethanol/tap water (1:9); dilution: physiological saline with 0.01% NaN_3	
	Solubility in receptor medium	undiluted: 46 mg/L dilution: 15 mg/L	
Sampling	Exposure time	8	hours
	Sampling duration	24	hours
	Sample intervals	(pre-dose, -15 min); 1; 2; 3; 4; 5; 6; 7; 8; 10; 12; 14; 16; 18; 21; 24 h after application	hours
	Skin wash/Swabbing	post exposure 8 hours and at termination 24 hours	
Tape strips	Tape stripping	Yes	
	Type of tape strips used	Scotch Crystal Tape 600 (3M, France)	
	TS 1-2 analysed separately?	Yes	

Remarks
Skin wash: 8-h post exposure: 2x with washing fluid (3% w/v Estesol® HAIR&BODY in tap water), gently swabbed 2x with cotton swabs soaked with washing fluid, 1x rinse with tap water, skin swabbed 1x with cotton swab soaked with tap water, dried with 1 dry cotton swab; at study termination skin was swabbed with washing fluid and thereafter with tap water.

Results and discussion

The preliminary permeability test (TEER) yielded resistances of above 1 kΩ for all cells which were consequently considered acceptable for the dermal absorption study.

The achieved actual concentrations of the application suspensions and the skin loading with the active substance was in good agreement with the calculated target values (see Table A 11).

Table A 11: Technical parameters of the dermal absorption study

Tested doses	Concentrate	Dilution 1 (1:200)	Dilution 1 (1:600)
Target concentration [mg/mL]	66.6	0.333	0.111
Surface area dose [µg/cm^2]	666	3.33	1.11
Total dose [µg/cell]	666	3.33	1.11
Specific activity [kBq/mL]	3700	2870	960
No. of donors	4	4	5
No. of replicates used/valid replicates*	8 / 8	8 / 8	8 / 8

The mean total recovery in all dose groups was greater than 95%. Therefore, no correction of the dermal penetration values was necessary.

For concentrate and the spray dilutions, dermal penetration was not essentially complete after 12 hours as indicated by the mean lower limit of confidence (LLC) values of 57.8, 46.3 and 59.1%. Therefore, the dose recovered from the 3rd to 20th tape strip was added to the absorbed dose for the concentrate and both spray dilutions. The dermal penetration estimates to be used for risk assessment were set at 0.2%, 6.3% and 7.8% for the formulation concentrate and the 1:200 and 1.600 spray dilutions, respectively. For details see Table A 12.

Table A 12: Dermal penetration of mefentrifluconazole formulated as BAS 758 00 F through human skin *in vitro*

	Concentrate (undiluted)		Dilution 1 (1:200)		Dilution 2 (1:600)	
Target concentration [mg/mL]	66.6		0.333		0.111	
Target dose [µg/cm²]	666		3.33		1.11	
Mean actual applied dose [µg/cm²]	663		3.38		1.10	
Recovery [%]	Mean	SD	Mean	SD	Mean	SD
Dislodgeable dose						
Skin wash after **8** and **24** hours	96.27	0.93	89.72	2.86	89.22	3.96
Donor chamber wash	0.22	0.11	1.39	1.08	1.36	0.81
Skin associated dose						
Tape strips 1-2	0.01 ~~0.06~~	0.0~~46~~	0.22	0.24	0.31	0.19
Tape strips 3-~~6~~-20	0.01 ~~0.02~~	0.01~~2~~	0.92	0.40	1.03	0.69
Skin preparation	0.08	0.11	0.75	0.34	0.38	0.47
Absorbed dose						
Receptor fluid	0.00~~2~~	N/A	0.09	0.05	0.03	0.05
Receptor chamber wash	N/A	N/A	3.22	1.33	3.89	2.36
Total recovery	96.59	0.91	96.32	0.61	96.21	1.42
LLC of t_0.5 absorption	57.80	29.70	46.28	16.26	59.05	23.63
Absorption complete?	No		No		No	
Measured absorption, if t_0.5<=75%	0.10	0.11	4.98	1.58	5.32	2.90
Measured absorption, if t_0.5>75%	N/A	N/A	N/A	N/A	N/A	N/A
Measured absorption corrected	0.10	0.11	4.98	1.58	5.32	2.90
Relevant absorption estimate	0.199		6.308		7.754	
Final estimate (rounded)	**0.2**		**6.3**		**7.8**	

Remarks

Recovery in receptor cell samples was zero in 7/8 cells of the concentrate group and in 3/8 cells of the dilution 2 group. Selecting an arbitrary T0.5 value for these cells (e.g. 100 or to 0.001) had no relevant influence on the final absorption estimate.

Conclusion:

The dermal penetration of ^{14}C-mefentrifluconazole (BAS 750 F) formulated as BAS 758 00 F through human dermatomed skin was determined in vitro. The % amount of applied dose (AD) considered absorbable within 24 hours was determined to be 0.10 ± 0.11% AD, 4.98 ± 1.58% AD, and 5.32 ± 2.90% AD for the formulation concentrate and the 1:200 and 1:600 spray dilutions, respectively. **The dermal**

penetration estimates to be used for risk assessment were set at 0.2% for the formulation concentrate, 6.3% for the 1:200 spray dilution and 7.8% for the 1:600 spray dilution based on current EFSA guidance criteria (2017).

A 2.10.2 ^{14}C-pyraclostrobin (BAS 500 F) in BAS 758 00 F

Comments of zRMS:	Study acceptable. The *in vitro* study on dermal absorption of pyraclostrobin in formulation 758 00 F was performed according to the OECD and EFSA guidance in compliance with GLP rules. No deviation was occurred during the study. The formulation was tested at the concentrated formulation (80 mg/mL of pyraclostrobin) and at the 1:200 and 1:400 dilutions which corresponds to the concentrations of 0.40 mg/mL and 0.20 mg/mL of pyraclostrobin, respectively. The dermal penetration was estimated as 0.0078% for the formulation concentrate, 2.6% for the 1:200 spray dilution and 2.2% for the 1:400 spray dilution based on current EFSA guidance criteria (2017).

