

REGISTRATION REPORT

Part B

Section 6

Mammalian Toxicology

Detailed summary of the risk assessment

Product code: HBZ10

Product name: Wizard

Chemical active substances:

Ethofumesate, 125 g/L

Phenmedipham, 125 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(Authorization - Art. 33 application)

Applicant: UPL Holdings Coöperatief U.A.

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Version history

When	What
October 2021	Applicant submission
June 2022	<p>Initial assessment by the zRMS</p> <p>The report in the dRR format has been prepared by the Applicant, therefore all comments, additional evaluations and conclusions of the zRMS are presented in grey commenting boxes. Minor changes are introduced directly in the text and highlighted in grey. Not agreed or not relevant information are struck through and shaded for transparency.</p>
August 2023	<p>Final report (Core Assessment updated following the commenting period)</p> <p>Additional information/assessments included by the zRMS in the report in response to comments received from the cMS and the Applicant are highlighted in yellow. Information no longer relevant is struck through and shaded.</p>

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Reviewer summary:

This part of dossier summarizes data related to the toxicological assessment and NDE data for the plant protection product Wizard/Beetup Pro/Betasana Max (product code HBZ10 an emulsifiable concentrate (EC) containing 125 g/L **L** phenmedipham and 125 g/L ethofumesate) which has been submitted to support registration according art. 33 of 1107/2009 in Poland also for zonal registration for which PL was designated zRMS.

Intended use of mentioned PPP is for beet crops (sugar beet, red beet, yellow beet, fodder beet and chards) for the control of broadleaved weeds.

The product Wizard/Beetup Pro/Betasana Max was not one of the representative products of the EU Review procedure for renewal of approval of ethofumesate or phenmedipham. Note, all data submitted with this dossier are owned by UPL Europe Ltd. Therefore, no letters of access are required for the relevant data package on the formulated product Wizard (HBZ10).

For the current product registration, UPL provided an assessment of the toxicological potential based on generic concentration limits of relevant ingredients. ZRMS PL, in accordance with the EC recommendations to avoid tests on animals, for the purposes of hazard classification use the data obtained using the calculation method and do not request for *in vivo* data.

Taking into account toxicological data of all ingredients also generic concentration limits (sum of relevant ingredients) Wizard/Beetup Pro/Betasana Max (HBZ10) is considered to cause skin irritation and serious eye damage, as well as respiratory irritation. No toxicological concern is expected after administration by the oral or dermal route and the formulation is not considered as a skin sensitiser.

NDE assessment for operator, workers and B&R has been calculated using the EFSA model and considering the worst-case exposure scenario to cover all the intended uses (highest application rate per application as well as the highest application rate per year with the shorter interval between each application):

- ☐ for operators results of the calculation show an acceptable risk for the critical use, leading to 13.25% of the combined systemic AOEL, without using Personal Protective Equipment,
- ☐ for a worker carrying out crop inspection tasks has been calculated to be 12.43 % of the combined systemic AOEL when wearing long sleeved shirt and long trousers (“permeable”) but no gloves,
- ☐ for B&R exposure assessment for residents covers bystander exposure to ethofumesate and phenmedipham (no AAOEL has been set for these active substances). Resident exposure after the application (according to the model calculations) is estimated to be 20.42% of the combined systemic AOEL for children. Adults are estimated to be exposed at levels not exceeding 8.56% of the combined systemic AOEL. Therefore, there is no undue risk for bystanders towards actives substances when Wizard is applied as recommended by the GAP.

6 Mammalian Toxicology (KCP 7)

6.1 Summary

Table 6.1-1: Information on Wizard*

Product name and code	Wizard / HBZ10
Formulation type	Emulsifiable Concentrate [EC]
Active substances (incl. content)	Ethofumesate; 125 g/L Phenmedipham; 125 g/L
Function	Herbicide
Product already evaluated as the ‘representative formulation’ during the approval of the active substances	No
Product previously evaluated in another MS according to Uniform Principles	No

* Information on the detailed composition of Wizard 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 HBZ10 according to Regulation (EC) No 1272/2008

Hazard classes, categories:	Skin Corrosion Irritation Category 2 - (H315) Serious eye damage/ eye irritation Category 1 - (H318) Specific target organ toxicity (single exposure) Category 3 - (H335)
Hazard pictograms or Codes for hazard pictograms:	GHS05, GHS07
Signal word:	Danger
Hazard statements:	H315 - Causes skin irritation H318 - Causes serious eye damage H335 - May cause respiratory irritation
Precautionary statements:	P261 - Avoid breathing dust/fume/gas/mist/vapours/spray. P264 - Wash hands, forearms and face thoroughly after handling. P271 - Use only outdoors or in a well-ventilated area. P280 - Wear protective gloves/ protective clothing eye protection/face protection. P302+P352 - IF ON SKIN: Wash with plenty of water. P304+P340 - IF INHALED: Remove person to fresh air and keep comfortable for breathing. P305+P351+P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P310 - Immediately call a POISON CENTER or doctor. P312 - Call a POISON CENTRE or doctor if you feel unwell. P321 - Specific treatment (see supplemental first aid instruction on this label). P332+P313 - If skin irritation occurs: Get medical advice/attention. 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/container to hazardous or special waste collection point, in accordance with local, regional, national and/or international regulation
Additional labelling phrases:	EUH401 - To avoid risks to human health and the environment, comply with the instructions for use

Table 6.1-3: Summary of risk assessment for operators, workers, bystanders and residents for HBZ10

	Result	PPE / Risk mitigation measures
Operators	Acceptable	None
Workers	Acceptable	None
Bystanders*	Acceptable	None
Residents	Acceptable	None

* Based on the results of the resident exposure according to the EFSA model. Bystander exposure is considered to be covered by resident exposure.

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.

#Reviewer comment: However NDE assessment indicates safe use (exposure E below limit AOEL) but due to the irritating effect on skin and serious eye damage effects, it is recommended ~~to require~~ the use of protective gloves and eye/face protection as prevention during handling and applying of the product.

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

Table 6.1-4 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. safen- er/synergist (L/ha)) critical gap for operator, worker, bystander or resident exposure based on [Expo- sure model]	Acceptability of exposure as- sessment			
			Method / Kind (incl. applica- tion technique ***	Max. number (min. interval between applications) a) per use b) per crop/ season	Max. application rate kg as/ha a) ethofumesate b) phenmedipham	Water L/ha min / max****			Operator	Worker	Bystander	Residents
2, 7, 12, 17, 22	Beet crops (sugar beet, red beet, yellow beet, fodder beet, chard)	F	Overall spray, BBCH 10-39 (TM / LC)	a) 3 (6d) b) 3 (6d)	a) 0.300 b) 0.300	80-400 200-400 ^a	-	Operators [EFSA OPEX model], workers, bystand- ers and residents			#	

* 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

^a for details refer dRR Part B Section 3 Efficacy Data and Information; see also comment point A 2.10

Based on the results of the resident exposure according to the EFSA model. Bystander exposure is considered to be covered by resident exposure.

**** Risk assessments performed by considering water volume of 80-400 L/ha, covering the 200-400 L/ha water volume proposed by zRMS Poland

Explanation for column 10 “Acceptability of exposure assessment”

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

Data gaps

Noticed data gaps are: None.

6.2 Toxicological Information on Active Substances

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 substances

	Ethofumesate	Phenmedipham
Common Name	Ethofumesate	Phenmedipham
CAS-No.	26225-79-6	13684-63-4
Classification and proposed labelling		
With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended)	Not classified	Not classified
Additional C&L proposal	None	None
Agreed EU endpoints		
AOEL systemic	2.5 mg/kg bw/d (no correction for oral absorption/bioavailability is needed)	0.13 mg/kg bw/day
Reference	SANTE/10119/2016 Rev. 3 – 12/07/2016 EFSA Journal 2016;14(1):4374	SANCO/4060/2001 final - 13 February 2004

	Ethofumesate	Phenmedipham
Conditions to take into account/critical areas of concern with regard to toxicology		
EFSA Conclusion for active substance	None	None

6.3 Toxicological Evaluation of Plant Protection Product

A summary of the toxicological evaluation for HBZ10 is given in the following tables. No new toxicological data is submitted.

