

REGISTRATION REPORT

Part B

Section 6

Mammalian Toxicology

Detailed summary of the risk assessment

Product code: GLOB2011I

Product name(s): SANKARI

Chemical active substance:

Pelargonic acid, 650 g/L

Central

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: Globachem NV

Submission date: 31/07/2023

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After commenting period: 05/05/2024

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Update list studies: 28/05/2024

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Version history

When	What
January 2024	zRMS assessment
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6 Mammalian Toxicology (KCP 7)

6.1 Summary

Table 6.1-1: Information on GLOB2011I *

Product name and code	GLOB2011I / SANKARI
Formulation type	Emulsifiable concentrate [Code: EC]
Active substance(s) (incl. content)	Pelargonic acid; 650 g/L
Function	Insecticide
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 GLOB2011I 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:

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Table 6.1-2: Justified proposals for classification and labelling for GLOB2011I according to Regulation (EC) No 1272/2008

	The classification for GLOB2011I according to Regulation (EC) No 1272/2008	The labelling for GLOB2011I according to Regulation (EC) No 1272/2008
Hazard class(es), categories	Skin eCorr. osion/irritation, Category 1, Sub-Categories 1B+1C Eye Dam. 1	
Hazard pictograms or Code(s) for hazard pictogram(s)		GHS05
Signal word		Danger
Hazard statement(s)	H314 H318*	H314 Causes severe skin burns and eye damage.
Precautionary statement(s)		P260, P264, P280, P301+P330+P331, P303+P361+P353, P363, P304+P340, P305+P351+P338, P310, P321, P405, P501
Additional labelling phrases		To avoid risks to man and the environment, comply with the instructions for use. [EUH401]
Contains		2-octadec-9-enoxyethanol;phosphoric acid

*according to Regulation (EC) No 1272/2008 if the statement H314 is assigned, the statement H318 may be omitted on the label

Table 6.1-3: Summary of risk assessment for operators, workers, residents and bystanders for GLOB2011I

	Result	PPE / Risk mitigation measures
Operators	Acceptable	PPE: Gloves during mixing/loading work wear, gloves and protective goggles or face protection during mixing/loading and application due to the fact that the product is classified as Skin Corr. 1C H314 and Eye Dam. 1 H318.
Workers	Acceptable	None
Residents	Acceptable	None
Bystanders	Acceptable	None

No unacceptable risk for operators, workers, residents and bystanders was identified when the product is used as intended and provided that the PPE/ risk mitigation measures stated in *according to Regulation (EC) No 1272/2008 if the statement H314 is assigned, the statement H318 may be omitted on the label Table 6.1-3 are applied.

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

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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 situ- ation (e.g. growth stage of crop)	F, Fn, Fpn G, Gn, Gpn or I **	Application		Application rate		PHI (d)	Remarks: (e.g. safener/syn- ergist (L/ha)) critical gap for operator, worker, resident or by- stander exposure based on [Expo- sure model]	Acceptability of exposure assess- ment			
			Method / Kind (incl. applica- tion technique ***	Max. number (min. interval between ap- plications) a) per use b) per crop/ season	Max. applica- tion rate kg as/ha a) a.s. 1	Water L/ha min / max			Operator	Worker	Residents	Bystander
13 (cover- ing uses 1 to 12)	Maize (BBCH 51-71)	F	Spraying, LCTM	a) 2 (14) b) 2 (14)	a) 1950	200 - 600	/	Guidance on the assessment of ex- posure of opera- tors, workers, resi- dents and bystand- ers in risk assess- ment for plant pro- tection products; EFSA Journal 2014;12(10):3874	R	A	A	A

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

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

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

Explanation for column 10 "Acceptability of exposure assessment"

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

Data gaps

Data gaps should be listed in the summary to give an overview (especially for cMS).