Reference:	CP 7.3/3
Report	^{14}C-BAS 500 F in BAS 758 00 F - Study of penetration through human skin in vitro Rieken, C., ~~2020~~ 2021 Report No. 10B0118/03B038 BASF DocID 2020/2093957 Authority registration No
Guideline(s):	OECD 428, OECD Guidance Document No. 28 for the conduct of skin absorption studies (March 2004)
Deviations:	No
GLP:	Yes (certified by Landesamt fuer Umwelt, Wasserwirtschaft und Gewerbeaufsicht, Mainz, Germany, Germany)
Acceptability:	Yes
Duplication (if vertebrate study)	No

Reference:	CP 7.3/4
Report	Excel file using "efs24873-sup-0001-supinfo_1.xlsx" (version 3) to support dermal absorption calculations according to EFSA Guidance on Dermal Absorption [EFSA Journal 2017;15(6):4873)] for study … BASF DocID 2020/2093957 Stinchcombe, S., 2021 BASF DocID 2021/2040396

Materials and methods

^{14}C-BAS 500 F formulated as emulsion concentrate (EC) formulation BAS 758 00 F was applied to dermatomed human skin membranes at three nominal dose levels ("concentrate", 1:200 and 1:400 dilutions). The "concentrate" was the undiluted formulation with spiked radiolabel at a nominal concentration of BAS 500 F of 80 mg/mL. The 1:200 and 1:400 dilutions were prepared with the radiolabeled test substance in combination with blank formulation, which resulted in nominal concentrations of 0.4 mg/mL and 0.2 mg/mL. For details see Table A 13.

Table A 13: General information on the test system and test material used

	Species	Human		
	Method	In vitro		
Test material				
Active substance	Name (Lot/Batch No.)	^{14}C-BAS 500 F (566-6501)		
	Test preparation	spiked		
	Radiochemical purity		>98	%
Product	Name (Lot/Batch No.)	BAS 758 00 F (FD-200124-0004)		
	Company code	BAS 758 00 F		
	Concentration a.s.		80	g/L
	Type of formulation	EC		
	Vehicle used (if any)	Drinking water		
Blank product	Name (Lot/Batch No.)	BAS 758 BE F		
	Concentration a.s.		0	g/L
	Type of formulation	EC		

The dermal penetration study used a flow-through system with cells having an exposed skin area of 1 cm². Eight cells were placed in an apparatus connected with a water bath for maintaining a skin temperature of 32 °C. Skin sections of 225 – 427 µm thickness from 4 human donors per dose were used (for details see Table A 14). Prior to the application of the test substance the integrity of the skin samples was investigated via TEER measurements. Measured values above 1 kΩ were expected for intact skin preparations.

Ethanol/tap water (3:7) and physiological saline with 0.01% NaN_3 were used as receptor fluids for the concentrate and the spray dilutions, respectively. The flow rate of the receptor was approx. 2.3 mL/h. The receptor fluid was sampled at hourly intervals during the first 8 hours, bi-hourly thereafter up to 18 hours and after 21 and 24 hours. The solubility of pyraclostrobin in the receptor fluids was determined to be 89 and 0.41 mg/L in the receptors used for the concentrate and the spray dilution, respectively. Taking into account the solubility, the actual applied doses and the total receptor volume of approx. 55.2 mL (over 24 hours), no rate limiting effects on the diffusion process by saturation of the receptor fluid was expected as ca. 15, 0.07 and 0.04 mg/L would have been the theoretically maximum achievable concentrations for the concentrate and 1:200 and 1:400 spray dilutions in the receptor fluid, respectively (for more details see Table A 14 and Table A 15).

A volume of 10 µL per chamber was applied to the skin. A first skin wash was performed after the 8-hour exposure. At the end of the study period of 24 hours a second skin wash was performed. Thereafter the diffusion cells were dismantled, and the skin samples removed and consecutively stripped with an adhesive tape. A total of 20 tape strips were performed. The tapes were pooled into five samples (2, 4, 4, 4 and 6 tape strips for samples 1-5, respectively) for analysis. More details are given in Table A 14.

Table A 14: Details on the test system and test material used (Excerpt from EFSA excel sheet)

Diffusion cell	Type of diffusion cell	Flow-through	
	(If dynamic) Flow rate	2.3	mL/h
	Exposed skin area	1	cm^2
	Cover	Semi-occluded	
Skin sample	Skin type	Dermatomed	
	Skin thickness range	225 – 427	µm
	Skin donor age	24 - 63	years
	Skin donor sex	Female	
	Site	Abdomen	
	Source	Surgery	
	Integrity test	TEER	
Receptor	Receptor medium	undiluted: ethanol/tap water (3:7); dilution: physiological saline with 0.01% NaN_3	
	Solubility in receptor medium	undiluted: 89 mg/L dilution: 0.41 mg/L	
Sampling	Exposure time	8	hours
	Sampling duration	24	hours
	Sample intervals	(pre-dose, -15 min); 1; 2; 3; 4; 5; 6; 7; 8; 10; 12; 14; 16; 18; 21; 24 h after application	hours
	Skin wash/Swabbing	post exposure 8 hours and at termination 24 hours	
Tape strips	Tape stripping	Yes	
	Type of tape strips used	Scotch Crystal Tape 600 (3M, France)	
	TS 1-2 analysed separately?	Yes	

Remarks
Skin wash: 8-h post exposure: 2x with washing fluid (3% w/v Estesol® HAIR&BODY in tap water), gently swabbed 2x with cotton swabs soaked with washing fluid, 1x rinse with tap water, skin swabbed 1x with cotton swab soaked with tap water, dried with 1 dry cotton swab; at study termination skin was swabbed with washing fluid and thereafter with tap water.

Results and discussion

The preliminary permeability test (TEER) yielded resistances of above 1 kΩ for all cells which were consequently considered acceptable for the dermal absorption study.

The achieved actual concentrations of the application suspensions and the skin loading with the active substance was in good agreement with the calculated target values (see Table A 15).