Table 6.3-1: Summary of evaluation of the studies on acute toxicity including irritancy and skin sensitisation for HBZ10

Sensitisation for H210				
Type of test, species, model system (Guideline)	Result	Acceptability	Classification (acc. to the criteria in Reg. 1272/2008)	Reference
LD ₅₀ oral, rat	> 2000 mg/kg bw	Yes, hazard classification has been based on generic concentration limits (sum of relevant ingredients).	None	Extrapolation from the composition of the formulation according to Reg. No (EC) 1272/2008 – please refer to Part C
LD ₅₀ dermal, rat	> 2000 mg/kg bw	Yes, hazard classification has been based on generic concentration limits (sum of relevant ingredients).	None	
LC ₅₀ inhalation, rat	> 5 mg/L	Yes, hazard classification has been based on generic concentration limits (sum of relevant ingredients).	None	
Skin irritation	Causes skin irritation	Yes, hazard classification has been based on generic concentration limits (sum of relevant ingredients).	H315	
Eye irritation	Causes serious eye damage	Yes, hazard classification has been based on generic concentration limits (sum of relevant ingredients).	H318	
Skin sensitisation	Non-sensitising to skin	Yes, hazard classification has been based on generic concentration limits (sum of relevant ingredients).	None	
Specific Target Organ Toxicity (STOT) – single exposure	May cause respiratory irritation	Yes	H335	
Supplementary studies for combinations of plant protection products	No data – not required			

Table 6.3-2: Additional toxicological information relevant for classification/labelling of HBZ10

	Substance (Concentration in product, % w/w)	Classification of the substance (acc. to the criteria in Reg. 1272/2008)	Reference	Classification of formulants (acc. to the criteria in Reg. 1272/2008)
Toxicological properties of active substances (relevant for classification of product)	Ethofumesate (10-20 % (w/w))	Not classified	Reg. 1272/2008	-
	Phenmedipham (10-20 % (w/w))	Not classified	Reg. 1272/2008	-
Toxicological properties of non-active substances (relevant for classification of product)	Solvent	Skin Irrit. 2 (H315) Eye Dam. 1 (H318) STOT SE 3 (H335)	MSDS	H315 (calculation method) H318 (calculation method) H335 (calculation method)
	Emulsifier	STOT SE 3 (H335) Skin Irrit. 2 (H315) Eye Irrit. 2 (H319) Acute Tox. 4 (H302) Acute Tox. 4 (H332)	MSDS	H335 (calculation method) H315 (calculation method)
	Adjuvant, Emulsifier, Wetter	Eye Dam. 1 (H318) Acute Tox. 4 (H302)	MSDS	H318 (calculation method)
	Stabilizer, Acid	Eye Dam. 1 (H318) Acute Tox. 4 (H302) Repro. 2 (H361d)	MSDS	H318 (calculation method)
Further toxicological information	No data – not required			

6.4 Toxicological Evaluation of Groundwater Metabolites

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

6.5 Dermal Absorption (KCP 7.3)

A summary of the dermal absorption rates for the active substances in HBZ10 are presented in the following table.

Table 6.5-1: Dermal absorption rates for active substances in HBZ10

	Ethofumesate		Phenmedipham	
	Value	Reference	Value	Reference
Concentrate	25 %	Guidance on Dermal Absorption (EFSA Journal 2017;15(6):4873)	0.44 %	██████████ (Study reported in Appendix 2)
Dilution (max dilution factor phenmedipham and ethofumesate is 0.375 g/L each)	70 %	Guidance on Dermal Absorption (EFSA Journal 2017;15(6):4873)	11 %	██████████ (Study reported in Appendix 2)

6.5.1 Justification for proposed values - Ethofumesate

No data on dermal absorption for Ethofumesate in HBZ10 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 6.5-2: Default dermal absorption rates for Ethofumesate

	Value	Justification for value	Acceptability of justification
Concentrate	25 %	Default value to be used in the absence of experimental data for an	Justification accepted. Endpoint can be used for current product

	Value	Justification for value	Acceptability of justification
Dilution	70 %	EC formulation according to EFSA Guidance on Dermal Absorption	Justification accepted. Endpoint can be used for current product

6.5.2 Justification for proposed values - Phenmedipham

Proposed dermal absorption values for Phenmedipham in HBZ10 are based on dermal absorption studies on the formulation HBZ10 (containing 125 g/l Phenmedipham). The study results are summarised in the following table. Full summaries of studies on the dermal absorption of Phenmedipham that have not previously been evaluated within an EU peer review process are described in detail in Appendix 2.

Table 6.5-3: Summary of the results for Phenmedipham in the submitted dermal absorption study with HBZ10.

Test	Concentrate	Spray dilution	Formulation in study	Acceptability of study	Justification provided on representativity of study formulation for current product	Acceptability of justification	Reference
<i>In vitro</i> (human)	0.44 %	9.8% (dilution of 3.75 g/L) 11% (dilution of 0.375 g/L)	HBZ10	Yes	Not required (study performed with formulation under evaluation)	Endpoint can be used for current product	(Study reported in Appendix 2)

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	Wizard / HBZ10	
Formulation type	EC	
Category	Herbicide	
Active substances (incl. content)	Ethofumesate 125 g/L	Phenmedipham 125 g/L
AOEL systemic	2.5 mg/kg bw/d	0.13 mg/kg bw/d
Inhalation absorption	100 %	100 %
Oral absorption	100 %	100 %
Dermal absorption	Concentrate: 25 % Dilution: 70 % (Default)	Concentrate: 0.44 % Dilution: 11 %

6.6.1 Selection of critical use and justification

The GAP used for the exposure assessment of the plant protection product is shown in Table 6.1-4. This refers to the highest application rate per application as well as the highest application rate per year with the shorter interval between each application, leading to the worst-case exposure for mixing/loading as well as for application and re-entry into the treated area. This is the same as the intended uses within the zone as given in Part B, Section 0.

6.6.2 Operator exposure (KCP 7.2.1)

No acute non-dietary risk assessment is included in this submission. Lack of scientific guidance or methodology is an acceptable reason for waiving according to Guidance of the European Commission¹.

¹ Guidance Document for applicants on preparing dossiers for the approval of a chemical new active substance and for the renewal of approval of a chemical active substance according to Regulation (EU) No 283/2013 and Regulation (EU) No 284/2013. SANCO/10181/2013, May 2013

The absence of such guidance on derivation of an appropriate reference dose (“AAOEL”) was recognized by

- the European Food Safety Authority², and
- the European Commission Standing Committee³.

Therefore, this waiver is presented in line with the Guidance of the European Commission. This applies for the same degree with regard to acute operator exposure estimates.

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 HBZ10 according to the critical uses is presented in Table 6.6-2. Outcome of the estimation is presented in

Table 6.6-3. Detailed calculations are in Appendix 3.

Table 6.6-2: Exposure models for intended uses

Use	Beet crops (2.4 L product/ha, 6d interval, worst-case)
Model	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 Calculator version: 30/03/2015

Table 6.6-3: Estimated operator exposure

		Ethofumesate		Phenmedipham		HBZ10
Model data	Level of PPE	Total absorbed dose (mg/kg/day)	% of systemic AOEL (RVNAS)	Total absorbed dose (mg/kg/day)	% of systemic AOEL (RVNAS)	Combined % of systemic AOEL (RVNAS)
Tractor mounted boom spray application outdoors to low crops (root and tuber vegetables) Application rate: 2.4 L product/ha (corresponding to 0.3 kg Ethofumesate/ha and 0.3 kg Phenmedipham/ha)						
Spray application (AOEM; 95 th percentile) Body weight: 60 kg	Potential exposure (no clothing)	0.3071	12.28	0.0113 ⁹⁹	8.73 ⁴⁰	20.68 21.01
	Work wear (arms, body and legs covered) M/L and A	0.1943	7.77	0.0071 ⁴	5.69 ⁴⁸	13.46 ²⁵

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)

6.6.4.1 Estimation of worker exposure

Table 6.6-4 shows the exposure model used for estimation of worker exposure after entry into a previously treated area or handling a crop treated with HBZ10 according to the critical use. Outcome of the estimation is presented in

Table 6.6-5. Detailed calculations are in Appendix 3.

² Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. EFSA Journal 2014;12(10):3874)

³ Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. SANTE-10832-2015 rev. 1.7 of 24 January 2017

Table 6.6-4: Exposure models for intended uses

Use	Beet crops (2.4 L product/ha, 6d interval, worst-case)
Model	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 Calculator version: 30/03/2015

Table 6.6-5: Estimated worker exposure for inspection, irrigation in beet crops

		Ethofumesate		Phenmedipham		HBZ10
Model data	Level of PPE	Total absorbed dose (mg/kg/day)	% of systemic AOEL (RVNAS)	Total absorbed dose (mg/kg/day)	% of systemic AOEL (RVNAS)	Combined % of systemic AOEL (RVNAS)
Number of applications and application rate:		3 x 0.3 kg a.s./ha		3 x 0.3 kg a.s./ha		
Inspection, irrigation Outdoor Work rate: 2 hours/day ⁽¹⁾ DT ₅₀ : 30 days TC: 1400 cm ² /person/h ⁽²⁾ Interval between treatments: 6 days Body weight: 60 kg	Potential exposure (no clothing)	0.6900	27.60	0.1084	83.40	111.00
	Worker wearing long sleeved shirt, long trousers (“permeable”) but no gloves	0.0773	3.09	0.0121	9.34	12.43
	with PPE ⁽³⁾	n.a. ⁽⁴⁾	n.a. ⁽⁴⁾	n.a. ⁽⁴⁾	n.a. ⁽⁴⁾	n.a. ⁽⁴⁾

(1) 2 h/day for professional applications 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) PPE (e.g. gloves) are not considered an appropriate PPE for crop inspection activities.

(4) No TC available for this assessment considering hands, arms, body and legs covered.

It is clear from Table 6.6-5 that 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 the worker is wearing long sleeved shirt, long trousers (“permeable”) but no gloves.

Table 6.6-6: Estimated worker exposure for manual removal of bolting beets

Estimated worker exposure for manual removal of bolting beets						
		Ethofumesate		Phenmedipham		HBZ10
Model data	Level of PPE	Total absorbed dose (mg/kg/day)	% of systemic AOEL (RVNAS)	Total absorbed dose (mg/kg/day)	% of systemic AOEL (RVNAS)	Combined % of systemic AOEL (RVNAS)
Number of applications and application rate:		3 x 0.3 kg a.s./ha		3 x 0.3 kg a.s./ha		
Manual removal of bolting beets Outdoor Work rate: 8 hours/day ⁽¹⁾ DT ₅₀ : 30 days Interval between treatments: 6 days Body weight: 60 kg	Potential exposure TC: 18600 cm ² /person/h ⁽²⁾	4.1066	164.27	0.6453	496.41	660.68
	T-shirt and shorts TC: 18300 cm ² /person/h ⁽²⁾	4.0404	161.62	0.6349	488.40	650.02
	T-shirt, shorts and gloves TC: 14300 cm ² /person/h ⁽²⁾	3.1572	126.29	0.4961	381.64	507.93
	T-shirt and long trousers TC: 4500 cm ² /person/h ⁽²⁾	0.9935	39.74	0.1561	120.10	159.84
	Long clothes (workwear) TC: 4400 cm ² /person/h ⁽²⁾	0.9715	38.86	0.1527	117.43	156.29
	T-shirt, long trousers and gloves TC: 530 cm ² /person/h ⁽²⁾	0.1170	4.68	0.0184	14.14	18.82
	Long clothes (workwear) and gloves TC: 430 cm ² /person/h ⁽²⁾	0.0949	3.80	0.0149	11.48	15.28

(1) 8 h/day for manual removal of bolting beets, in accordance with EFSA Journal 2022;20(1):7032 recommendations.

(2) Proposed TC values in accordance with EFSA Journal 2022;20(1):7032 recommendations

According to results given in Table 6.6-6, the worker exposure estimations indicate that the acceptable operator exposure level (AOEL) will not be exceeded for specific task consisting of manual removal of bolting beets when considering worker is wearing T-shirt, long trousers and gloves, or long clothes (workwear) and gloves.

6.6.4.2 Refinement of generic DFR value (KCP 7.2)

Not relevant.

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 PPE, 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)

No acute non-dietary risk assessment is included in this submission. Lack of scientific guidance or methodology is an acceptable reason for waiving according to Guidance of the European Commission⁴. The absence of such guidance on derivation of an appropriate reference dose (“AAOEL”) was recognized by:

- the European Food Safety Authority⁵, and
- the European Commission Standing Committee⁶.

Therefore, this waiver is presented in line with the Guidance of the European Commission. According to EFSA longer term exposure of bystanders is covered by the resident scenario.

6.6.5.1 Estimation of bystander and resident exposure

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

Table 6.6-6 shows the exposure model used for estimation of resident exposure to Ethofumesate and Phenmedipham. Outcome of the estimation is presented in Table 6.6-7. Detailed calculations are in Appendix 3.

Table 6.6-67: Exposure models for intended uses

Use	Beet crops (2.4 L product/ha, 6d interval, worst-case)
Model	<p>Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015</p> <p>The EFSA Model uses standard figures for different parameters. The following points are of particular importance when considering the estimates: The EFSA Model assumes:</p> <ul style="list-style-type: none"> • Body weight <ul style="list-style-type: none"> ○ Adult resident: 60 kg ○ Child resident: 10 kg • Transfer coefficients specific to the application procedure and crop are considered, here for application in fields (use in sugar and fodder beet)⁷: <ul style="list-style-type: none"> ○ Adult resident: 7500 cm²/h (75th percentile), 5980 cm²/h (mean) ○ Child resident: 2250 cm²/h (75th percentile), 1794 cm²/h (mean) • Oral and inhalation exposure (default): 100% • Multiple application factor is considered taking into account the maximum number of applications, the minimum interval and the DT₅₀ • Air concentration: 0.001 mg/m³ for low volatile substance • Spray drift values specific to the application procedure /crop and distance (buffer strip) are considered, here for application in fields (use in sugar and fodder beet) • Dermal exposure (75th percentile) to spray drift, surface deposits and entry into treated crops is considered as well as exposure to spray drift and oral exposure for children (hand to mouth and object to mouth). • For a summary of all pathways the mean values are considered.

⁴ Guidance Document for applicants on preparing dossiers for the approval of a chemical new active substance and for the renewal of approval of a chemical active substance according to Regulation (EU) No 283/2013 and Regulation (EU) No 284/2013. SANCO/10181/2013, May 2013

⁵ Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. EFSA Journal 2014;12(10):3874)

⁶ Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. SANTE-10832-2015 rev. 1.7 of 24 January 2017.

⁷ The transfer coefficients employed in the EFSA model are extremely high for low crops with early applications (exceeding the transfer coefficient for re-entry worker) leading to very conservative exposure estimates for residents upon entry into treated crops.

Table 6.6-78: Estimated resident exposure (longer-term exposure)

		Ethofumesate		Phenmedipham		HBZ10
Model data		Total absorbed dose (mg/kg/day)	% of systemic AOEL	Total absorbed dose (mg/kg/day)	% of systemic AOEL	Combined % of systemic AOEL (RVNAS)
Tractor mounted boom spray application outdoors to low crops Application rate: 3 x 0.3 kg a.s./ha Buffer strip: 2 – 3 m Drift reduction technology: no DT ₅₀ Ethofumesate and Phenmedipham: 30 days DFR: 3 µg/cm ² /kg a.s./ha (equivalent to 0.9 µg a.s./cm ²) Interval between treatments: 6 days						
Residents (children) Body weight: 10 kg	Drift (75 th perc.)	0.0705	2.82	0.0111	8.57	11.39
	Vapour (75 th perc.)	0.0011	0.04	0.0011	0.82	0.86
	Deposits (75 th perc.)	0.0087	0.35	0.0019	1.46	1.81
	Re-entry (75 th perc.)	0.0931	3.73	0.0146	11.26	14.99
	Sum (mean)	0.1205	4.82	0.0203	15.60	20.42
Residents (adult) Body weight: 60 kg	Drift (75 th perc.)	0.0169	0.67	0.0027	2.04	2.71
	Vapour (75 th perc.)	0.0002	0.01	0.0002	0.18	0.19
	Deposits (75 th perc.)	0.0038	0.15	0.0006	0.45	0.60
	Re-entry (75 th perc.)	0.0517	2.07	0.0081	6.26	8.33
	Sum (mean)	0.0523	2.09	0.0084	6.47	8.56

6.6.5.2 Measurement of bystander and/or resident exposure

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

6.6.6 Combined exposure

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

The product is a mixture of two active substances. 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. In all cases the %AOEL of Ethofumesate and Phenmedipham added together, does not exceed 100% (see above tables). Thus, combined exposure to all active substances in HBZ10 is not expected to present a risk for operators, workers, bystanders, and residents. No further refinement of the assessment is required.

