FINAL REGISTRATION REPORT

Part B

Section 6

Mammalian Toxicology

Detailed summary of the risk assessment

Product code: GLOB2007bF

Product name: Observer Pro

Chemical active substances:

Zoxamide, 67.5 g/L
Propamocarb-HCl, 450 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

Applicant: Globachem NV

Submission date: November 2023

MS Finalisation date: 31/10/2024

Version history

When	What
November 2023	Initial dossier submission by applicant for approval of new product
March 2024	Dossier sent for evaluation
July 2024	zRMS finalised evaluation
October 2024	zRMS finalised evaluation after commenting period

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

6 Mammalian Toxicology (KCP 7)

6.1 Summary

Table 6.1-1: Information on GLOB2007bF *

Product name and code	GLOB2007bF
Formulation type	Suspension Concentrate (SC)
Active substance(s) (incl. content)	zoxamide; 67.5 g/L propamocarb-HCl; 450 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 GLOB2007bF 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 GLOB2007bF according to Regulation (EC) No 1272/2008

Hazard class(es), categories	Skin Sens. 1
Hazard pictograms or Code(s) for hazard pictogram(s)	GHS07
Signal word	Warning
Hazard statement(s)	H317 - May cause an allergic skin reaction.
Precautionary statement(s)	P261 - Avoid breathing dust/fume/ gas/mist/vapours/spray. P272 - Contaminated work clothing should not be allowed out of the workplace. P280 - Wear protective gloves/ protective clothing/eye protection/face protection. P302 + P352 - IF ON SKIN: Wash with plenty of water/… P333 + P313 - If skin irritation or rash occurs: Get medical advice/attention P321 - Specific treatment (see on this label). P362 + 364 - Take off contaminated clothing and wash it before reuse. P501 - Dispose of contents/ container to in accordance with local regulation.
Additional labelling phrases	To avoid risks to man and the environment, comply with the instructions for use. [EUH401]
	Contains 1,2-Benzisothiazolin-3-one. ~~May produce an allergic reaction. [EUH 208]~~

Table 6.1-3: Summary of risk assessment for operators, workers, residents and bystanders for GLOB2007bF

	Result	PPE / Risk mitigation measures
Operators	Acceptable	No PPE (work wear - arms , body and legs covered) – according to the exposure assessment Due to the product classification (Skin Sens. 1, H317), it is reccomended to use protective gloves at the M/L step.
Workers	Acceptable	No PPE (work wear - arms , body and legs covered)
Residents	Acceptable	None
Bystanders	Acceptable	None

No unacceptable risk for operators, workers, residents and bystanders was identified when the product is used as intended. No specific PPE is necessary.

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

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

1	2	3	4	5	6	7	8	9	10			
Use-No.*	**Crops and situation (e.g. growth stage of crop)**	**F, Fn, Fpn G, Gn, Gpn or I ******	**Application**		**Application rate**		**PHI (d)**	**Remarks: (e.g. safener/synergist (L/ha)) critical gap for operator, worker, resident or bystander exposure based on [Exposure model]**	**Acceptability of exposure assessment**			
			Method / Kind (incl. application technique ***)**	**Max. number (min. interval between applications) a) per use b) per crop/ season**	**Max. application rate kg as/ha a) a.s. 1 b) a.s. 2**	**Water L/ha min / max**			**Operator**	**Worker**	**Residents**	**Bystander**
	Potato (BBCH 21-79)	F	Spraying, LCTM	3 (7)	a) 0.135 b) 0.900	150-300	7	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2022;20(1):7032, 134 pp.	A	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

Noticed data gaps are:

- None

6.2 Toxicological Information on Active Substance(s)

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

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

	Zoxamide	**Propamocarb**
Common Name	Zoxamide	Propamocarb (unless otherwise stated, the following data relate to the variant propamocarb hydrochloride)
CAS-No.	156052-68-5	24579-73-5 (Propamocarb) 25606-41-1 (Propamocarb-HCl)
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, H317 Code(s) for hazard pictogram(s): GHS07 Signal word: Warning Hazard statement(s): H317 Precautionary statement(s): *Not aplicable for a.s.*	Hazard classes (s), categories: Skin Sens. 1B, H317 [1)] Code(s) for hazard pictogram(s): GHS07 Signal word: Warning Hazard statement(s): H317 Precautionary statement(s): *Not aplicable for a.s.*
Additional C&L proposal	-	Propamocarb HCl: CLH report (RMS Portugal): Proposed harmonised classification by the dossier submitter: Skin Sens. 1B, H317 CLH report is not yet available. *Link: https://echa.europa.eu/cs/registry-of-clh-intentions-until-outcome/-/dislist/details/0b0236e18272dbc8*
Agreed EU endpoints		
AOEL systemic	0.3 mg/kg bw/d	0.29 mg/kg bw/d
Reference	EFSA Journal 2017; 15 (9):4980	EFSA Scientific Report (2006) 78, 1-80
Conditions to take into account/critical areas of concern with regard to toxicology		
According to Review Report/EFSA Conclusion for active substance	~~None~~ *The groundwater relevance assessment for groundwater metabolite RH-141455 predicted to be in annual average recharge leaving the top 1 m soil layer at > 0.75 µg/L could not be finalised, whilst the consumer risk assessment from drinking water originating from groundwater cannot be completed, as the available data are insufficient to set a reference value to complete the consumer risk assessment (see Sections 2 and 4).* (SANTE/10052/2018 Rev 2 23 March 2018)	~~None~~ *The operator, worker and bystander risk assessment is inconclusive.* EFSA Scientific Report (2006) 78, 1-80 *Member States should pay particular attention to: - the operators and workers safety.* SANCO/10057/2006 final, 25 April 2007