Table A 15: Technical parameters of the dermal absorption study

Tested doses	Concentrate	Dilution 1 (1:200)	Dilution 1 (1:400)
Target concentration [mg/mL]	80	0.4	0.2
Surface area dose [µg/cm^2]	800	4	2
Total dose [µg/cell]	800	4	2
Specific activity [kBq/mL]	3700	2130	1060
No. of donors	4	8	8
No. of replicates used/valid replicates*	8 / 8	16 / 16	16 / 16

The mean total recovery in all dose groups was greater than 95%. Therefore, no correction of the dermal penetration values was necessary.

For the 1:200 and 1:400 spray dilutions, dermal penetration was essentially complete after 12 hours as indicated by the mean lower limit of confidence (LLC) value of 100%. However, for the formulation

concentrate, absorption was not essentially complete within 12 hours (LLC value of -17.2). Therefore, the dose recovered from the 3rd to 20th tape strip was added to the absorbed dose for the concentrate only. The dermal penetration estimates to be used for risk assessment were set at ~~0.2~~ 0.0078%, ~~6.3~~ 2.6% and ~~7.8~~ 2.2% for the formulation concentrate and the 1:200 and 1.400 spray dilutions, respectively. For details see Table A 16.

Table A 16: Dermal penetration of pyraclostrobin formulated as BAS 758 00 F through human skin *in vitro*

	Concentrate (undiluted)		Dilution 1 (1:200)		Dilution 2 (1:400)	
Target concentration [mg/mL]	80		0.4		0.2	
Target dose [µg/cm²]	800		4		2	
Mean actual applied dose [µg/cm²]	812		4.1		2	
Recovery [%]	Mean	SD	Mean	SD	Mean	SD
Dislodgeable dose						
Skin wash after **8** and **24** hours	94.77	4.77	91.65	3.02	92.53	3.90
Donor chamber wash	1.05	0.38	1.80	1.27	1.86	1.35
Skin associated dose						
Tape strips 1-2	0.00	N/A	0.50 ~~0.58~~	0.74 ~~0.77~~	0.58	0.54
Tape strips 3-~~6~~ 20	N/A	N/A	0.95 ~~1.01~~	0.74	1.46	1.43
Skin preparation	0.00	0.00	1.02	0.59	0.85	0.90
Absorbed dose						
Receptor fluid	0.00	N/A	0.02	0.02	0.01	0.01
Receptor chamber wash	0.00	0.00	1.03	0.44	0.68	0.45
Total recovery	95.82	4.92	96.97	1.20	97.97	2.78
LLC of t_0.5 absorption	-17.20	29.70	100.00	0.00	100.00	0.00
Absorption complete?	No		Yes		Yes	
Measured absorption, if t_0.5<=75%	0.00	0.00	N/A	N/A	N/A	N/A
Measured absorption, if t_0.5>75%	N/A	N/A	2.07	0.98	1.54	1.26
Measured absorption corrected	0.00	0.00	2.07	0.98	1.54	1.26
Relevant absorption estimate	0.008		2.592		2.213	
Final estimate (rounded)	**0.0078**		**2.6**		**2.2**	

Conclusion:

The dermal penetration of ^{14}C-pyraclostrobin (BAS 500 F) formulated as BAS 758 00 F through human dermatomed skin was determined in vitro. The % amount of applied dose (AD) considered absorbable within 24 hours was determined to be 0.005 ± 0.004% AD, 2.07 ± 0.98% AD, and 1.54 ± 1.26% AD for the formulation concentrate and the 1:200 and 1:400 spray dilutions, respectively. **The dermal penetration estimates to be used for risk assessment were set at 0.0078% for the formulation concentrate, 2.6% for the 1:200 spray dilution and 2.2% for the 1:400 spray dilution based on current EFSA guidance criteria (2017).**

A 2.11 Other/Special Studies

None available.

Exposure calculations

A 2.12 Operator exposure calculations (KCP 7.2.1.1)

A 2.12.1 Calculations for mefentrifluconazole

A 3.1.1-1 Input parameters considered for the estimation of operator exposure to mefentrifluconazole

Application rate of active substance	**0,1**	kg a.s./ha
Assumed area treated	**50**	ha/day
Amount of active substance applied	**5**	kg a.s./day
Dermal absorption of the product	**0,20%**	
Dermal absorption of in-use dilution	**6,30%**	
Formulation type	**Soluble concentrates, emulsifiable concentrate, etc.**	
Indoor or Outdoor application	**Outdoor**	
Application method	**Downward spraying**	
Application equipment	**Vehicle-mounted**	
Season	**not relevant**	

A 3.1.1-2 Estimation of operator exposure towards mefentrifluconazole using the EFSA model (without PPE)

	Exposure values	µg exposure/day mixed and loaded 75th centile	95th centile	Reference	Comment
Mixing and loading	Hands	16767	62314	AOEM	
	Body	11058	114960	AOEM	
	Head	259	1423	AOEM	
	Protected hands (gloves)	98	990	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	99	731	AOEM	
	Protected head (hood and face shield)	4	81	AOEM	
	Inhalation	6	30	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	ork wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied 75th centile	95th centile	Reference	Comment
Application	Hands	742	7449	AOEM	
	Body	415	2138	AOEM	
	Head	20	59	AOEM	
	Protected hands (gloves)	102	4021	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	11	28	AOEM	
	Inhalation	2	7	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	ork wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

	Without RPE/PPE	With RPE/PPE
Longer term		
Total systemic exposure from mixing, loading and application (mg a.s./day)	**0,1385431**	**0,0912189**
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	**0,0023091**	**0,0015203**
% of RVNAS	**6,60%**	**4,34%**
Acute		
Total systemic exposure from mixing, loading and application (mg a.s./day)	**1,0022392**	**0,6408721**
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	**0,0167040**	**0,0106812**
% of RVAAS	**11,14%**	**7,12%**

A 3.1.1-3 Estimation of operator exposure towards mefentrifluconazole using the EFSA model (with PPE)

	Exposure values	µg exposure/day mixed and loaded 75th centile	µg exposure/day mixed and loaded 95th centile	Reference	Comment
Mixing and loading	Hands	16767	62314	AOEM	
	Body	11058	114960	AOEM	
	Head	259	1423	AOEM	
	Protected hands (gloves)	98	990	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	99	731	AOEM	
	Protected head (hood and face shield)	4	81	AOEM	
	Inhalation	6	30	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	Yes		Incl. in AOEM model	
	Clothing	ork wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied 75th centile	µg exposure/day applied 95th centile	Reference	Comment
Application	Hands	742	7449	AOEM	
	Body	415	2138	AOEM	
	Head	20	59	AOEM	
	Protected hands (gloves)	102	4021	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	11	28	AOEM	
	Inhalation	2	7	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	Yes		Incl. in AOEM model	
	Clothing	ork wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