Reviewer comment:

However currently no commonly accepted guidance on the risk assessment considering combined exposure to multiple active substances but most assessment approaches employed make use of the Hazard Index (HI) concept. This approach is supported by the ZRMS PL as a first tier assessment. Thus, ZRMS PL decided to add mentioned above calculation (combined exposure based on HI) to the dRR.

Table 6.6-98: Acute risk assessment from combined exposure

Application scenario	Active Ingredient	Estimated exposure / AOEL (HQ)
Operators; [Work wear (arms, body and legs covered) M/L and A; no PPE]	Ethofumesate	0.07 0.08
	Phenmedipham	0.05 0.06
	Cumulative risk Operators (HI)	0.12 0.14
Workers; Inspection, irrigation [wearing long sleeved shirt, long trousers (“permeable”) but no gloves]	Ethofumesate	0.03
	Phenmedipham	0.09
	Cumulative risk Workers (HI)	0.12
Workers; Manual removal of bolting beets [T-shirt, long trousers and gloves]	Ethofumesate	0.05
	Phenmedipham	0.14
	Cumulative risk Workers (HI)	0.19
Bystander	Assessment for residents covers bystander exposure to Ethofumesate and Phenmedipham (no AAEL has been set for these active substances).	
Resident – Adult (Sum of all exposure roads)	Ethofumesate	0.024
	Phenmedipham	0.06
	Cumulative risk Resident – Adult (HI)	0.084 0.09
Resident – Child (Sum of all exposure roads)	Ethofumesate	0.048 0.05
	Phenmedipham	0.165
	Cumulative risk Resident – Child (HI)	0.20

The Hazard Index is < 1. Thus combined exposure to all active substances in Wizard/Beetup Pro/Betasana Max (HBZ10) 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 7.3/01	[REDACTED]	2020	[REDACTED] Report No. [REDACTED] GLP Unpublished	N	UPL

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

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

List of data submitted by the applicant and not relied on

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

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

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

Appendix 2 Detailed evaluation of the studies relied upon

A 2.1 Statement on bridging possibilities

Not relevant.

Reviewer comment:

Hazard assessment and proposed classification of the product based on content of relevant ingredients of the mixture (calculation plus additivity formula) (for details see Part C) are reliable and accepted.

A 2.2 Acute oral toxicity (KCP 7.1.1)

Not applicable. No acute oral toxicity studies have been conducted with the formulation, HBZ10, since a conclusion on hazard has been drawn following the calculation method using ingredient data given under EC Regulation No. 1272/2008.

As per EC Regulation No 1272/2008, the calculation method using ingredient data apply to determine the acute toxicity estimate (ATE) of the mixture. The ATE_{mix} is calculated under consideration of the amount of substance classified for acute oral toxicity. For details please refer to Part C.

In the light of these consideration and for animal welfare reasons, no new study was submitted. No classification for acute oral toxicity is warranted according to EC Regulation No 1272/2008 based on the composition of HBZ10.

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

Not applicable. No acute percutaneous toxicity studies have been conducted with the formulation, HBZ10, since a conclusion on hazard has been drawn following the calculation method using ingredient data given under EC Regulation No. 1272/2008.

As per EC Regulation No 1272/2008, the calculation method using ingredient data apply to determine the acute toxicity estimate (ATE) of the mixture. The ATE_{mix} is calculated under consideration of the amount of substance classified for acute oral toxicity. For details please refer to Part C.

In the light of these consideration and for animal welfare reasons, no new study was submitted. No classification for acute dermal toxicity is warranted according to EC Regulation No 1272/2008 based on the composition of HBZ10.

A 2.4 Acute inhalation toxicity (KCP 7.1.3)

Not applicable. No acute inhalation toxicity studies have been conducted with the formulation, HBZ10, since a conclusion on hazard has been drawn following the calculation method using ingredient data given under EC Regulation No. 1272/2008.

Since the formulation will be applied by spraying, toxicity and exposure via the inhalation route need to be considered and a conclusion reached on classification according to EC Regulation No 1272/2008.

As per EC Regulation No 1272/2008, the calculation method using ingredient data apply to determine the acute toxicity estimate (ATE) of the mixture. The ATE_{mix} is calculated under consideration of the amount of substance classified for acute inhalation toxicity. For details, please refer to Part C.

In the light of these consideration and for animal welfare reasons, a study was considered not to be necessary. No classification for acute inhalation toxicity is warranted according to EC Regulation No 1272/2008 based on the composition of HBZ10.

A 2.5 Skin irritation (KCP 7.1.4)

Not applicable. No skin irritation studies have been conducted with the formulation, HBZ10, since a conclusion on hazard has been drawn following the calculation method using ingredient data given under EC

Regulation No. 1272/2008.

In accordance with EC Regulation No 1272/2008, classification for skin irritating potential of a mixture may be derived from the labelling of the individual ingredients and their content in the formulated product. For details please refer to Part C.

In the light of these considerations and for animal welfare reasons, unnecessary animal testing should be avoided. Thus, it could be concluded that HBZ10 requires classification for skin irritation Category 2, H315, according to EC Regulation No. 1272/2008 and based on the composition of HBZ10.

A 2.6 Eye irritation (KCP 7.1.5)

Not applicable. No eye irritation studies have been conducted with the formulation, HBZ10, since a conclusion on hazard has been drawn following the calculation method using ingredient data given under EC Regulation No. 1272/2008.

In accordance with EC Regulation No 1272/2008, classification for eye irritating potential of a mixture may be derived from the labelling of the individual ingredients and their content in the formulated product. For details please refer to Part C.

In the light of these considerations and for animal welfare reasons, unnecessary animal testing should be avoided. Thus, it could be concluded that HBZ10 HBZ10 requires classification for serious eye damage Category 1, H318, according to EC Regulation No. 1272/2008 and based on the composition of HBZ10.

A 2.7 Skin sensitisation (KCP 7.1.6)

Not applicable. No skin sensitization studies have been conducted with the formulation, HBZ10, since a conclusion on hazard has been drawn following the calculation method using ingredient data given under EC Regulation No. 1272/2008.

In accordance with EC Regulation No 1272/2008, classification for skin sensitizing potential of a mixture may be derived from the labelling of the individual ingredients and their content in the formulated product. For details please refer to Part C.

In the light of these considerations and for animal welfare reasons, unnecessary animal testing should be avoided. Thus, it could be concluded that HBZ10 does not require classification for skin sensitizing according to EC Regulation No 1272/2008 and based on the composition of HBZ10.

Specific Target Organ Toxicity (STOT) – single exposure

Not applicable. No Specific Target Organ Toxicity studies have been conducted with the formulation, HBZ10 (Ethofumesate 125 + Phenmedipham 125 g/L EC), since a conclusion on hazard has been drawn following the calculation method using ingredient data given under EC Regulation No. 1272/2008.

In accordance with EC Regulation No 1272/2008, classification for Specific Target Organ Toxicity potential of a mixture may be derived from the labelling of the individual ingredients and their content in the formulated product. For details please refer to Part C.

In the light of these considerations and for animal welfare reasons, unnecessary animal testing should be avoided. Thus, it could be concluded that HBZ10 requires classification for STOT-SE Category 3, Respiratory system, H335 (May cause respiratory irritation), according to EC Regulation No 1272/2008 and based on the composition of HBZ10.

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

Supplementary studies on HBZ10 were considered not to be necessary.

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

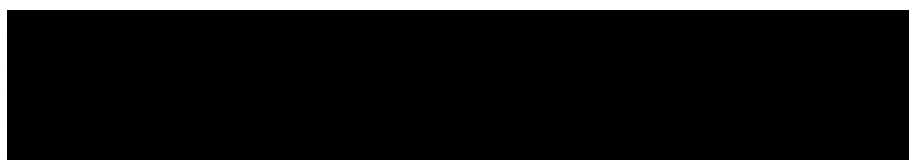
Available toxicological data for each co-formulant can be found in the confidential dossier of this submission (Registration Report - Part C).