[1)] *Note: Skin Sens. 1B, H317: Skin sensitisation studies with the active substance propamocarb HCl (M&S test, Coleman, D. 1999 and LLNA, Repetto-Larsay, M, 2005)*

6.3 Toxicological Evaluation of Plant Protection Product

A summary of the toxicological evaluation for GLOB2007bF 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 GLOB2007bF

Type of test, species, model system (Guideline)	Result	Acceptability	Classification (acc. to the criteria in Reg. 1272/2008)	Reference
LD_{50} oral, rat	Study not necessary	Y	None	Theoretical calculations (see Part C)
LD_{50} dermal, rat	Study not necessary	Y	None	Theoretical calculations (see Part C)
LC_{50} inhalation, rat	Study not necessary	Y	None	Theoretical calculations (see Part C)
Skin irritation	Study not necessary	Y	None	Theoretical calculations (see Part C)
Eye irritation	Study not necessary	Y	None	Theoretical calculations (see Part C)
Skin sensitisation	Study not necessary	Y	Skin Sens. 1, H317	Theoretical calculations (see Part C)
Supplementary studies for combinations of plant protection products	No data – not required			

Table 6.3-2: Additional toxicological information relevant for classification/labelling of GLOB2007bF

	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)	Zoxamide (5.64 - 6.9 % (w/w))	Skin Sens. 1, H317	Reg. (EC) No 1272/2008 as amended	Skin Sens. 1, H317
	Propamocarb hydrochloride (42.29 - 46.74 % (w/w))	Skin Sens. 1B, H317	Reg. (EC) No 1272/2008 as amended	Skin Sens. 1, H317
Toxicological properties of non-active substance(s)	–	–	–	–

	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)
(relevant for classification of product)				
Further toxicological information	See Part C	–	–	~~EUH 208~~ Contains 1,2-Benzisothiazolin-3-one. ~~May produce an allergic reaction~~

* Please use concentration range or concentration limit (e.g. 1-10 % or > 1 %) as provided in MSDS.
** Material safety data sheet by the applicant

6.4 Toxicological Evaluation of Groundwater Metabolites

The predicted Environmental Concentration in groundwater calculated for zoxamide metabolite RH-141455 is greater than the regulatory threshold of 0.1 µg/L in the proposed use.

Propamocarb-HCl has no relevant metabolites to be considered in groundwater.

The following data on metabolites with the potential to reach the groundwater in concentrations above 0.1 µg/L and requiring relevance assessment were submitted. Note that the relevance assessment of the metabolites is reported in Part B.10; the submitted toxicological studies are summarised in this document.

6.4.1 RH-141455

An overview of the results of the accepted toxicological studies for groundwater metabolite RH-141455 is given in the following table. Full summaries of studies on the metabolite that have not previously been considered within an EU peer review process are described in detail in Appendix 2 (A 2.11 Other/Special Studies).

Table 6.4-1: Summary of the results of toxicity studies for RH-141455

Type of test, species (Guideline)	Result	Acceptability	Reference*
Ames Test (OECD 471)	Non mutagenic	Y	Sames, J.L. Ciaccia, P.J. (1998b)*
In vitro mouse lymphoma Assay	Non mutagenic	Y	Woods, I. (2014a)**
In vitro Micronucleus Assay	Non mutagenic	Y	Woods, I. (2014b)**

* indicates that a study was reviewed at EU level
** Matching studies have been submitted as part of a data matching package in order to compensate for access to these references

6.5 Dermal Absorption (KCP 7.3)

A summary of the dermal absorption rates for the active substances in GLOB2007bF are presented in the following table.
According to Guidance on dermal absorption (EFSA Journal 2017;15(6):4873) the default values to be used in the absence of experimental data for formulation type: suspension concentrate (SC) should be for Concentrate: 10% and for Dilution; 50%

Table 6.5-1: Dermal absorption rates for active substances in GLOB2007bF

	zoxamide		propamocarb-HCl	
	Value	**Reference**	**Value**	**Reference**
Concentrate	10%	default value (EFSA Journal 2017;15(6):4873)	10%	default value (EFSA Journal 2017;15(6):4873)
Dilution	50%		50%	

6.5.1 Justification for proposed values - zoxamide

No data on dermal absorption for zoxamide in GLOB2007bF 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 zoxamide

	Value	**Justification for value**	**Acceptability of justification**
Concentrate	10%	EFSA Journal 2017;15(6):4873	Y
Dilution	50%	EFSA Journal 2017;15(6):4873	Y