	Without RPE/PPE	With RPE/PPE
Longer term		
Total systemic exposure from mixing, loading and application (mg a.s./day)	**0,1385431**	**0,0175577**
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	**0,0023091**	**0,0002926**
% of RVNAS	**6,60%**	**0,84%**
Acute		
Total systemic exposure from mixing, loading and application (mg a.s./day)	**1,0022392**	**0,3022773**
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	**0,0167040**	**0,0050380**
% of RVAAS	**11,14%**	**3,36%**

A 2.12.2 Calculations for pyraclostrobin

A 3.1.2-1 Input parameters considered for the estimation of operator exposure to pyraclostrobin

Application rate of active substance	**0,12**	kg a.s./ha
Assumed area treated	**50**	ha/day
Amount of active substance applied	**6**	kg a.s./day
Dermal absorption of the product	**0,01%**	
Dermal absorption of in-use dilution	**2,60%**	
Formulation type	**Soluble concentrates, emulsifiable concentrate, etc.**	
Indoor or Outdoor application	**Outdoor**	
Application method	**Downward spraying**	
Application equipment	**Vehicle-mounted**	
Season	**not relevant**	

A 3.1.2-2 Estimation of operator exposure towards pyraclostrobin using the EFSA model (without PPE)

	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75th centile	95th centile		
Mixing and loading	Hands	19293	71819	AOEM	
	Body	12569	121213	AOEM	
	Head	311	1707	AOEM	
	Protected hands (gloves)	111	1188	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	116	878	AOEM	
	Protected head (hood and face shield)	5	97	AOEM	
	Inhalation	6	30	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	ork wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied		Reference	Comment
		75th centile	95th centile		
Application	Hands	890	8513	AOEM	
	Body	498	2565	AOEM	
	Head	24	71	AOEM	
	Protected hands (gloves)	112	4107	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	14	33	AOEM	
	Inhalation	3	8	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	ork wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

	Without RPE/PPE	With RPE/PPE
Longer term		
Total systemic exposure from mixing, loading and application (mg a.s./day)	**0,0481118**	**0,0345330**
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	**0,0008019**	**0,0005755**
% of RVNAS	**5,35%**	**3,84%**

A 3.1.2-3 Estimation of operator exposure towards pyraclostrobin using the EFSA model (with PPE)

Mixing and loading

Exposure values	µg exposure/day mixed and loaded		Reference	Comment
	75th centile	95th centile		
Hands	19293	71819	AOEM	
Body	12569	121213	AOEM	
Head	311	1707	AOEM	
Protected hands (gloves)	111	1188	AOEM	
Protected body (workwear or protective garment and sturdy footwear)	116	878	AOEM	
Protected head (hood and face shield)	5	97	AOEM	
Inhalation	6	30	AOEM	
Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
Gloves	Yes		Incl. in AOEM model	
Clothing	ork wear - arms, body and legs covered		Incl. in AOEM model	
Head and respiratory PPE	None		1	1
Water soluble bag	No		1	

Application

Exposure values	µg exposure/day applied		Reference	Comment
	75th centile	95th centile		
Hands	890	8513	AOEM	
Body	498	2565	AOEM	
Head	24	71	AOEM	
Protected hands (gloves)	112	4107	AOEM	
Protected body (workwear or protective garment and sturdy footwear)	14	33	AOEM	
Inhalation	3	8	AOEM	
Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
Gloves	Yes		Incl. in AOEM model	
Clothing	ork wear - arms, body and legs covered		Incl. in AOEM model	
Head and respiratory PPE	None		1	1
Closed cab	No		vehicle mounted upward spraying only	

	Without RPE/PPE	With RPE/PPE
Longer term		
Total systemic exposure from mixing, loading and application (mg a.s./day)	**0,0481118**	**0,0127751**
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	**0,0008019**	**0,0002129**
% of RVNAS	**5,35%**	**1,42%**

A 2.12.3 Calculations for metrafenone

A 3.1.3-1 Input parameters considered for the estimation of operator exposure to metrafenone

Application rate of active substance	**0,15**	kg a.s./ha
Assumed area treated	**50**	ha/day
Amount of active substance applied	**7,5**	kg a.s./day
Dermal absorption of the product	**25,00%**	
Dermal absorption of in-use dilution	**705,00%**	
Formulation type	**Soluble concentrates, emulsifiable concentrate, etc.**	
Indoor or Outdoor application	**Outdoor**	
Application method	**Downward spraying**	
Application equipment	**Vehicle-mounted**	
Season	**not relevant**	

A 3.1.3-2 Estimation of operator exposure towards metrafenone using the EFSA model (without PPE)

	Exposure values	µg exposure/day mixed and loaded 75th centile	95th centile	Reference	Comment
Mixing and loading	Hands	22909	85448	AOEM	
	Body	14704	129332	AOEM	
	Head	389	2134	AOEM	
	Protected hands (gloves)	128	1486	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	142	1097	AOEM	
	Protected head (hood and face shield)	6	121	AOEM	
	Inhalation	7	30	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	ork wear - arms, body and legs covered		cl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied 75th centile	95th centile	Reference	Comment
Application	Hands	1112	10024	AOEM	
	Body	622	3206	AOEM	
	Head	29	89	AOEM	
	Protected hands (gloves)	127	4216	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	17	42	AOEM	
	Inhalation	3	9	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	ork wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

	Without RPE/PPE	With RPE/PPE
Longer term		
Total systemic exposure from mixing, loading and application (mg a.s./day)	**10,8330207**	**6,7387553**
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	**0,1805503**	**0,1123126**
% of RVNAS	**41,99%**	**26,12%**