A 2.10 Studies on dermal absorption (KCP 7.3)

Comments of zRMS:	Study () was conducted according to OECD Guideline 428 and in compliance with GLP. All the recoveries were between the recovery boundaries mentioned in the dermal absorption guidance (Guidance on Dermal Absorption (EFSA Journal, 2017, 15(6): 4873). DA values obtained from the study are reliable and can be used for risk assessment. ZRMS consider study to be acceptable and dermal absorption for radiolabeled phenmedipham is covered by this <i>in vitro</i> study. Change in the critical GAP (refer table 6.1-4; p.7) does not affect the final conclusion of the DA study. Highest in use-dilution (Test Preparation 3) remain still the worst case, thus pro-rata correction is not required.
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Reference KCP 7.3/01

Report



Guideline(s): OECD Guideline for Testing of Chemicals, Guideline No. 428: Skin Absorption: *In Vitro* Method (2004); OECD Guidance Notes on Dermal Absorption No. 156, ENV/JM/MONO (2011) 36, 2011; Council Regulation (EC) No. 440/2008, Method B.45, Skin Absorption: In Vitro Method, Brussels, May 2008; OECD Environmental Health and Safety Publications Series on Testing and Assessment No. 28. Guidance Document for the Conduct of Skin Absorption Studies (2004); European Commission Guidance Document on Dermal Absorption, Sanco/222/2000/Rev. 7 (19 March 2004); Guidance on Dermal Absorption (EFSA Journal, 2017, 15(6): 4873)

Deviations: No

GLP: Yes

Acceptability: Yes

Duplication (if vertebrate study) No

Executive Summary

The objective of this study was to determine the dermal absorption of the test item, phenmedipham, an active ingredient in an emulsifiable concentrate (EC) formulation (HBZ10), containing nominally 125 g/L of the active ingredient phenmedipham. The highest concentration in-use spray dilution was *ca* 3.75 g/L. The lowest concentration spray dilution was *ca* 0.375 g/L.

Human skin was mounted into static diffusion cells and exposed to Phenmedipham test preparations (10 µL/cm²) for 8 h under unoccluded conditions. The skin integrity was checked by determination of electrical resistance. At 8 h post dose, the exposure was terminated by washing the skin samples. At 24 h

post dose the skin was washed a second time. The receptor fluid was collected at 0, 1, 2, 4, 8, 12 and 24 h post dose. At the end of the experiment the entire bulk receptor fluid was analysed. The amount of radioactivity was determined in the skin (tape-stripping and total skin), the receptor fluid, skin wash samples (including pipette tip, tissue swabs and soap wash) and in the cell apparatus (donor chamber wash and receptor chamber wash).

The results for the dermal absorption of phenmedipham from all test preparations are summarised in Table A 2.10-1

Table A 2.10-1 Summary of dermal distribution results of phenmedipham at three concentrations using human skin in vitro

Concentration of phenmedipham	Test Preparation 1 125 g/L		Test Preparation 2 3.75 g/L		Test Preparation 3 0.375 g/L	
	%	SD	%	SD	%	SD
Overall absorption						
Total % potentially absorbable (without tape strips 1 & 2) ^a	0.34	0.12	7.75	2.42	9.01	2.50
Total % absorbed ^b	0.07	0.07	2.75	2.12	4.98	2.59
Total % dermal delivery ^b	0.20	0.08	5.66	2.50	7.18	2.63
Total % non-absorbed	110.41 100.41	1.80	91.39	1.51	92.53	4.89
Total % recovery of radioactivity	100.61	1.81	97.06	2.54	99.71	3.30

^a Potentially absorbable dose (equivalent to the dermal delivery and tape strips 3-20) was only calculated where absorption was considered “incomplete” according to the Guidance on Dermal Absorption (EFSA Journal 2017, 15(6): 4873), where less than 75% of the absorption occurs within the first half of the study.

^b The Guidance on Dermal Absorption (EFSA Journal 2017, 15(6): 4873) recommends that the SD is multiplied by a defined multiplication factor (k) based on the number of replicates (for 8 replicates, k=0.84), and that the resultant value is added to the mean value. This is applicable for the total dermal delivery, total absorbed dose and potentially absorbable dose for all groups. The mean + (k)SD value for total absorbed dose for the 125 g/L Phenmedipham formulation concentrate was 0.13%. The mean + (k)SD value for total dermal delivery for the 125 g/L Phenmedipham formulation concentrate was 0.27%. The mean + (k)SD value for potentially absorbable dose for the 125 g/L Phenmedipham formulation concentrate was 0.44%. The mean + (k)SD value for total absorbed dose for the 3.75 g/L Phenmedipham Spray Dilution 1 was 4.53%. The mean + (k)SD value for total dermal delivery for the 3.75 g/L Phenmedipham Spray Dilution 1 was 7.76%. The mean + (k)SD value for potentially absorbable dose for the 3.75 g/L Phenmedipham Spray Dilution 1 was 9.78%. The mean + (k)SD value for total absorbed dose for the 0.375 g/L Phenmedipham Spray Dilution 2 was 7.16%. The mean + (k)SD value for total dermal delivery for the 0.375 g/L Phenmedipham Spray Dilution 2 was 9.39%. The mean + (k)SD value for potentially absorbable dose for the 0.375 g/L Phenmedipham Spray Dilution 2 was 11.11%.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Radiolabelled Test Material:

[3 methylphenyl U 14C] Phenmedipham
[3-(methoxycarbonylamino)phenyl]

Specific Activity:

46 mCi/mmol

Batch:

11448CEO001-2

Radiochemical Purity:

98.5%

2. Non-Radiolabelled Test Material:

Phenmedipham Working Standard

Batch:

LDSFPMP130

Purity:

97.1%

3. Formulation:

Ethofumesate/Phenmedipham 125/125 g/L EC

Batch:

FL20-024-5A

4. Blank Formulation:
Batch:

Blank of HBZ10 with Ethofumesate
FL20-024-6A

B. METHODS

1. Preparation of dosing solutions

The radiolabelled test item was mixed with Phenmedipham Working Standard and the blank formulation to prepare the formulation concentrate. The radiolabelled test item was mixed with Phenmedipham Working Standard, the blank formulation and ultrapure water to prepare the in-use dilutions at the required concentrations.

2. Test System

Dermatomed human skin (200-400 µm) from the abdomen and arm. Full thickness skin was obtained from elective plastic surgery (Tissue Solutions Ltd, Scotland, UK) and delivered to the test facility on ice and stored in a freezer set to maintain a temperature of -20°C for a maximum of 5 years.

C. STUDY DESIGN AND METHODS:

1. In life dates: 03 June 2020 – 22 June 2020

2. Animal assignment and treatment: Not Applicable

3. Statistics:

The data did not warrant statistical analysis.

4. Percutaneous absorption study:

Each test preparation was applied to 8 samples of split-thickness skin samples mounted into static diffusion cells *in vitro*. Percutaneous absorption was assessed by collecting receptor fluid. At 8 h post application, the exposure was terminated by washing the skin surface and drying the skin surface with tissue paper (tissue swabs). At 24 h post application, the skin was washed again and removed from the static diffusion cells and dried. The *stratum corneum* was removed with 20 successive tape strips. The remaining skin was divided into exposed and unexposed skin and solubilised with Solvable[®] tissue solubiliser. All samples were analysed by liquid scintillation counting.

II. RESULTS AND DISCUSSION

In this study, the dermal absorption of Phenmedipham at three different concentrations was investigated using human skin *in vitro*. The concentrations tested were 125 g/L in formulation concentrate (Test Preparation 1), 3.75 g/L in Spray Dilution 1 (Test Preparation 2) and 0.375 g/L in Spray Dilution 2 (Test Preparation 3).

Total recovery percentage for Phenmedipham to human skin was 100.61% ± 1.81%, 97.06% ± 2.54% and 99.71% ± 3.30%, for Test Preparation 1, Test Preparation 2 and Test Preparation 3, respectively.