6.5.2 Justification for proposed values - propamocarb-HCl

No data on dermal absorption for propamocarb-HCl in GLOB2007bF 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 propamocarb-HCl

	Value	**Justification for value**	**Acceptability of justification**
Concentrate	10%	EFSA Journal 2017;15(6):4873	Y
Dilution	50%	EFSA Journal 2017;15(6):4873	Y

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	GLOB2007bF	
Formulation type	SC	
Category	Fungicide	
Active substance(s) (incl. content)	**zoxamide** 67.5 g/L or g/kg	**propamocarb-HCl** 450 g/L or g/kg
AOEL systemic	0.3 mg/kg bw/d	0.29 mg/kg bw/d
Inhalation absorption	100%	100%
Oral absorption	~~100%~~ 60% (based on EFSA Journal 2017;15(9):4980).	100%
Dermal absorption	Concentrate: 10% Dilution: 50% (Default)	Concentrate: 10% Dilution: 50% (Default)

6.6.1 Selection of critical use(s) and justification

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

Justification

The exposure assessment was performed with intended uses.

6.6.2 Operator exposure (KCP 7.2.1)

zRMS's comment	Acceptable. The Applicant performed operator exposure calculations using the EFSA OPEX calculator version 1.0.1 (01/07/2023). The calculation results revealed that the use of GLOB2007bF is safe for the operator if the product is used as intended, without PPE, also taking into account the combined exposure to both active substances. However, taking into account the GLOB2007bF classification (Skin Sens. 1, H317), the operator should use protective gloves during the mixing/loading step.

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 GLOB2007bF according to the critical use(s) is presented in Table 6.6-2. The outcome of the estimation is presented in Table 6.6-3 (longer term exposure). Detailed calculations are in Appendix 3.

Table 6.6-2: Exposure models for intended uses

Critical use(s)	Potato (max. 2 L product/ha)
Model(s)	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment of plant protection products. EFSA Journal 2022;20(1):7032, 134 pp. calculator version: v 1.0.1 (01/07/2023)

Table 6.6-3: Estimated operator exposure (longer term exposure) using OPEX v 1.0.1

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL
Low vegetables/Outdoor/Downward spraying/Vehicle-mounted/Drift reduction: 0 %/75th percentile Crop density: Normal			
Zoxamide	Number of applications and application rate: 3 x 0.135 kg a.s./ha Dermal absorption (concentrate): 10 % Dermal absorption (in-use dilution): 50 %		
	M/L: Workwear App: Workwear	0.06	18.6
Propamocarb-HCl	Number of applications and application rate: 3 x 0.9 kg a.s./ha Dermal absorption (concentrate): 10 % Dermal absorption (in-use dilution): 50 %		
	M/L: Workwear App: Workwear	0.2	75.4
Combined exposure			Hazard index
	M/L: Workwear App: Workwear		0.9

6.6.2.2 Measurement of operator exposure

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

6.6.3 Worker exposure (KCP 7.2.3)

zRMS's comment	Acceptable. The Applicant performed worker exposure calculations using the EFSA OPEX calculator version 1.0.1 (01/07/2023). The calculation results (also for combined exposure) revealed that the worker exposure to GLOB2007bF is acceptable if worker is wearing the workwear.

6.6.3.1 Estimation of worker exposure

Table 6.6-4 shows the exposure model(s) used for estimation of worker exposure after entry into a previously treated area or handling a crop treated with GLOB2007bF according to the critical use(s). Outcome of the estimation is presented in Table 6.6-5 (longer term exposure). Detailed calculations are in Appendix 3.

Table 6.6-4: Exposure models for intended uses

Critical use(s)	Potato (max. 2 L product/ha)
Model(s)	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment of plant protection products. EFSA Journal 2022;20(1):7032, 134 pp. calculator version: v 1.0.1 (01/07/2023)

Table 6.6-5: Estimated worker exposure (longer term exposure) using OPEX v 1.0.1

	Level of PPE	**Total absorbed dose [mg/kg bw per day]**	**% of systemic AOEL**	**Re-entry restriction [days]**
			Inspection, irrigation (All) / Outdoor Work rate: 2 hours/day Interval: 7 days Body weight: 60 kg TC (potential): 12500 cm²/h TC (workwear (arms, body and legs covered)): 1400 cm²/h TC (workwear (arms, body and legs covered) and gloves): 1250 cm²/h TC (gloves): NA cm²/h	
	Zoxamide		Number of applications & application rate: 3 x 0.135 kg a.s./ha Dermal absorption: 50 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days	
	Potential	0.2	72.3	0
	Workwear	0.02	8.1	0
	Workwear and gloves	0.02	7.2	0
	Hands covered, no workwear			
	Propamocarb-HCl		Number of applications & application rate: 3 x 0.9 kg a.s./ha Dermal absorption: 50 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days	
	Potential	1.4	498	70
	Workwear	0.2	55.8	0
	Workwear and gloves	0.1	49.8	0
	Hands covered, no workwear			
	Combined		Hazard index	

Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL	Re-entry restriction [days]
potential		5.7	76
Workwear		0.6	0
Workwear and gloves		0.6	0
Hands covered, no workwear			0

6.6.3.2 Refinement of generic DFR value (KCP 7.2)

Refinement of the generic Dislodgeable Foliar Residues (DFR) was not necessary since the risk to workers was acceptable based on the standard values.