Noticed data gaps are:

- data gap 1
- data gap 2
- data gap 3

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)

	Pelargonic acid
Common Name	Pelargonic acid
IUPAC name	Nonanoic acid

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	Pelargonic acid
CAS-No.	112-05-0
Classification and proposed labelling	
With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended)	Hazard classes (s), categories: Skin Irrit. ant 2, Eye Irrit. ant 2 Code(s) for hazard pictogram(s): GHS07 Signal word: Warning Hazard statement(s): H315 Causes skin irritation H319 Causes serious eye irritation Precautionary statement(s): P264, P280, P302+352, P305+P351+P338, P321, P332+P313, P337+P313, P362+P364, P501
Additional C&L proposal	-
Agreed EU endpoints	
AOEL systemic	Not set, not needed considering food grade quality *
Reference	EFSA Conclusions 2013 2021 (EFSA Journal 2013;11(1):3023 2021;19(8):6813)
Normal dietary intake	821 mg/kg bw /day
Conditions to take into account/critical areas of concern with regard to toxicology	
EFSA Conclusion for active substance	None

* the normal dietary intake of fatty acids of 821 mg/kg bw per day has been used instead of an AOEL for the conduction of an indicative non-dietary exposure assessment

6.3 Toxicological Evaluation of Plant Protection Product

A summary of the toxicological evaluation for GLOB2011I 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.

Comments on zRMS:	<p>For the acute toxicity including irritancy and skin sensitisation the assessments have been conducted by the applicant based on the calculation method according to the Regulation (EC) 1272/2008. Proposed classification based on calculation method according to Regulation (EC) 1272/2008 is acceptable by the zRMS.</p> <p>In addition to the calculation method, the applicant submitted toxicology studies (in vitro and in vivo), that were performed to obtain the registration in Brazil. Results of studies match with classification results from calculation approach. zRMS do not accept those in vivo studies within EU region as there was no justified reason to perform those studies, while there is sufficient data on individual ingredients and calculation method is reliably applicable.</p> <p>zRMS accepts skin irritation and skin corrosion in-vitro studies submitted by the applicant. The submitted studies are considered by zRMS in addition to the calculation method in order to support proposed classification.</p> <p>According to the Regulation (EC) 1272/2008 possible skin corrosion has to be evaluated prior to consideration of any testing for serious eye damage/eye irritation in order to avoid testing for local effects on eyes with skin corrosive substances. Skin corrosive substances shall be considered as leading to serious eye damage (Category 1) as well. Eye irritation in-vitro test was not required.</p>
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Table 6.3-1: Summary of evaluation of the studies on acute toxicity including irritancy and skin sensitisation for GLOB2011I

Type of test, species, model system (Guideline)	Result	Acceptability	Classification (acc. to the criteria in Reg. 1272/2008)	Reference
LD ₅₀ oral, rat (calculation)	> 2000 mg/kg bw	Yes / No / Supplementary	None	Calculation method (Part C)
LD ₅₀ oral, rat (OECD 423 (2001))	> 2000 mg/kg bw	Yes / No / Supplementary	None	██████████, Study 2022a, Study ██████████
LD ₅₀ dermal, rat (calculation)	> 2000 mg/kg bw	Yes / No / Supplementary	None	Calculation method (Part C)
LD ₅₀ dermal, rat (OECD 402 (2017))	> 2000 mg/kg bw	Yes / No / Supplementary	None	██████████, Study 2022b, Study ██████████
LC ₅₀ inhalation, rat (calculation)	> 5 mg/L air	Yes / No / Supplementary	None	Calculation method (Part C)
LC ₅₀ inhalation, rat (calculation OECD 403 (2009))	> 5.212 mg/L air	Yes / No / Supplementary	None	██████████, Study 2022c, Study ██████████
Skin irritation/corrosion (calculation)	Irritant/Corrosive	Yes / No / Supplementary	Skin corrosion/irritation, Category 1, Sub-Category 1C / H314	Calculation method (Part C)
Skin irritation, in-vitro, Reconstructed Human Epidermis (RHE) (OECD 439 (2021))	Irritant	Yes / No / Supplementary	Skin irritation, Category 2 / H315	Mecatti Elias L., 2022a, Study No. TX 2284 083 21 B
Skin corrosion, in-vitro, Reconstructed Human Epidermis (RHE) (OECD 431 (2019))	Corrosive	Yes / No / Supplementary	Skin corrosive, Sub-categories 1B+1C / H314	Ammirabile L., 2022, Study No. TX 2284 082 21 B
Eye irritation, (calculation)	Irritant	Yes / No / Supplementary	Eye irritant, Category 1 / H318	Calculation method (Part C)
Eye irritation, in-vitro, enucleated bovine eyes (OECD 437 (2020))	Irritant	Yes / No / Supplementary	Eye irritant, Category 1 / H318	Mecatti Elias L., 2022b, Study No. TX 2284 013 21 B
Skin sensitisation (calculation)	Non-sensitising	Yes / No / Supplementary	None	Calculation method (Part C)
Skin sensitisation, Local Lymph	Non-sensitising	Yes / No /	None	██████████