Results for the percutaneous absorption of Phenmedipham are summarised in Table A 2.10-2

Table A 2.10-2 Dermal distribution parameters and percentage absorption of radioactivity of Phenmedipham in human skin *in vitro*

Formulation	Test Preparation 1 125 g/L		Test Preparation 2 3.75 g/L		Test Preparation 3 0.375 g/L	
	%	SD	%	SD	%	SD

SURFACE COMPARTMENT						
Total dislodgeable dose 24 h ^c	100.24	1.80	88.65	3.00	90.04	3.68
Total % unabsorbed ^d	100.41	1.80	91.39	1.51	92.53	4.89
SKIN COMPARTMENT						
Exposed Skin	0.13	0.07	2.91	1.31	2.20	0.70
<i>Stratum corneum</i> (tape strips 3-20)	0.14	0.09	2.09	1.62	1.83	1.77
<i>Stratum corneum</i>	0.17	0.12	2.72	1.94	2.46	2.13
Unexposed skin	0.00	0.00	0.02	0.02	0.02	0.01
RECEPTOR COMPARTMENT						
Receptor fluid (collected over 24 h)	0.07	0.07	2.59	2.04	4.72	2.53
Receptor wash	0.01	0.00	0.17	0.10	0.27	0.07
Total % absorbed ^e	0.07	0.07	2.75	2.12	4.98	2.59
Total % dermal delivery ^f	0.20	0.08	5.66	2.50	7.18	2.63
OVERALL ABSORPTION						
Total % recovery	100.61	1.81	97.06	2.54	99.71	3.30

^c Total dislodgeable dose = skin wash 8 h + tissue swab 8 h + pipette tip 8 h + donor wash + tissue swab 24 h + skin wash 24 h + pipette tip 24 h

^d Total % unabsorbed = total dislodgeable dose + *stratum corneum* + unexposed skin

^e Total % absorbed = receptor fluid + receptor wash

^f Total % dermal delivery = total absorbed + exposed skin

DEFICIENCIES No significant deficiencies in the procedure were identified.

III. CONCLUSIONS

In vitro, the total absorption of Phenmedipham to human skin was 0.07%, 2.75% and 4.98% for Test Preparation 1 (125 g/L), Test Preparation 2 (3.75 g/L) and Test Preparation 3 (0.375 g/L), respectively. The dermal delivery of Phenmedipham to human skin was 0.20%, 5.66% and 7.18% for Test Preparation 1 (125 g/L), Test Preparation 2 (3.75 g/L) and Test Preparation 3 (0.375 g/L), respectively. The potentially absorbable dose of Phenmedipham to human skin was 0.34%, 7.75%, and 9.01% for Test Preparation 1 (125 g/L), Test Preparation 2 (3.75 g/L) and Test Preparation 3 (0.375 g/L), respectively.

IV. EVALUATION ACCORDING TO THE EFSA GUIDANCE⁸

1. Test item

The dermal absorption study was conducted with HBZ10 (Ethofumesate 125 + Phenmedipham 125 g/L EC), which is equivalent to the formulation under evaluation.

2. Tape strips

The potentially absorbed dose of Phenmedipham after 24 h study includes recovery from the receptor fluid, receptor compartment wash, the skin and the tape strips (except the first 2 tapes strips). For *in vitro* studies permeation is considered essentially complete when > 75% of the amount that has permeated into the receptor fluid at the end of sampling (usually 24 h) has reached the receptor fluid at the half time of the sampling period (usually 12 h). The mean relative permeation into the receptor fluid within half of the samples period ($t_{0.5}$) was 38.6%, 52.9% and 66.7% for Test Preparation 1 (125 g/L), Test Preparation 2 (3.75 g/L) and Test Preparation 3 (0.375 g/L), respectively.

3. Recovery

Recovery was 100.61% for Test Preparation 1 (125 g/L), 97.06% for Test Preparation 2 (3.75 g/L) and 99.71% for Test Preparation 3 (0.375 g/L). For all samples the recovery exceeded 95%. No correction for recovery is required.

4. Variability of results

According to the EFSA Guidance (2017), in order to address variability between replicates, dermal absorption should be calculated by adding to the mean value the standard deviation multiplied by a factor that depends on the number of replicates.

Dermal absorption = Absorption (mean value) + $k \times SD$, where k is a factor depending on the number of replicates and SD is the standard deviation.

A factor k (0.84 for a number of 8 replicates) is considered for all test preparations.

Dermal absorption Test Preparation 1 (125 g/L) = $0.34 + 0.84 \times 0.12 = 0.44\%$

Dermal absorption Test Preparation 2 (3.75 g/L) = $7.75 + 0.84 \times 2.42 = 9.78\%$

Dermal absorption Test Preparation 3 (0.375 g/L) = $9.01 + 0.84 \times 2.5 = 11.11\%$

5. Tested concentrations during the study

Table A 2.10-3 Tested concentrations

Phenmedipham	Test preparation 1 (concentrate)	Test preparation 2	Test preparation 3
Concentrations employed in the study	125 g/L	3.75 g/L	0.375 g/L
Worst-case scenario according to GAP	125 g/L	3.75 g/L	0.375 g/L

The tested dilution in test preparation 3 (0.375 g/L) is equivalent to the in-use dilution for the worst-case scenario according to the GAP evaluated. This can therefore directly be used.

6. Rounding of values

Final absorption rates that may be transferred to practical uses of HBZ10 are calculated by rounding the values:

Dermal absorption Test Preparation 1 (125 g/L) = 0.44% → **0.44%**

⁸ EFSA (European Food Safety Authority). Guidance on dermal absorption. EFSA Journal 2017;15(6):4873, 60 pp. <https://doi.org/10.2903/j.efsa.2017.4873>

Dermal absorption Test Preparation 2 (3.75 g/L) = 9.78% → **9.8%**

Dermal absorption Test Preparation 3 (0.375 g/L) = 11.11% → **11%**

V. FINAL CONCLUSIONS

Phenmedipham

Based on the experimental study by Paulo (2020) (KCP 7.3/01) and according to the EFSA Guidance on dermal absorption (2017), an absorption value for Phenmedipham of 0.4% from the concentrate and 11% from the in-use dilution is used during the risk assessment of HBZ10.

A 2.11 Other/Special Studies

None.

Appendix 3 Exposure calculations

A 3.1 Operator exposure calculations (KCP 7.2.1.1)

A 3.1.1 Calculations for Ethofumesate by using vehicle-mounted for application

Table A 1: Input parameters considered for the estimation of operator exposure
3 x 2.4L HBZ10/ha, 6d interval, vehicle-mounted

Substance name	Ethofumesate
Product name	HBZ10
Reference value non acutely toxic active substance (RVNAS)	2.5 mg/kg bw/day
Reference value acutely toxic active substance (RVAAS)	mg/kg bw/day
Crop type	Root and tuber vegetables
Substance properties	
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.
Minimum volume water for application (liquids)	80 L/ha
Maximum application rate of active substance	0.3 kg a.s. /ha
50% Dissipation Time DT50	30 days
Initial Dislodgeable Foliar Residue	3 µg/cm ² of foliage/kg a.s. applied/ha
Dermal absorption of product	25.00%
Dermal absorption of in-use dilution	70.00%
Oral absorption of active substance	100.00%
Inhalation absorption of active substance	100.00%
Vapour pressure of active substance	low volatile substances having a vapour pressure of <5*10 ⁻³ Pa
Scenario	
Indoor or Outdoor application	Outdoor
Application method	Downward spraying
Application equipment	Vehicle-mounted
Buffer strip	2-3 m
Number of applications	3
Interval between multiple applications	6 days
Season (upward spraying orchards only)	not relevant

Table A 2: Estimation of operator exposure towards Ethofumesate using the EFSA model
3 x 2.4L HBZ10/ha, 6d interval, vehicle-mounted

Operator exposure for HBZ10 outdoor spray applications

Application rate of active substance		0.3 kg a.s./ha	<i>i_AppRate</i>		
Assumed area treated		50 ha/day	<i>d_AreaTreated</i>		
Amount of active substance applied		15 kg a.s./day	<i>i_AmountAS</i>		
Dermal absorption of the product		25.00%	<i>i_AbsorpProduct</i>		
Dermal absorption of in-use dilution		70.00%	<i>i_AbsorInuse</i>		
Formulation type		Soluble concentrates, emulsifiable concentrate, etc.			
Indoor or Outdoor application		Outdoor			
Application method		Downward spraying			
Application equipment		Vehicle-mounted			
Season		not relevant			
OutdoorSoluble concentrates, emulsifiable concentrate, etc Downward sprayingVehicle-mounted					
Mixing and loading	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75 th centile	95 th centile		
	Hands	39062	146589	AOEM	
	Body	23935	158184	AOEM	
	Head	778	4268	AOEM	
	Protected hands (gloves)	201	2971	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	262	2194	AOEM	
	Protected head (hood and face shield)	12	242	AOEM	
	Inhalation	8	31	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
		75 th centile	95 th centile		
	Hands	2225	16655	AOEM	
	Body	1244	6413	AOEM	
	Head	59	177	AOEM	
	Protected hands (gloves)	184	4571	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	34	84	AOEM	
	Inhalation	4	14	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)	18.4254625	11.6602399
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.3070910	0.1943373
% of RVNAS	12.28%	7.77%