6.6.3.3 Measurement of worker exposure

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

6.6.4 Resident and bystander exposure (KCP 7.2.2)

zRMS's comment	Acceptable. The Applicant performed resident exposure calculations using the EFSA OPEX calculator version 1.0.1 (01/07/2023). The calculation results (also for combined exposure) revealed that resident exposure both for child and adult is acceptable (below the AOEL) considering all pathways of exposure – drift, vapour, deposit and re-entry. The AAOEL values for zoxamide and propamocarb-HCl are not specified, therefore it is assumed that the bystander exposure estimation is covered by the calculated resident exposure to both substances.

6.6.4.1 Estimation of resident and bystander exposure

The acute exposure assessment for bystanders covers the exposure that a resident could reasonably be expected to incur in a single day. Therefore, there is no need for a separate acute risk assessment for residents.

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

Table 6.6-6 shows the exposure model(s) used for estimation of resident and bystander exposure to zoxamide and propamocarb-HCl. The outcome of the estimation is presented in Table 6.6-7 (longer term resident exposure). Detailed calculations are in Appendix 3.

Table 6.6-6: Exposure models for intended uses

Critical use(s)	Potato (max. 2 L product/ha)
Model	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment of plant protection products. EFSA Journal 2022;20(1):7032, 134 pp. calculator version: v 1.0.1 (01/07/2023)

Table 6.6-7: Estimated resident exposure (longer term exposure) using OPEX v 1.0.1

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL
			Season: Not relevant Buffer zone: 2-3 m Drift reduction technology: 0 % Interval between treatments: 7 days Minimum volume of water: 150 l
Zoxamide			Number of applications and application rate: 3 x 0.135 kg a.s./ha Dermal absorption: 50 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days
Resident child Body weight: 10 kg	Drift (75th perc.)	0.01	4.1
	Vapour (75th perc.)	0.0008	0.3
	Deposits (75th perc.)	0.003	0.9
	Re-entry (75th perc.)	0.03	9.8
	Sum (mean)	0.03	10.9
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.003	1
	Vapour (75th perc.)	0.0003	0.09
	Deposits (75th perc.)	0.001	0.4
	Re-entry (75th perc.)	0.02	5.4
	Sum (mean)	0.02	5.2
Propamocarb-HCl			Number of applications and application rate: 3 x 0.9 kg a.s./ha Dermal absorption: 50 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days
Resident child Body weight: 10 kg	Drift (75th perc.)	0.08	28
	Vapour (75th perc.)	0.0008	0.3
	Deposits (75th perc.)	0.02	6.5
	Re-entry (75th perc.)	0.2	67.3
	Sum (mean)	0.2	74
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.02	6.6
	Vapour (75th perc.)	0.0003	0.09

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL
	Deposits (75th perc.)	0.008	2.7
	Re-entry (75th perc.)	0.1	37.4
	Sum (mean)	0.1	35
Combined exposure			Hazard index
Resident child Body weight: 10 kg	Drift (75th perc.)		0.3
	Vapour (75th perc.)		0.005
	Deposits (75th perc.)		0.07
	Re-entry (75th perc.)		0.8
	Sum (mean)		0.8
Resident adult Body weight: 60 kg	Drift (75th perc.)		0.08
	Vapour (75th perc.)		0.002
	Deposits (75th perc.)		0.03
	Re-entry (75th perc.)		0.4
	Sum (mean)		0.4

No bystander acute exposure estimation is required as Acute AOEM has not be set (SANTE-10832-2015 rev. 2; 18 May 2022), therefore no unacceptable risk is expected for bystanders due to short-term single exposure.
It is then concluded that there is no undue risk to any bystander after accidental short-term exposure or to any resident after long-term exposure to GLOB2007bF.

6.6.4.2 Measurement of resident and/or bystander exposure

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

6.6.5 Combined exposure

zRMS's comment	The combined exposure calculations for operator, workers and residents conducted by the Applicant are acceptable. The Hazard Index is <1, therefore combined exposure to both active substances (zoxamide and propamocarb-HCl in GLOB2007bF) is not expected to pose a risk for operators and workers and residents. The exposure assessment of residents also covers the bystander exposure, therefore the combined exposure of bystanders is also not expected.

The product is a mixture of two 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 harmonised "scientific methods accepted by the Authority to assess such effects are available."

6.6.5.1 Exposure assessment of zoxamide and propamocarb-HCl in GLOB2007bF

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 converted to decimal. The Hazard Index (HI) is the sum of the individual HQs and is presented in Tables 6.6-3, 6.6-5 and 6.6-7.

The Hazard Index is < 1. Thus, combined exposure to all active substances in GLOB2007bF is not expected to present a risk for operators, workers, residents and bystanders. No further refinement of the assessment is required.