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Node Assay (LLNA) (OECD 442B (2018))		Supplementary		2022d, study # [REDACTED]
Supplementary studies for combinations of plant protection products	No data – not required			

Table 6.3-2: Additional toxicological information relevant for classification/labelling of GLOB2011I

	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)	Pelargonic acid (71.36 % (w/w))	H315, H319 (criteria: ≥ 10 %)	Harmonized classification from ECHA website Regulation (EC) 1272/2008	H315, H319
Toxicological properties of non-active substance(s) (relevant for classification of product)	Emulsifier (≥ 5 % (w/w))*	H314 (≥ 5 %) H318 (≥ 3 %)	Reg. Regulation (EC) 1272/2008	H314 H318
Further toxicological information	No data – not required			

* Please refer to Part C for more detailed information

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 GLOB2011I are presented in the following table.

Table 6.5-1: Dermal absorption rates for active substances in GLOB2011I

	Pelargonic acid	
	Value	Reference
Concentrate	25 %	Default value
Dilution	70 %	Default value

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6.5.1 Justification for proposed values – pelargonic acid

No data on dermal absorption for pelargonic acid in GLOB2011I is available. Justifications for default values according to Guidance on Dermal Absorption (EFSA Journal 2012;10(4):2665 2017;15(6):4873) are presented in the following table.

Table 6.5-2: Default dermal absorption rates for pelargonic acid

	Value	Justification for value	Acceptability of justification
Concentrate	25 %	Default value	Yes
Dilution	70 %	Default value	Yes

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	GLOB2011I/Sankari
Formulation type	EC
Category	Insecticide
Container size(s), short description	Size: 0.1-20 L Material: HDPE-PA, HDPE-EVOH or HDPE-F Opening: 42-63 mm
Active substance(s) (incl. content)	Pelargonic acid 650 g/L
AOEL systemic	Not set, not needed considering food grade quality *
Inhalation absorption	100 %
Oral absorption	100 %
Dermal absorption	Concentrate: 25 % Dilution: 70 % (Default)

* the normal dietary intake of fatty acids of 821 mg/kg bw per day has been used instead of an AOEL for the conduction of an indicative non-dietary exposure assessment

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 use 13 (maize) was selected as critical GAP as it has the highest application rate and the wider volume of application (200-600 L water/Ha). As a matter of fact, all crops are field crops and all other parameters (maximum number and interval of application) are identical.

6.6.2 Operator exposure (KCP 7.2.1)

No AOEL has been set and no operator longer term exposure calculation is deemed necessary. Nevertheless, as done in the EU review, an indicative calculation of longer-term exposure is provided using the surrogate normal dietary intake of fatty acids of 821 mg/kg bw per day.

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 GLOB2011I 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 (acute exposure) and Table 6.6-4 (longer term exposure). Detailed calculations are in Appendix 1.