A 3.1.2 Calculations for Phenmedipham by using vehicle-mounted for application

Table A 3: Input parameters considered for the estimation of operator exposure
3 x 2.4L HBZ10/ha, 6d interval, vehicle-mounted

Substance name	Phenmedipham
Product name	HBZ10
Reference value non acutely toxic active substance (RVNAS)	0.13 mg/kg bw/day
Reference value acutely toxic active substance (RVAAS)	mg/kg bw/day
Crop type	Root and tuber vegetables
Substance properties	
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.
Minimum volume water for application (liquids)	80 L/ha
Maximum application rate of active substance	0.3 kg a.s. /ha
50% Dissipation Time DT50	30 days
Initial Dislodgeable Foliar Residue	3 µg/cm2 of foliage/kg a.s. applied/ha
Dermal absorption of product	0.40%
Dermal absorption of in-use dilution	11.00%
Oral absorption of active substance	100.00%
Inhalation absorption of active substance	100.00%
Vapour pressure of active substance	low volatile substances having a vapour pressure of <5*10 ⁻³ Pa
Scenario	
Indoor or Outdoor application	Outdoor
Application method	Downward spraying
Application equipment	Vehicle-mounted
Buffer strip	2-3 m
Number of applications	3
Interval between multiple applications	6 days
Season (upward spraying orchards only)	not relevant

Substance name	Phenmedipham
Product name	HBZ10
Reference value non acutely toxic active substance (RVNAS)	0.13 mg/kg bw/day
Reference value acutely toxic active substance (RVAAS)	mg/kg bw/day
Crop type	Root and tuber vegetables
Substance properties	
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.
Minimum volume water for application (liquids)	80 L/ha
Maximum application rate of active substance	0.3 kg a.s. /ha
50% Dissipation Time DT50	30 days
Initial Dislodgeable Foliar Residue	3 µg/cm2 of foliage/kg a.s. applied/ha
Dermal absorption of product	0.40%
Dermal absorption of in-use dilution	11.00%
Oral absorption of active substance	100.00%
Inhalation absorption of active substance	100.00%
Vapour pressure of active substance	low volatile substances having a vapour pressure of <5*10 ⁻³ Pa
Scenario	
Indoor or Outdoor application	Outdoor
Application method	Downward spraying
Application equipment	Vehicle-mounted
Buffer strip	2-3 m
Number of applications	3
Interval between multiple applications	6 days
Season (upward spraying orchards only)	not relevant

Substance name	Phenmedipham
Product name	HBZ10
Reference value non acutely toxic active substance (RVNAS)	0.13 mg/kg bw/day
Reference value acutely toxic active substance (RVAAS)	mg/kg bw/day
Crop type	Root and tuber vegetables
Substance properties	
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.
Minimum volume water for application (liquids)	80 L/ha
Maximum application rate of active substance	0.3 kg a.s. /ha
50% Dissipation Time DT50	30 days
Initial Dislodgeable Foliar Residue	3 µg/cm2 of foliage/kg a.s. applied/ha
Dermal absorption of product	0.44%
Dermal absorption of in-use dilution	11.00%
Oral absorption of active substance	100.00%
Inhalation absorption of active substance	100.00%
Vapour pressure of active substance	low volatile substances having a vapour pressure of <5*10-3Pa
Scenario	
Indoor or Outdoor application	Outdoor
Application method	Downward spraying
Application equipment	Vehicle-mounted
Buffer strip	2-3 m
Number of applications	3
Interval between multiple applications	6 days
Season (upward spraying orchards only)	not relevant

Table A 4: Estimation of operator exposure towards Phenmedipham using the EFSA model
3 x 2.4L HBZ10/ha, 6d interval, vehicle-mounted

Operator exposure for HBZ10 outdoor spray applications

Application rate of active substance	0.3 kg a.s./ha		i_AppRate		
Assumed area treated	50 ha/day		d_AreaTreated		
Amount of active substance applied	15 kg a.s./day		i_AmountAS		
Dermal absorption of the product	0.40%		i_AbsorpProduct		
Dermal absorption of in-use dilution	11.00%		i_AbsorInuse		
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.				
Indoor or Outdoor application	Outdoor				
Application method	Downward spraying				
Application equipment	Vehicle-mounted				
Season	not relevant				
OutdoorSoluble concentrates, emulsifiable concentrate, etc. Downward sprayingVehicle-mounted					
Mixing and loading	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75 th centile	95 th centile		
	Hands	39062	146589	AOEM	
	Body	23935	158184	AOEM	
	Head	778	4268	AOEM	
	Protected hands (gloves)	201	2971	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	262	2194	AOEM	
	Protected head (hood and face shield)	12	242	AOEM	
	Inhalation	8	31	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
		75 th centile	95 th centile		
	Hands	2225	16635	AOEM	
	Body	1244	6413	AOEM	
	Head	59	177	AOEM	
	Protected hands (gloves)	184	4571	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	34	84	AOEM	
	Inhalation	4	14	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)	0.6554498	0.4276715
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0109242	0.0071279
% of RVNAS	8.40%	5.48%

Operator exposure for HBZ10 outdoor spray applications

Application rate of active substance 0.3 kg a.s./ha *i_AppRate*
Assumed area treated 50 ha/day *d_AreaTreated*
Amount of active substance applied 15 kg a.s./day *i_AmountAS*
Dermal absorption of the product 0.40% *i_AbsorpProduct*
Dermal absorption of in-use dilution 11.00% *i_AbsorInuse*
Formulation type Soluble concentrates, emulsifiable concentrate, etc.
Indoor or Outdoor application Outdoor
Application method Downward spraying
Application equipment Vehicle-mounted
Season not relevant

Mixing and loading	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75 th centile	95 th centile		
	Hands	39062	146589	AOEM	
	Body	23935	158184	AOEM	
	Head	778	4268	AOEM	
	Protected hands (gloves)	201	2971	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	262	2194	AOEM	
	Protected head (hood and face shield)	12	242	AOEM	
	Inhalation	8	31	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	
	Water soluble bag	No		1	
Application					
	Exposure values	µg exposure/day applied		Reference	Comment
		75 th centile	95 th centile		
	Hands	2225	16655	AOEM	
	Body	1244	6413	AOEM	
	Head	59	177	AOEM	
	Protected hands (gloves)	184	4571	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	34	84	AOEM	
	Inhalation	4	14	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	
	Closed cab	No		vehicle mounted upward spraying only	

Operator exposure for HBZ10 outdoor spray applications

Application rate of active substance	0.3 kg a.s./ha	<i>i_AppRate</i>
Assumed area treated	50 ha/day	<i>d_AreaTreated</i>
Amount of active substance applied	15 kg a.s./day	<i>i_AmountAS</i>
Dermal absorption of the product	0.44%	<i>i_AbsorpProduct</i>
Dermal absorption of in-use dilution	11.00%	<i>i_AbsorInuse</i>
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Indoor or Outdoor application	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Season	not relevant	
	OutdoorSoluble concentrates, emulsifiable concentrate, etc. Downward sprayingVehicle-mounted	

Mixing and loading	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75 th centile	95 th centile		
	Hands	39062	146589	AOEM	
	Body	23935	158184	AOEM	
	Head	778	4268	AOEM	
	Protected hands (gloves)	201	2971	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	262	2194	AOEM	
	Protected head (hood and face shield)	12	242	AOEM	
	Inhalation	8	31	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
		75 th centile	95 th centile		
	Hands	2225	16655	AOEM	
	Body	1244	6413	AOEM	
	Head	59	177	AOEM	
	Protected hands (gloves)	184	4571	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	34	84	AOEM	
	Inhalation	4	14	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)	0.6554498	0.4276715
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0109242	0.0071279
% of RVNAS	8.40%	5.48%

1. Total		
	Without RPE/PPE	With RPE/PPE
Longer term		
Total systemic exposure from mixing, loading and application (mg a.s./day)	0.6809599	0.4437123
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0113493	0.0073952
% of RVNAS	8.73%	5.69%

A 3.2 Worker exposure calculations (KCP 7.2.3.1)

A 3.2.1 Calculations for Ethofumesate by using vehicle-mounted for application

Table A 5: Input parameters considered for the estimation of worker exposure
3 x 2.4L HBZ10/ha, 6d interval, vehicle-mounted