Appendix 1 Lists of data considered in support of the evaluation

List of data submitted by the applicant and relied on

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

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

*Studies in the table below were generated to data match the AIR protected studies from the main notifier. The data matching package has been evaluated by the RMS Latvia and a copy was already sent to all MS.

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
KCA 5.2.7	Brinkmann, C.	2022	In Vitro 3T3 NRU Phototoxicity Test with Zoxamide Tech, Eurofins Biopharma Product Testing Munich Gmbh, Report No.: STUGC22AA0666-2, GLP, Unpublished	N	Globachem NV
KCA 5.8.1	Schmidt, E.	2022	In vitro Mammalian Cell Gene Mutation Assay (Thymidine Kinase Locus/tk+/-) in L5178Y Mouse Lymphoma Cells with Zoxamide metabolite RH-141455, Eurofins Biopharma Product Testing Munich Gmbh, Report No.: STUGC22AA1264-3, GLP, Unpublished	N	Globachem NV
KCA 5.8.1	Graf, J.	2022	In vitro Mammalian Micronucleus Assay in Human Lymphocytes with Zoxamide metabolite RH-141455, Eurofins Biopharma Product Testing Munich Gmbh, Report No.: STUGC22AA1264-4, GLP, Unpublished	N	Globachem NV

Appendix 2 Detailed evaluation of the studies relied upon

zRMS's comment	The toxicological assessment of the GLOB2007bF formulation was carried out using the calculation method in accordance with the principles of Regulation 1272/2008. Details in Doc. C.

A 2.1 Statement on bridging possibilities

Not relevant.

A 2.2 Acute oral toxicity (KCP 7.1.1)

No new studies were submitted.

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

No new studies were submitted.

A 2.4 Acute inhalation toxicity (KCP 7.1.3)

No new studies were submitted.

A 2.5 Skin irritation (KCP 7.1.4)

No new studies were submitted.

A 2.6 Eye irritation (KCP 7.1.5)

No new studies were submitted.

A 2.7 Skin sensitisation (KCP 7.1.6)

No new studies were submitted.

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

7.1.7)

No new studies were submitted.

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)

No new studies were submitted.

zRMS's comment	In the absence of experimental data for GLOB2007bF, default values for formulation type: suspension concentrate (SC) were used according to the Guidance on dermal absorption (EFSA Journal 2017;15(6):4873).

A 2.11 Other/Special Studies

No other/special studies were submitted.

Appendix 3 Exposure calculations

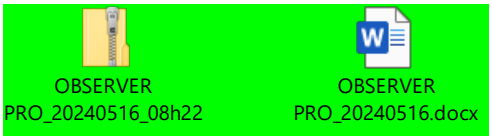

Table A 1: Information on product and active substance(s)

Product name	GLOB2007bF
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.
Product category	Other
Name of active substance	Zoxamide
Concentration of active substance [g a.s./l or kg]	67.5
AOEL [mg/kg bw/day]	0.3
AAOEL [mg/kg bw]	
Inhalation absorption [%]	100
Oral absorption [%]	100
Dermal absorption [%] (concentrate)	10
Dermal absorption [%] (dilution) 0.45 [g a.s./l or kg]	50
Dermal absorption [%] (dilution) 0.225 [g a.s./l or kg]	50
Name of active substance	Propamocarb-HCl
Concentration of active substance [g a.s./l or kg]	450
AOEL [mg/kg bw/day]	0.29
AAOEL [mg/kg bw]	
Inhalation absorption [%]	100
Oral absorption [%]	100
Dermal absorption [%] (concentrate)	10
Dermal absorption [%] (dilution) 3 [g a.s./l or kg]	50
Dermal absorption [%] (dilution) 1.5 [g a.s./l or kg]	50

Table A 2: Assessed uses

Use	Crops	Max. application rate of the product [l or kg/ha]	Unit	Max. no. of applications	Interval between multiple applications [days]	Min. volume water [l/ha]	Max. volume water [l/ha]	Indoor/outdoor	Application method	Type of cultivation	Application technique	Buffer strip [m]	Drift reduction [%]
Use 1	Low vegetables	2	l/ha	3	7	150	300	Outdoor	Downward spraying	Normal	Vehicle-mounted	2-3	0
Use 1	Low vegetables	2	l/ha	3	7	150	300	Outdoor	Downward spraying	Normal	Manual-hand held	2-3	0
Use 1	Low vegetables	2	l/ha	3	7	150	300	Outdoor	Downward spraying	Normal	Manual-knapsack	2-3	0

A 3.1 Operator exposure calculations (KCP 7.2.1.1)

A 3.1.1 Use 1 : Low vegetables

Mixing/loading	Application	Zoxamide (% AOEL)			Propamocarb-HCl (% AOEL)			Combined (hazard index)		
		Normal & vehicle-mounted	Normal & manual-hand held	Normal & manual-knapsack	Normal & vehicle-mounted	Normal & manual-hand held	Normal & manual-knapsack	Normal & vehicle-mounted	Normal & manual-hand held	Normal & manual-knapsack
		**28.3**	256	257	120	640	266	1.49	8.96	5.23
		18.6	**32.3**	**34.7**	**75.4**	**83.3**	**35.9**	**0.94**	1.16	**0.706**
 	 	0.9	25	25.1	4	62.2	26	0.049	**0.872**	0.512