Mixing and loading

Exposure values	µg exposure/day mixed and loaded		Reference	Comment
	75th centile	95th centile		
Hands	22909	85448	AOEM	
Body	14704	129332	AOEM	
Head	389	2134	AOEM	
Protected hands (gloves)	128	1486	AOEM	
Protected body (workwear or protective garment and sturdy footwear)	142	1097	AOEM	
Protected head (hood and face shield)	6	121	AOEM	
Inhalation	7	30	AOEM	
Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
Gloves	No			
Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
Head and respiratory PPE	None		1	1
Water soluble bag	No		1	

Application

Exposure values	µg exposure/day applied		Reference	Comment
	75th centile	95th centile		
Hands	1112	10024	AOEM	
Body	622	3206	AOEM	
Head	29	89	AOEM	
Protected hands (gloves)	127	4216	AOEM	
Protected body (workwear or protective garment and sturdy footwear)	17	42	AOEM	
Inhalation	3	9	AOEM	
Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
Gloves	No			
Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
Head and respiratory PPE	None		1	1
Closed cab	No		vehicle mounted upward spraying only	

1. Total

	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	10.7448298	6.6808111	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.1790805	0.1113469	
% of RVNAS	41.65%	25.89%	

A 3.1.3-3 Estimation of operator exposure towards metrafenone using the EFSA model (with PPE)

	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75th centile	95th centile		
Mixing and loading	Hands	22909	85448	AOEM	
	Body	14704	129332	AOEM	
	Head	389	2134	AOEM	
	Protected hands (gloves)	128	1486	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	142	1097	AOEM	
	Protected head (hood and face shield)	6	121	AOEM	
	Inhalation	7	30	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	Yes		Incl. in AOEM model	
	Clothing	ork wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied		Reference	Comment
		75th centile	95th centile		
Application	Hands	1112	10024	AOEM	
	Body	622	3206	AOEM	
	Head	29	89	AOEM	
	Protected hands (gloves)	127	4216	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	17	42	AOEM	
	Inhalation	3	9	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	Yes		Incl. in AOEM model	
	Clothing	ork wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

	Without RPE/PPE	With RPE/PPE
Longer term		
Total systemic exposure from mixing, loading and application (mg a.s./day)	**10,8330207**	**0,3040294**
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	**0,1805503**	**0,0050672**
% of RVNAS	**41,99%**	**1,18%**

	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75th centile	95th centile		
Mixing and loading	Hands	22909	85448	AOEM	
	Body	14704	129332	AOEM	
	Head	389	2134	AOEM	
	Protected hands (gloves)	128	1486	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	142	1097	AOEM	
	Protected head (hood and face shield)	6	121	AOEM	
	Inhalation	7	30	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	Yes		Incl. in AOEM model	
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied		Reference	Comment
		75th centile	95th centile		
Application	Hands	1112	10024	AOEM	
	Body	622	3206	AOEM	
	Head	29	89	AOEM	
	Protected hands (gloves)	127	4216	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	17	42	AOEM	
	Inhalation	3	9	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	Yes		Incl. in AOEM model	
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

1. Total

	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	10.7448298	0.2953781	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.1790805	0.0049230	
% of RVNAS	41.65%	1.14%	

A 2.13 Worker exposure calculations (KCP 7.2.3.1)

A 2.13.1 Calculations for mefentrifluconazole

A 3.2.1-1 Input parameters considered for the estimation of worker exposure to mefentrifluconazole

Crop type	Cereals	
Indoor or outdoor	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Worker's task	Inspection, irrigation	
Main body parts in contact with foliage	Hand and body	
Application rate of active substance	0,1	kg a.s./ha
Number of applications	2	
Interval between multiple applications	14	days
Half-life of active substance	30	days
Multiple application factor	1,7	
Dermal absorption of the product	0,20%	
Dermal absorption of the in-use dilution	6,30%	
Dislodgeable foliar residue (i_AppRate*i_DFR)	0,3	µg a.s./cm^2
Working hours	2	hr
Dermal transfer coefficient - Total potential exposure	12500	cm^2/hr
Dermal transfer coefficient - arms, body and legs covered	1400	cm^2/hr
Dermal transfer coefficient - hands, arms, body and legs covered	no TC available for this assessment	cm^2/hr

A 3.2.1-2 Estimation of worker exposure to mefentrifluconazole

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves
Total systemic exposure (mg a.s./day)	**0,8144174**	**0,0912147**	**no TC available for this assessment**
Total systemic exposure per kg body weight (mg/kg bw/day)	**0,0135758**	**0,0015202**	
% of RVNAS	**38,78%**	**4,34%**	

A 2.13.2 Calculations for pyraclostrobin

A 3.2.2-1 Input parameters considered for the estimation of worker exposure to pyraclostrobin

Crop type	Cereals	
Indoor or outdoor	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Worker's task	Inspection, irrigation	
Main body parts in contact with foliage	Hand and body	
Application rate of active substance	0,12	kg a.s./ha
Number of applications	2	
Interval between multiple applications	14	days
Half-life of active substance	30	days
Multiple application factor	1,7	
Dermal absorption of the product	0,01%	
Dermal absorption of the in-use dilution	2,60%	
Dislodgeable foliar residue (i_AppRate*i_DFR)	0,36	µg a.s./cm²
Working hours	2	hr
Dermal transfer coefficient - Total potential exposure	12500	cm²/hr
Dermal transfer coefficient - arms, body and legs covered	1400	cm²/hr
Dermal transfer coefficient - hands, arms, body and legs cov	no TC available for this assessment	cm²/hr

A 3.2.2-2 Estimation of worker exposure to pyraclostrobin

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves
Total systemic exposure (mg a.s./day)	**0,4033305**	**0,0451730**	**no TC available for this assessment**
Total systemic exposure per kg body weight (mg/kg bw/day)	**0,0067222**	**0,0007529**	
% of RVNAS	**44,81%**	**5,02%**	

A 2.13.3 Calculations for metrafenone

A 3.2.3-1 Input parameters considered for the estimation of worker exposure to metrafenone