Worker exposure from residues on foliage for HBZ10	
Crop type	Root and tuber vegetables
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	0.3 kg a.s./ha
Number of applications	3
Interval between multiple applications	6 days
Half-life of active substance	30 days
Multiple application factor	2.6
Dermal absorption of the product	25.00%
Dermal absorption of the in-use dilution	70.00%
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.9 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
Inhalation transfer coefficient for automated applications	NA ha/hr*10 ⁻³
Inhalation transfer coefficient for cutting ornamentals	NA ha/hr*10 ⁻³
Inhalation transfer coefficient for sorting / bundling ornamentals	NA ha/hr*10 ⁻³

Table A 6: Estimation of worker exposure towards Ethofumesate using the EFSA model
3 x 2.4L HBZ10/ha, 6d interval, vehicle-mounted

1. Total			
	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves
Total systemic exposure (mg a.s./day)	41.3974393	4.6365132	no TC available for this assessment
Total systemic exposure per kg body weight (mg/kg bw/day)	0.6899573	0.0772752	
% of RVNAS	27.60%	3.09%	

A 3.2.2 Calculations for Phenmedipham by using vehicle-mounted for application

Table A 7: Input parameters considered for the estimation of worker exposure
3 x 2.4L HBZ10/ha, 6d interval, vehicle-mounted

Worker exposure from residues on foliage for HBZ10	
Crop type	Root and tuber vegetables
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	0.3 kg a.s./ha
Number of applications	3
Interval between multiple applications	6 days
Half-life of active substance	30 days
Multiple application factor	2.6
Dermal absorption of the product	0.40%
Dermal absorption of the in-use dilution	11.00%
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.9 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
Inhalation transfer coefficient for automated applications	NA ha/hr*10 ^{^(-3)}
Inhalation transfer coefficient for cutting ornamentals	NA ha/hr*10 ^{^(-3)}
Inhalation transfer coefficient for sorting / bundling ornamentals	NA ha/hr*10 ^{^(-3)}

Table A 8: Estimation of worker exposure towards Phenmedipham using the EFSA model
3 x 2.4L HBZ10/ha, 6d interval, vehicle-mounted

1. Total			
	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves
Total systemic exposure (mg a.s./day)	6.5053119	0.7285949	no TC available for this assessment
Total systemic exposure per kg body weight (mg/kg bw/day)	0.1084219	0.0121432	
% of RVNAS	83.40%	9.34%	

Worker exposure from residues on foliage for HBZ10	
Crop type	Root and tuber vegetables
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	0.3 kg a.s./ha
Number of applications	3
Interval between multiple applications	6 days
Half-life of active substance	30 days
Multiple application factor	2.6
Dermal absorption of the product	0.40%
Dermal absorption of the in-use dilution	11.00%
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.9 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
Inhalation transfer coefficient for automated applications	NA ha/hr*10 ^{^(-3)}
Inhalation transfer coefficient for cutting ornamentals	NA ha/hr*10 ^{^(-3)}
Inhalation transfer coefficient for sorting / bundling ornamentals	NA ha/hr*10 ^{^(-3)}

Worker exposure from residues on foliage for HBZ10	
Crop type	Root and tuber vegetables
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	0.3 kg a.s./ha
Number of applications	3
Interval between multiple applications	6 days
Half-life of active substance	30 days
Multiple application factor	2.6
Dermal absorption of the product	0.44%
Dermal absorption of the in-use dilution	11.00%
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.9 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
Inhalation transfer coefficient for automated applications	NA ha/hr*10 ⁽⁻³⁾
Inhalation transfer coefficient for cutting ornamentals	NA ha/hr*10 ⁽⁻³⁾
Inhalation transfer coefficient for sorting / bundling ornamentals	NA ha/hr*10 ⁽⁻³⁾

Table A 9: Estimation of worker exposure towards Phenmedipham using the EFSA model
3 x 2.4L HBZ10/ha, 6d interval, vehicle-mounted

1. Total			
	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves
Total systemic exposure (mg a.s./day)	6.5053119	0.7285949	no TC available for this assessment
Total systemic exposure per kg body weight (mg/kg bw/day)	0.1084219	0.0121432	
% of RVNAS	83.40%	9.34%	

A 3.3 Bystander and resident exposure calculations (KCP 7.2.2.1)

A 3.3.1 Calculations for Ethofumesate by using vehicle-mounted for application

Table A 10: Estimation of resident exposure towards Ethofumesate using the EFSA model
3 x 2.4L HBZ10/ha, 6d interval, vehicle-mounted

Resident exposure for HBZ10	
Croptype	Root and tuber vegetables
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	0.3 kg a.s./ha
Concentration of active substance (in-use dilution for liquid applications)	3.75 g a.s./l
Dermal absorption of product	25.00%
Dermal absorption of in-use dilution	70.00%
Oral absorption	100.00%
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.9 µg a.s./cm ²
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10 ⁻³ 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) - adult	7500 cm ² /h
Transfer coefficient for entry into treated crops (75th percentile) - child	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

1. Total					
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)	0.7046925	0.0107000	0.0867690	0.9314424	1.2049849
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0704693	0.0010700	0.0086769	0.0931442	0.1204985
% of RVNAS	2.82%	0.04%	0.35%	3.73%	4.82%
1.2 Adult					
	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	1.0120500	0.0138000	0.2256436	3.1048079	3.1353027
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0168675	0.0002300	0.0037607	0.0517468	0.0522550
% of RVNAS	0.67%	0.01%	0.15%	2.07%	2.09%

A 3.3.2 Calculations for Phenmedipham by using vehicle-mounted for application

Table A 11: Estimation of resident exposure towards Phenmedipham using the EFSA model
3 x 2.4L HBZ10/ha, 6d interval, vehicle-mounted

Resident exposure for HBZ10	
Croptype	Root and tuber vegetables
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	0.3 kg a.s./ha
Concentration of active substance (in-use dilution for liquid applications)	3.75 g a.s./l
Dermal absorption of product	0.40%
Dermal absorption of in-use dilution	11.00%
Oral absorption	100.00%
Dislodgeable foliar residue ($i_{\text{appRate}} \cdot i_{\text{DFR}}$)	0.9 $\mu\text{g a.s./cm}^2$
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of $<5 \cdot 10^{-3} \text{ Pa}$
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 $\text{m}^3/\text{day/kg}$
Breathing rate child (1-3 year old)	1.07 $\text{m}^3/\text{day/kg}$
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	21.00%
Transfer coefficient for entry into treated crops (75th percentile) - adult	7500 cm^2/h
Transfer coefficient for entry into treated crops (75th percentile) - child	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

1. Total					
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)	0.1114328	0.0107000	0.0190318	0.1463695	0.2028618
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0111433	0.0010700	0.0019032	0.0146370	0.0202862
% of RVNAS	8.57%	0.82%	1.46%	11.26%	15.60%
1.2 Adult					
	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.1593525	0.0138000	0.0354583	0.4878984	0.5046063
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0026559	0.0002300	0.0005910	0.0081316	0.0084101
% of RVNAS	2.04%	0.18%	0.45%	6.26%	6.47%

Resident exposure for HBZ10	
Croptype	Root and tuber vegetables
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	0.3 kg a.s./ha
Concentration of active substance (in-use dilution for liquid applications)	3.75 g a.s./l
Dermal absorption of product	0.40%
Dermal absorption of in-use dilution	11.00%
Oral absorption	100.00%
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.9 µg a.s./cm ²
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10 ⁻³ 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	0.00000 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) - adult	7500 cm ² /h
Transfer coefficient for entry into treated crops (75th percentile) - child	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

Resident exposure for HBZ10	
Croptype	Root and tuber vegetables
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	0.3 kg a.s./ha
Concentration of active substance (in-use dilution for liquid applications)	3.75 g a.s./l
Dermal absorption of product	0.44%
Dermal absorption of in-use dilution	11.00%
Oral absorption	100.00%
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.9 µg a.s./cm ²
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10 ⁻³ Pa
Concentration in air	0.001 mg/m ³
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Resident inhal. spray drift exposure 75th percentile - child	0.00022 ml spray dilution/person
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Resident inhal. spray drift exposure mean - child	0.00017 ml spray dilution/person
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% of RVNAS	2.04%	0.18%	0.45%	6.26%	6.47%

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

Not relevant.