A 3.1.1.1 Scenario 1 : Outdoor, normal, downward spraying, vehicle-mounted

Table A 3: Zoxamide , Input Data

Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	**Name of active substance**	Zoxamide
Concentration of active substance [g a.s./l or kg]	67.5	**Crops**	Low vegetables
Area treated [ha/day]	50	**Application method**	Downward spraying
Dermal absorption [%] (concentrate)	10	**Application technique**	Vehicle-mounted
Dermal absorption [%] (dilution)	50	**Indoor/outdoor**	Outdoor
Oral absorption [%]	100	**Drift reduction [%]**	0
Inhalation absorption [%]	100	**Type of cultivation**	Normal
Body weight (kg)	60		
AOEL [mg/kg bw/day]	0.3		
AAOEL [mg/kg bw]			

Table A 4: Zoxamide , Per body part - Short term exposure

Activity	Systemic exposure per body part	With workwear	With workwear + PPE/RPE
Mixing and loading (µg/kg bw per day)	*Hand protection*	*None*	*None*
	Hands exposure	**46**	**46**
	Body protection	*Workwear*	*Workwear*
	Body exposure	**0.3**	**0.3**
	Head protection	*None*	*None*

Activity	Systemic exposure per body part	With workwear	With workwear + PPE/RPE
Application (µg/kg bw per day)	**Head exposure**	**0.7**	**0.7**
	Inhalation protection	*None*	*None*
	Inhalation exposure	**0.1**	**0.1**
	Hand protection	*None*	*None*
	Hands exposure	**8.3**	**8.3**
	Body protection	*Workwear*	*Workwear*
	Body exposure	**0.1**	**0.1**
	Head protection	*None*	*None*
	Head exposure	**0.2**	**0.2**
	Inhalation protection	*None*	*None*
	Inhalation exposure	**0.05**	**0.05**
Total	Total systemic exposure [mg/kg bw per day]	0.06	0.06
	% of AOEL	18.6	18.6

Table A 5: Propamocarb-HCl , Input Data

Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	**Name of active substance**	Propamocarb-HCl
Concentration of active substance [g a.s./l or kg]	450	**Crops**	Low vegetables
Area treated [ha/day]	50	**Application method**	Downward spraying
Dermal absorption [%] (concentrate)	10	**Application technique**	Vehicle-mounted
Dermal absorption [%] (dilution)	50	**Indoor/outdoor**	Outdoor
Oral absorption [%]	100	**Drift reduction [%]**	0
Inhalation absorption [%]	100	**Type of cultivation**	Normal
Body weight (kg)	60		
AOEL [mg/kg bw/day]	0.29		
AAOEL [mg/kg bw]			

Table A 6: Propamocarb-HCl , Per body part - Short term exposure

Activity	Systemic exposure per body part	With workwear	With workwear + PPE/RPE
Mixing and loading (µg/kg bw per day)	*Hand protection*	*None*	*None*
	Hands exposure	**155**	**155**
	Body protection	*Workwear*	*Workwear*
	Body exposure	**0.9**	**0.9**
	Head protection	*None*	*None*
	Head exposure	**4.7**	**4.7**
	Inhalation protection	*None*	*None*
	Inhalation exposure	**0.2**	**0.2**
	Hand protection	*None*	*None*

Activity	Systemic exposure per body part	With workwear	With workwear + PPE/RPE
Application (µg/kg bw per day)	**Hands exposure**	**55.5**	**55.5**
	Body protection	*Workwear*	*Workwear*
	Body exposure	**0.8**	**0.8**
	Head protection	*None*	*None*
	Head exposure	**1.5**	**1.5**
	Inhalation protection	*None*	*None*
	Inhalation exposure	**0.1**	**0.1**
Total	Total systemic exposure [mg/kg bw per day]	0.2	0.2
	% of AOEL	75.4	75.4

A 3.1.1.2 Scenario 2 : Outdoor, normal, downward spraying, manual-hand held

Table A 7: Zoxamide , Input Data

Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	**Name of active substance**	Zoxamide
Concentration of active substance [g a.s./l or kg]	67.5	**Crops**	Low vegetables
Area treated [ha/day]	4	**Application method**	Downward spraying
Dermal absorption [%] (concentrate)	10	**Application technique**	Manual-hand held
Dermal absorption [%] (dilution)	50	**Indoor/outdoor**	Outdoor
Oral absorption [%]	100	**Drift reduction [%]**	0
Inhalation absorption [%]	100	**Type of cultivation**	Normal
Body weight (kg)	60		
AOEL [mg/kg bw/day]	0.3		
AAOEL [mg/kg bw]			

Table A 8: Zoxamide , Per body part - Short term exposure

Activity	Systemic exposure per body part	With workwear	With workwear + PPE/RPE
Mixing and loading (µg/kg bw per day)	*Hand protection*	*None*	*None*
	Hands exposure	**9.1**	**9.1**
	Body protection	*Workwear*	*Workwear*
	Body exposure	**0.06**	**0.06**
	Head protection	*None*	*None*
	Head exposure	**0.06**	**0.06**
	Inhalation protection	*None*	*None*
	Inhalation exposure	**0.04**	**0.04**
Application (µg/kg bw per day)	*Hand protection*	*None*	*None*
	Hands exposure	**12.9**	**12.9**