Table 6.6-2: Exposure models for intended uses

Critical use(s)	Maize (max. 3 L product/ha)
Model(s)	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2022;20(1):7032 Online model OPEX version 1.0.0

Table 6.6-3: Estimated operator exposure (acute exposure)

		Pelargonic acid	
Model data	Level of PPE	Total absorbed dose (mg/kg/day)	% of systemic AAOEL
Normal and vehicle mounted boom spray application outdoors to low crops			
Application rate		1.95 kg a.s./ha	
Spray application outdoor (online AOEM; 95 th percentile) Body weight: 60 kg	Work wear (arms, body and legs covered) M/L and A	No acute exposure calculation necessary	No acute exposure calculation necessary
	Work wear (arms, body and legs covered) M/L and A + type of PPE/RPE	No acute exposure calculation necessary	No acute exposure calculation necessary

Table 6.6-4: Estimated operator exposure (longer term exposure)

		Pelargonic acid	
Model data	Level of PPE	Total absorbed dose (mg/kg/day)	% of systemic AOEL
Normal and vehicle mounted boom spray application outdoors to low crops			
Application rate		1.95 kg a.s./ha	

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Spray application (online AOEM; 75 th percentile) Body weight: 60 kg	Work wear (arms, body and legs covered) M/L and A	0.8	0.1
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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.

Study comment 6.6.2:	<p>The applicant presented calculations for the application of Sankari (GLOB2011I) on maize: max dose 2x3 L/ha (Field) as the worst case. zRMS agrees with Applicant that the use 13 (maize) is critical GAP as it has the highest application rate and the wider volume of application (200-600 L water/ha). Additionally, all crops provided in Part B, Section 0 are field crops and all other parameters (maximum number and interval of application) are identical.</p> <p>The exposure calculations were conducted using the EFSA online calculator 2022 v 1.0.0. (OPEX). The calculations provided by Applicant were done correctly.</p>
Agreed endpoint 6.6.2:	<p>According to EFSA OPEX calculations, it can be concluded that the risk of operator exposure during mixing & loading and application using the tractor-mounted on field on maize is acceptable under conditions of intended use when the work wear (long sleeved shirt, long trousers) is worn during loading, mixing and application.</p> <p>Due to the fact that the product is classified as Skin Corr. 1C H314 and Eye Dam. 1 H318, the operator should wear work wear, gloves and protective goggles or face protection during mixing/loading and application operations.</p> <p>Thus, the operator using Sankari (GLOB2011I) will be safe as long as he wears work wear, gloves and protective goggles or face protection.</p>

6.6.3 Worker exposure (KCP 7.2.3)

6.6.3.1 Estimation of worker exposure

Table 6.6-5 shows the exposure model(s) used for estimation of worker exposure after entry into a previously treated area or handling a crop treated with GLOB2011I according to the critical use(s). Outcome of the estimation is presented in Table 6.6-6 (acute exposure) and Table 6.6-7 (longer term exposure). Detailed calculations are in Appendix 1.

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Table 6.6-5: Exposure models for intended uses

Critical use(s)	Maize (max. 3 L product/ha)
Model	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2022;20(1):7032 Online model OPEX version 1.0.0

Table 6.6-6: Estimated worker exposure (acute exposure)

		Pelargonic acid	
Model data	Level of PPE	Total absorbed dose (mg/kg bw/day)	% of systemic AAOEL
Inspection, irrigation/Outdoor Work rate: 2 hours/day DT ₅₀ : 30 days DFR: 3 µg/cm ² /kg a.s./ha			
Application rate		1.95 kg a.s./ha	
Body weight: 60 kg	Potential TC: 12500 cm ² /person/h	No acute exposure calculation necessary	No acute exposure calculation necessary
	Work wear (arms, body and legs covered) TC: 1400 cm ² /person/h	No acute exposure calculation necessary	No acute exposure calculation necessary
	Work wear (arms, body and legs covered) and gloves TC: 1250 cm ² /person/h	No acute exposure calculation necessary	No acute exposure calculation necessary

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

		Pelargonic acid	
Model data	Level of PPE	Total absorbed dose (mg/kg bw/day)	% of systemic AOEL
Inspection, irrigation/Outdoor Work rate: 2 hours/day DT ₅₀ : 30 days DFR: 3 µg/cm ² /kg a.s./ha Interval between treatments: 14 days			
Number of applications and application rate		1.95 kg a.s./ha	
Body weight: 60 kg	Potential TC: 12500 cm ² /person/h	2.9	0.4
	Work wear (arms, body and legs covered) TC: 1400 cm ² /person/h	0.3	0.04
	Work wear (arms, body and legs covered) and gloves TC: 1250 cm ² /person/h	0.3	0.04

6.6.3.2 Refinement of generic DFR value (KCP 7.2)

Not required as default DFR value is used.