Crop type	Cereals	
Indoor or outdoor	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Worker's task	Inspection, irrigation	
Main body parts in contact with foliage	Hand and body	
Application rate of active substance	0,15	kg a.s./ha
Number of applications	2	
Interval between multiple applications	14	days
Half-life of active substance	30	days
Multiple application factor	1,7	
Dermal absorption of the product	25,00%	
Dermal absorption of the in-use dilution	75,00%	
Dislodgeable foliar residue (i_AppRate*i_DFR)	0,45	µg a.s./cm^2
Working hours	2	hr
Dermal transfer coefficient - Total potential exposure	12500	cm^2/hr
Dermal transfer coefficient - arms, body and legs covered	1400	cm^2/hr
Dermal transfer coefficient - hands, arms, body and legs covered	no TC available for this assessment	cm^2/hr

Crop type	Cereals		
Indoor or outdoor	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Worker's task	Inspection, irrigation		
Main body parts in contact with foliage	Hand and body		
Application rate of active substance	0.15	kg a.s./ha	*i_AppRate*
Number of applications	2		*i_AppNo*
Interval between multiple applications	14	days	*i_AppInt*
Half-life of active substance	30	days	*d_HalflifeAS*
Multiple application factor	1.7		*d_MAF*
Dermal absorption of the product	25.00%		*i_AbsorpProduct*
Dermal absorption of the in-use dilution	70.00%		*i_AbsorpInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.45	µg a.s./cm^2	*d_DFR*
Working hours	2	hr	*d_WorkHr*
Dermal transfer coefficient - Total potential exposure	12500	cm^2/hr	*d_DermTcUCV*
Dermal transfer coefficient - arms, body and legs covered	1400	cm^2/hr	*d_DermTcCV1*
Dermal transfer coefficient - hands, arms, body and legs covered	no TC available for this assessment	cm^2/hr	*d_DermTcCV2*
Inhalation transfer coefficient for automated applications	NA	ha/hr*10^(-3)	*d_InhalTcAut*
Inhalation transfer coefficient for cutting ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcCut*
Inhalation transfer coefficient for sorting / bundling ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcSort*

A 3.2.3-2 Estimation of worker exposure to metrafenone

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves
Total systemic exposure (mg a.s./day)	14,5431671	1,6288347	no TC available for this assessment
Total systemic exposure per kg body weight (mg/kg bw/day)	0,2423861	0,0271472	
% of RVNAS	56,37%	6,31%	

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves
Total systemic exposure (mg a.s./day)	13.5736226	1.5202457	no TC available for this assessment
Total systemic exposure per kg body weight (mg/kg bw/day)	0.2262270	0.0253374	
% of RVNAS	52.61%	5.89%	

A 2.14 Bystander and resident exposure calculations (KCP 7.2.2.1)

A 2.14.1 Calculations for mefentrifluconazole

A 3.3.1-1 Input parameters considered for the estimation of bystander exposure to mefentrifluconazole

Croptype	Cereals	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Formulation type	oluble concentrates, emulsifiable concentrate, etc.	
Application rate of the product	0,1	kg a.s./ha
Buffer strip	2-3	m
Concentration of active substance (in-use dilution for liquid applications)	1	g a.s./l
Dermal absorption of product	0,20%	
Dermal absorption of in-use dilution	6,30%	
Oral absorption	100,00%	
Dislodgeable foliar residue (i_AppRate*i_DFI	0,3	µg a.s./cm^2
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-	Pa
Concentration in air	0,001	mg/m^3
Bystander dermal spray drift exposure - adult	1,21	ml spray dilution/person
Bystander dermal spray drift exposure - child	0,74	ml spray dilution/person
Bystander inhal. spray drift exposure - adult	0,00050	ml spray dilution/person
Bystander inhal. spray drift exposure - child	0,00112	ml spray dilution/person
Exposure duration	2	hours
Exposure duration entry into treated crops	0,25	hours
Light clothing adjustment factor	18,0%	
Breathing rate adult	0,23	m^3/kg bw/day
Breathing rate child (1-3 year old)	1,07	m^3/kg bw/day
Drift percentage on surface (90th percentile)	8,50%	
Turf transferable residues percentage	5,00%	
Transfer coeff. of surface deposits-adult	14500	cm^2/hour
Transfer coeff. of surface deposits-child (1-3 year old)	5200	cm^2/hour
Saliva extraction percentage	50,00%	
Surface area of hands mouthed	20	cm^2
Frequency of hand to mouth activity	20	events/hour
Ingestion rate for mouthing of grass per day	25	cm^2
Dislodgeable residues percentage transferability for object to mouth	20,00%	
Transfer coefficient for entry into treated crop	7500	cm^2/h
Transfer coefficient for entry into treated crop	2250	cm^2/h

A 3.3.1-2 Estimation of bystander exposure to mefentrifluconazole

1.1 1-3 year old child

	Spray drift	Vapour	Surface depo-sits	Entry into treated crops
Total systemic exposure (mg a.s./day)	**0,0393484**	**0,0107000**	**0,0084624**	**0,0183244**
Total systemic exposure per kg body weight (mg/kg bw/day)	**0,0039348**	**0,0010700**	**0,0008462**	**0,0018324**
% of RVAAS	**2,62%**	**0,71%**	**0,56%**	**1,22%**

1.2 Adult

	Spray drift	Vapour	Surface depo-sits	Entry into treated crops
Total systemic exposure (mg a.s./day)	**0,0630086**	**0,0138000**	**0,0133836**	**0,0610813**
Total systemic exposure per kg body weight (mg/kg bw/day)	**0,0010501**	**0,0002300**	**0,0002231**	**0,0010180**
% of RVAAS	**0,70%**	**0,15%**	**0,15%**	**0,68%**

A 3.3.1-3 Input parameters considered for the estimation of resident exposure to mefentrifluconazole