Activity	Systemic exposure per body part	With workwear	With workwear + PPE/RPE
	Body protection	*Workwear*	*Workwear*
	Body exposure	**74.2**	**74.2**
	Head protection	*None*	*None*
	Head exposure	**0.1**	**0.1**
	Inhalation protection	*None*	*None*
	Inhalation exposure	**0.4**	**0.4**
Total	Total systemic exposure [mg/kg bw per day]	0.1	0.1
	% of AOEL	32.3	32.3

Table A 9: Propamocarb-HCl , Input Data

Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	**Name of active substance**	Propamocarb-HCl
Concentration of active substance [g a.s./l or kg]	450	**Crops**	Low vegetables
Area treated [ha/day]	4	**Application method**	Downward spraying
Dermal absorption [%] (concentrate)	10	**Application technique**	Manual-hand held
Dermal absorption [%] (dilution)	50	**Indoor/outdoor**	Outdoor
Oral absorption [%]	100	**Drift reduction [%]**	0
Inhalation absorption [%]	100	**Type of cultivation**	Normal
Body weight (kg)	60		
AOEL [mg/kg bw/day]	0.29		
AAOEL [mg/kg bw]			

Table A 10: Propamocarb-HCl, Per body part - Short term exposure

Activity	Systemic exposure per body part	With workwear	With workwear + PPE/RPE
Mixing and loading (µg/kg bw per day)	*Hand protection*	*None*	*None*
	Hands exposure	**30.8**	**30.8**
	Body protection	*Workwear*	*Workwear*
	Body exposure	**0.2**	**0.2**
	Head protection	*None*	*None*
	Head exposure	**0.4**	**0.4**
	Inhalation protection	*None*	*None*
	Inhalation exposure	**0.09**	**0.09**
Application (µg/kg bw per day)	*Hand protection*	*None*	*None*
	Hands exposure	**30.9**	**30.9**
	Body protection	*Workwear*	*Workwear*
	Body exposure	**178**	**178**
	Head protection	*None*	*None*

Activity	Systemic exposure per body part	With workwear	With workwear + PPE/RPE
	Head exposure	**0.2**	**0.2**
	Inhalation protection	*None*	*None*
	Inhalation exposure	**1**	**1**
Total	Total systemic exposure [mg/kg bw per day]	0.2	0.2
	% of AOEL	83.3	83.3

A 3.1.1.3 Scenario 3 : Outdoor, normal, downward spraying, manual-knapsack

Table A 11: Zoxamide , Input Data

Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	**Name of active substance**	Zoxamide
Concentration of active substance [g a.s./l or kg]	67.5	**Crops**	Low vegetables
Area treated [ha/day]	1	**Application method**	Downward spraying
Dermal absorption [%] (concentrate)	10	**Application technique**	Manual-knapsack
Dermal absorption [%] (dilution)	50	**Indoor/outdoor**	Outdoor
Oral absorption [%]	100	**Drift reduction [%]**	0
Inhalation absorption [%]	100	**Type of cultivation**	Normal
Body weight (kg)	60		
AOEL [mg/kg bw/day]	0.3		
AAOEL [mg/kg bw]			

Table A 12: Zoxamide , Per body part - Short term exposure

Activity	Systemic exposure per body part	With workwear	With workwear + PPE/RPE
Mixing and loading (µg/kg bw per day)	*Hand protection*	*None*	*None*
	Hands exposure	**15.8**	**15.8**
	Body protection	*Workwear*	*Workwear*
	Body exposure	**0.04**	**0.04**
	Head protection	*None*	*None*
	Head exposure	**0.009**	**0.009**
	Inhalation protection	*None*	*None*
	Inhalation exposure	**0.6**	**0.6**
Application (µg/kg bw per day)	*Hand protection*	*None*	*None*
	Hands exposure	**12.9**	**12.9**
	Body protection	*Workwear*	*Workwear*
	Body exposure	**74.2**	**74.2**

Activity	Systemic exposure per body part	With workwear	With workwear + PPE/RPE
	Head protection	*None*	*None*
	Head exposure	**0.1**	**0.1**
	Inhalation protection	*None*	*None*
	Inhalation exposure	**0.4**	**0.4**
Total	Total systemic exposure [mg/kg bw per day]	0.1	0.1
	% of AOEL	34.7	34.7

Table A 13: Propamocarb-HCl , Input Data

Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	**Name of active substance**	Propamocarb-HCl
Concentration of active substance [g a.s./l or kg]	450	**Crops**	Low vegetables
Area treated [ha/day]	1	**Application method**	Downward spraying
Dermal absorption [%] (concentrate)	10	**Application technique**	Manual-knapsack
Dermal absorption [%] (dilution)	50	**Indoor/outdoor**	Outdoor
Oral absorption [%]	100	**Drift reduction [%]**	0
Inhalation absorption [%]	100	**Type of cultivation**	Normal
Body weight (kg)	60		
AOEL [mg/kg bw/day]	0.29		
AAOEL [mg/kg bw]			