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.

Study comment 6.6.4:	The evaluator agrees with Applicant's estimation of worker exposure after entry into a previously treated area or handling a crop treated with Sankari (GLOB2011I) according to the critical use on maize. The calculations were made by means of EFSA OPEX calculator for dose 2 x 3 L product/ha as the worst case. The calculations were done correctly.
Agreed endpoint 6.6.4:	According to the calculations, it can be concluded that the risk of worker exposure during re-entry activities is acceptable. The risk for worker exposure during re-entry activities on area treated with Sankari (GLOB2011I) is acceptable without the PPE but worker should be wearing the adequate work clothing for its intended use within good agricultural practice.

6.6.4 Resident and bystander exposure (KCP 7.2.2)

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 6.6-8 shows the exposure model(s) used for estimation of resident and bystander exposure to pelargonic acid. The outcome of the estimation is presented in Table 6.6-10 (longer term resident exposure) and Table 6.6-9 (acute bystander exposure). Detailed calculations are in Appendix 1.

According to the EFSA guidance, an assessment of recreational exposure is required for the proposed uses on golf courses, turf or other sports lawns. The outcome of the estimation is presented in **Błąd! Nie można odnaleźć źródła odwołania..**

Table 6.6-8: Exposure models for intended uses

Critical use(s)	Maize (max. 3 L product/ha)
Model	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2022;20(1):7032 Online model OPEX version 1.0.0

Table 6.6-9: Estimated resident exposure (longer term exposure)

		Pelargonic acid	
Model data		Total absorbed dose (mg/kg bw/day)	% of systemic AOEL
Normal and vehicle mounted boom spray application outdoors to low crops Buffer zone: 2-3 m Drift reduction technology: no DT ₅₀ : 30 days DFR: 3 µg/cm ² /kg a.s./ha Interval between treatments: 14 days			
Number of applications and application rate		1.95 kg a.s./ha	
Resident child Body weight: 10 kg	Drift (75 th perc.)	0.2	0.02
	Vapour (75 th perc.)	0	0
	Deposits (75 th perc.)	0.04	0.004
	Re-entry (75 th perc.)	0.4	0.05
	Sum (mean)	0.4	0.05
Resident adult Body weight: 60 kg	Drift (75 th perc.)	0.04	0.005
	Vapour (75 th perc.)	0	0
	Deposits (75 th perc.)	0.02	0.002

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	Re-entry (75 th perc.)	0.2	0.03
	Sum (mean)	0.2	0.03

Table 6.6-10: Estimated bystander exposure (acute exposure)

		Pelargonic acid	
Model data		Total absorbed dose (mg/kg bw/day)	% of systemic AAOEL
Normal and vehicle mounted boom spray application outdoors to low crops Buffer zone: 2-3 m Drift reduction technology: no DFR: 3 µg/cm ² /kg a.s./ha			
Application rate		1.95 kg a.s./ha	
Bystander child Body weight: 10 kg	Drift (95 th perc.)	0.4	No acute exposure calculation necessary
	Vapour (95 th perc.)	0	No acute exposure calculation necessary
	Deposits (95 th perc.)	0.1	No acute exposure calculation necessary
	Re-entry (95 th perc.)	0.4	No acute exposure calculation necessary
Bystander adult Body weight: 60 kg	Drift (95 th perc.)	0.1	No acute exposure calculation necessary
	Vapour (95 th perc.)	0	No acute exposure calculation necessary
	Deposits (95 th perc.)	0.05	No acute exposure calculation necessary
	Re-entry (95 th perc.)	0.2	No acute exposure calculation necessary

6.6.4.2 Measurement of resident and/or bystander exposure

Since the indicative resident and/or bystander exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) for pelargonic acid 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.