Croptype	Cereals	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Buffer strip	2-3	m
Application rate of the product	0,1	kg a.s./ha
Concentration of active substance (in-use dilution for liquid applications)	1	g a.s./l
Dermal absorption of product	0,20%	
Dermal absorption of in-use dilution	6,30%	
Oral absorption	100,00%	
Dislodgeable foliar residue (i_AppRate*i_DFR)	0,3	µg a.s./cm²
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa
Concentration in air	0,001	mg/m³
Resident dermal spray drift exposure 75th percentile - adult	0,47	ml spray dilution/person
Resident dermal spray drift exposure 75th percentile - child	0,327	ml spray dilution/person
Resident inhal. spray drift exposure 75th percentile - adult	0,00010	ml spray dilution/person
Resident inhal. spray drift exposure 75th percentile - child	0,00022	ml spray dilution/person
Resident dermal spray drift exposure mean - adult	0,22318	ml spray dilution/person
Resident dermal spray drift exposure mean - child	0,18	ml spray dilution/person
Resident inhal. spray drift exposure mean - adult	0,00009	ml spray dilution/person
Resident inhal. spray drift exposure mean - child	0,00017	ml spray dilution/person
Exposure duration dermal	2	hours
Exposure duration inhalation	24	hours
Exposure duration entry into treated crops	0,25	hours
Light clothing adjustment factor	18,0%	
Breathing rate adult	0,23	m³/day/kg
Breathing rate child (1-3 year old)	1,07	m³/day/kg
Drift percentage on surface (75th percentile)	5,60%	
Drift percentage on surface (mean)	4,10%	
Turf transferable residues percentage	5,00%	
Transfer coeff. of surface deposits-adult	7300	cm²/hour
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm²/hour
Saliva extraction percentage	50,00%	
Surface area of hands mouthed	20	cm²
Frequency of hand to mouth activity	9,5	events/hour
Ingestion rate for mouthing of grass per day	25	cm²
Dislodgeable residues percentage transferability for object to mouth	20,00%	
Transfer coefficient for entry into treated crops (75th percentile) -	7500	cm²/h
Transfer coefficient for entry into treated crops (75th percentile) -	2250	cm²/h
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm²/h
Transfer coefficient for entry into treated crops (mean) - child	1794	cm²/h

A 3.3.1-4 Estimation of resident exposure to mefentrifluconazole

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	**0,0171128**	**0,0107000**	**0,0029806**	**0,0183244**	**0,0369617**
Total systemic exposure per kg body weight (mg/kg bw/day)	**0,0017113**	**0,0010700**	**0,0002981**	**0,0018324**	**0,0036962**
% of RVNAS	**4,89%**	**3,06%**	**0,85%**	**5,24%**	**10,56%**

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	**0,0243802**	**0,0138000**	**0,0044391**	**0,0610813**	**0,0773717**
Total systemic exposure per kg body weight (mg/kg bw/day)	**0,0004063**	**0,0002300**	**0,0000740**	**0,0010180**	**0,0012895**
% of RVNAS	**1,16%**	**0,66%**	**0,21%**	**2,91%**	**3,68%**

A 2.14.2 Calculations for pyraclostrobin

A 3.3.2-1 Input parameters considered for the estimation of resident exposure to pyraclostrobin

Croptype	Cereals	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Buffer strip	2-3	m
Application rate of the product	0,12	kg a.s./ha
Concentration of active substance (in-use dilution for liquid applications)	1,2	g a.s./l
Dermal absorption of product	0,01%	
Dermal absorption of in-use dilution	2,60%	
Oral absorption	50,00%	
Dislodgeable foliar residue (i_AppRate*i_DFR)	0,36	µg a.s./cm^2
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa
Concentration in air	0,001	mg/m^3
Resident dermal spray drift exposure 75th percentile - adult	0,47	ml spray dilution/person
Resident dermal spray drift exposure 75th percentile - child	0,327	ml spray dilution/person
Resident inhal. spray drift exposure 75th percentile - adult	0,00010	ml spray dilution/person
Resident inhal. spray drift exposure 75th percentile - child	0,00022	ml spray dilution/person
Resident dermal spray drift exposure mean - adult	0,22318	ml spray dilution/person
Resident dermal spray drift exposure mean - child	0,18	ml spray dilution/person
Resident inhal. spray drift exposure mean - adult	0,00009	ml spray dilution/person
Resident inhal. spray drift exposure mean - child	0,00017	ml spray dilution/person
Exposure duration dermal	2	hours
Exposure duration inhalation	24	hours
Exposure duration entry into treated crops	0,25	hours
Light clothing adjustment factor	18,0%	
Breathing rate adult	0,23	m^3/day/kg
Breathing rate child (1-3 year old)	1,07	m^3/day/kg
Drift percentage on surface (75th percentile)	5,60%	
Drift percentage on surface (mean)	4,10%	
Turf transferable residues percentage	5,00%	
Transfer coeff. of surface deposits-adult	7300	cm^2/hour
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm^2/hour
Saliva extraction percentage	50,00%	
Surface area of hands mouthed	20	cm^2
Frequency of hand to mouth activity	9,5	events/hour
Ingestion rate for mouthing of grass per day	25	cm^2
Dislodgeable residues percentage transferability for object to mouth	20,00%	
Transfer coefficient for entry into treated crops (75th percentile) -	7500	cm^2/h
Transfer coefficient for entry into treated crops (75th percentile) -	2250	cm^2/h
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm^2/h
Transfer coefficient for entry into treated crops (mean) - child	1794	cm^2/h

A 3.3.2-2 Estimation of resident exposure to pyraclostrobin

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	**0,0086300**	**0,0107000**	**0,0016228**	**0,0090749**	**0,0239330**
Total systemic exposure per kg body weight (mg/kg bw/day)	**0,0008630**	**0,0010700**	**0,0001623**	**0,0009075**	**0,0023933**
% of RVNAS	**5,75%**	**7,13%**	**1,08%**	**6,05%**	**15,96%**

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	**0,0121445**	**0,0138000**	**0,0021984**	**0,0302498**	**0,0453466**
Total systemic exposure per kg body weight (mg/kg bw/day)	**0,0002024**	**0,0002300**	**0,0000366**	**0,0005042**	**0,0007558**
% of RVNAS	**1,35%**	**1,53%**	**0,24%**	**3,36%**	**5,04%**

A 2.14.3 Calculations for metrafenone

A 3.3.3-1 Input parameters considered for the estimation of resident exposure to metrafenone