Table A 14: Propamocarb-HCl, Per body part - Short term exposure

Activity	Systemic exposure per body part	With workwear	With workwear + PPE/RPE
Mixing and loading (µg/kg bw per day)	*Hand protection*	*None*	*None*
	Hands exposure	**15.8**	**15.8**
	Body protection	*Workwear*	*Workwear*
	Body exposure	**0.04**	**0.04**
	Head protection	*None*	*None*
	Head exposure	**0.009**	**0.009**
	Inhalation protection	*None*	*None*
	Inhalation exposure	**0.6**	**0.6**
Application (µg/kg bw per day)	*Hand protection*	*None*	*None*
	Hands exposure	**12.9**	**12.9**
	Body protection	*Workwear*	*Workwear*
	Body exposure	**74.2**	**74.2**
	Head protection	*None*	*None*
	Head exposure	**0.1**	**0.1**
	Inhalation protection	*None*	*None*

Activity	Systemic exposure per body part	With workwear	With workwear + PPE/RPE
	Inhalation exposure	**0.4**	**0.4**
Total	Total systemic exposure [mg/kg bw per day]	0.1	0.1
	% of AOEL	35.9	35.9

A 3.2 Worker exposure calculations (KCP 7.2.3.1)

A 3.2.1 Low vegetables

A 3.2.1.1 Scenario 1 : Outdoor, normal

Table A 15: Zoxamide , Input data

Indoor/outdoor	Outdoor	**AOEL [mg/kg bw/day]**	0.3
Re-entry activity	Inspection, irrigation (All)	**Dermal transfer coefficient - Total potential exposure [cm²/h]**	12500
Crops	Low vegetables	**Dermal transfer coefficient - Arm, body and legs covered [cm²/h]**	1400
Application method	Downward spraying	**Dermal transfer coefficient - Hands, arm, body and legs covered [cm²/h]**	1250
Application technique	Vehicle-mounted; manual-hand held; manual-knapsack	**Dermal transfer coefficient - Hands covered, no workwear [cm²/h]**	
Max. application rate of the product [l or kg/ha]	2	**DFR refined worker [µg/cm² foliage per kg a.s./ha]**	3
Max. no. of applications	3	**DT50 foliar worker [days]**	30
Interval between multiple applications [days]	7	**Inhalation task specific factor [ha/h*10^-3]**	0.01
Multiple application factor	2.57		
Body weight (kg)	60		
Name of active substance	Zoxamide		
Dermal absorption [%] (dilution)	50		
Inhalation absorption [%]	100		
Time [hours per day]	2		

Table A 16: Zoxamide , Exposure per body part

Exposure route	Description	Potential	Workwear	Workwear and gloves	Gloves
Dermal	Systemic dermal exposure [mg a.s. per day]	13	1.5	1.3	NA
Inhalation	Systemic inhalation exposure [mg a.s. per day]				NA
Total	Total systemic exposure [mg a.s. per day]	13	1.5	1.3	NA
	Total systemic exposure [mg/kg bw per day]	0.2	0.02	0.02	NA
	% of AOEL	72.3	8.1	7.2	NA

Table A 17: Propamocarb-HCl , Input data

Indoor/outdoor	Outdoor	**AOEL [mg/kg bw/day]**	0.29
Re-entry activity	Inspection, irrigation (All)	**Dermal transfer coefficient - Total potential exposure [cm²/h]**	12500
Crops	Low vegetables	**Dermal transfer coefficient - Arm, body and legs covered [cm²/h]**	1400
Application method	Downward spraying	**Dermal transfer coefficient - Hands, arm, body and legs covered [cm²/h]**	1250
Application technique	Vehicle-mounted; manual-hand held; manual-knapsack	**Dermal transfer coefficient - Hands covered, no workwear [cm²/h]**	
Max. application rate of the product [l or kg/ha]	2	**DFR refined worker [µg/cm² foliage per kg a.s./ha]**	3
Max. no. of applications	3	**DT50 foliar worker [days]**	30
Interval between multiple applications [days]	7	**Inhalation task specific factor [ha/h*10^-3]**	0.01
Multiple application factor	2.57		
Body weight (kg)	60		
Name of active substance	Propamocarb-HCl		
Dermal absorption [%] (dilution)	50		
Inhalation absorption [%]	100		
Time [hours per day]	2		

Table A 18: Propamocarb-HCl , Exposure per body part

Exposure route	Description	Potential	Workwear	Workwear and gloves	Gloves
Dermal	Systemic dermal exposure [mg a.s. per day]	86.7	9.7	8.7	NA
Inhalation	Systemic inhalation exposure [mg a.s. per day]				NA
Total	Total systemic exposure [mg a.s. per day]	86.7	9.7	8.7	NA

Exposure route	Description	Potential	Workwear	Workwear and gloves	Gloves
	Total systemic exposure [mg/kg bw per day]	1.4	0.2	0.1	NA
	% of AOEL	498	55.8	49.8	NA