Croptype	Cereals	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Buffer strip	2-3	m
Application rate of the product	0,15	kg a.s./ha
Concentration of active substance (in-use dilution for liquid applications)	1,5	g a.s./l
Dermal absorption of product	25,00%	
Dermal absorption of in-use dilution	75,00%	
Oral absorption	100,00%	
Dislodgeable foliar residue (i_AppRate*i_DFR)	0,45	µg a.s./cm²
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa
Concentration in air	0,001	mg/m³
Resident dermal spray drift exposure 75th percentile - adult	0,47	ml spray dilution/person
Resident dermal spray drift exposure 75th percentile - child	0,327	ml spray dilution/person
Resident inhal. spray drift exposure 75th percentile - adult	0,00010	ml spray dilution/person
Resident inhal. spray drift exposure 75th percentile - child	0,00022	ml spray dilution/person
Resident dermal spray drift exposure mean - adult	0,22318	ml spray dilution/person
Resident dermal spray drift exposure mean - child	0,18	ml spray dilution/person
Resident inhal. spray drift exposure mean - adult	0,00009	ml spray dilution/person
Resident inhal. spray drift exposure mean - child	0,00017	ml spray dilution/person
Exposure duration dermal	2	hours
Exposure duration inhalation	24	hours
Exposure duration entry into treated crops	0,25	hours
Light clothing adjustment factor	18,0%	
Breathing rate adult	0,23	m³/day/kg
Breathing rate child (1-3 year old)	1,07	m³/day/kg
Drift percentage on surface (75th percentile)	5,60%	
Drift percentage on surface (mean)	4,10%	
Turf transferable residues percentage	5,00%	
Transfer coeff. of surface deposits-adult	7300	cm²/hour
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm²/hour
Saliva extraction percentage	50,00%	
Surface area of hands mouthed	20	cm²
Frequency of hand to mouth activity	9,5	events/hour
Ingestion rate for mouthing of grass per day	25	cm²
Dislodgeable residues percentage transferability for object to mouth	20,00%	
Transfer coefficient for entry into treated crops (75th percentile) -	7500	cm²/h
Transfer coefficient for entry into treated crops (75th percentile) -	2250	cm²/h
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm²/h
Transfer coefficient for entry into treated crops (mean) - child	1794	cm²/h

Croptype	Cereals		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		*i_AppEquip*
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		*i_FormVal*
Buffer strip	2-3	m	*i_Buffer*
Application rate of the product	0.15	kg a.s./ha	*i_AppRate*
Concentration of active substance (in-use dilution for liquid applications)	1.5	g a.s./l	*d_ConcAS*
Dermal absorption of product	25.00%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	70.00%		*i_Absorpinuse*
Oral absorption	100.00%		*i_AbsorpOralInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.45	µg a.s./cm^2	*d_DFR*
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa	*i_Volat*
Concentration in air	0.001	mg/m^3	*d_AirCon*
Resident dermal spray drift exposure 75th percentile - adult	0.47	ml spray dilution/person	
Resident dermal spray drift exposure 75th percentile - child	0.327	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - adult	0.00010	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - child	0.00022	ml spray dilution/person	
Resident dermal spray drift exposure mean - adult	0.22318	ml spray dilution/person	
Resident dermal spray drift exposure mean - child	0.18	ml spray dilution/person	
Resident inhal. spray drift exposure mean - adult	0.00009	ml spray dilution/person	
Resident inhal. spray drift exposure mean - child	0.00017	ml spray dilution/person	
Exposure duration dermal	2	hours	*d_ReExpDur*
Exposure duration inhalation	24	hours	*d_ReExpDurInhal*
Exposure duration entry into treated crops	0.25	hours	*d_ExpDurTreatCrop*
Light clothing adjustment factor	18.0%		*d_ClothAF*
Breathing rate adult	0.23	m^3/day/kg	*d_BreathRAd*
Breathing rate child (1-3 year old)	1.07	m^3/day/kg	*d_BreathRCh*
Drift percentage on surface (75th percentile)	5.60%		
Drift percentage on surface (mean)	4.10%		
Turf transferable residues percentage	5.00%		*d_Turf*
Transfer coeff. of surface deposits-adult	7300	cm^2/hour	*d_ReTCAd*
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm^2/hour	*d_ReTCCh*
Saliva extraction percentage	50.00%		*d_SalExt*
Surface area of hands mouthed	20	cm^2	*d_AreaHM*
Frequency of hand to mouth activity	9.5	events/hour	*d_ReFreqHM*
Ingestion rate for mouthing of grass per day	25	cm^2	*d_MouthGrass*
Dislodgeable residues percentage transferability for object to mouth	20.00%		*d_DRP*
Transfer coefficient for entry into treated crops (75th percentile)	7500	cm^2/h	*d_TcEntryAd*
Transfer coefficient for entry into treated crops (75th percentile)	2250	cm^2/h	*d_TcEntryCh*
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm^2/h	*d_TcEntryAd*
Transfer coefficient for entry into treated crops (mean) - child	1794	cm^2/h	*d_TcEntryCh*

A 3.3.3-2 Estimation of resident exposure to metrafenone

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0,3019875	0,0107000	0,0303325	0,3272213	0,4601172
Total systemic exposure per kg body weight (mg/kg bw/day)	0,0301988	0,0010700	0,0030333	0,0327221	0,0460117
% of RVNAS	7,02%	0,25%	0,71%	7,61%	10,70%

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (me
Total systemic exposure (mg a.s./day)	0.2818770	0.0107000	0.0284503	0.3054065	0.4302755
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0281877	0.0010700	0.0028450	0.0305407	0.0430275
% of RVNAS	6.56%	0.25%	0.66%	7.10%	10.01%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0,4337250	0,0138000	0,0792700	1,0907375	1,1475369
Total systemic exposure per kg body weight (mg/kg bw/day)	0,0072288	0,0002300	0,0013212	0,0181790	0,0191256
% of RVNAS	1,68%	0,05%	0,31%	4,23%	4,45%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0121445	0.0138000	0.0021984	0.0302498	0.0453466
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0002024	0.0002300	0.0000366	0.0005042	0.0007558
% of RVNAS	1.35%	1.53%	0.24%	3.36%	5.04%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.4048200	0.0138000	0.0739853	1.0180217	1.0719634
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0067470	0.0002300	0.0012331	0.0169670	0.0178661
% of RVNAS	1.57%	0.05%	0.29%	3.95%	4.15%