Study comment 6.6.4:	<p>The evaluator agrees with estimation of resident exposure after application of Sankari (GLOB2011I) on maize.</p> <p>The exposure estimation of resident (adult and child) to pelargonic acid, applied on a field of maize at dose of 2x3 L product/ha, using tractor-mounted, calculated with the the EFSA OPEX calculator demonstrates that such a exposure for adult and</p>
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	<p>child resident amounted 0.03 % to 0.05% of respective AOEL, thus not causing an unacceptable risk.</p> <p>The calculations were done correctly. The exposure assessment for residents also covers bystander exposure.</p>
Agreed endpoint 6.6.4:	According to calculations, it can be concluded that there is no unacceptable risk to any resident (child and adult) and bystander after application product Sankari (GLOB2011I) on maize.

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Appendix 1 Lists of data considered in support of the evaluation

Tables considered not relevant can be deleted as appropriate.
 MS to blacken authors of vertebrate studies in the version made available to third parties/public.

List of data submitted by the applicant and relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 7.1.1		2022a	ACUTE ORAL TOXICITY STUDY IN RATS AFTER THE ADMINISTRATION OF GLOB2011I GLP Unpublished	Y	Globachem NV
KCP 7.1.2		2022b	ACUTE DERMAL TOXICITY STUDY IN RATS AFTER THE ADMINISTRATION OF GLOB2011I GLP Unpublished	Y	Globachem NV
KCP 7.1.3		2022e	ACUTE INHALATION TOXICITY STUDY IN RATS AFTER THE ADMINISTRATION OF GLOB2011I GLP Unpublished	Y	Globachem NV
KCP 7.1.4	Mecatti Elias, L.	2022a	IN VITRO SKIN IRRITATION TEST FOR GLOB2011I: RECONSTRUCTED HUMAN EPIDERMIS	N	Globachem

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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
			(RHE) TEST METHOD Report No. TX 2284 083 21 B PLANTEC Laboratórios GLP Unpublished		NV
KCP 7.1.4	Ammirabile, L.	2022	IN VITRO SKIN CORROSION TEST FOR GLOB2011I: ASSAY WITH RECONSTRUCTED HUMAM EPIDERMIS (RHE) Report No. TX 2284 082 21 B PLANTEC Laboratórios GLP Unpublished	N	Globachem NV
KCP 7.1.5	Mecatti Elias, L	2022b	BOVINE CORNEAL OPACITY AND PERMEABILITY TEST (BCOP) AFTER APPLICATION OF GLOB2011I Report No. TX 2284 013 21 B PLANTEC Laboratórios GLP Unpublished	N	Globachem NV
KCP 7.1.6		2022d	LOCAL LYMPH NODE ASSAY (LLNA): BRDU ELISA FOR SKIN SENSITIZATION BY GLOB2011I [REDACTED] GLP Unpublished	Y	Globachem NV

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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
-	-	-	-	-	-

The following tables are to be completed by MS

List of data submitted by the applicant and not relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 7.1.1		2022a	ACUTE ORAL TOXICITY STUDY IN RATS AFTER THE ADMINISTRATION OF GLOB2011I GLP Unpublished	Y	Globachem NV
KCP 7.1.2		2022b	ACUTE DERMAL TOXICITY STUDY IN RATS AFTER THE ADMINISTRATION OF GLOB2011I GLP Unpublished	Y	Globachem NV
KCP 7.1.3		2022c	ACUTE INHALATION TOXICITY STUDY IN RATS AFTER THE ADMINISTRATION OF GLOB2011I	Y	Globachem NV

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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
			██████████ GLP Unpublished		
KCP 7.1.5	Mecatti Elias, L	2022b	BOVINE CORNEAL OPACITY AND PERMEABILITY TEST (BCOP) AFTER APPLICATION OF GLOB2011I Report No. TX 2284 013 21 B PLANTEC Laboratórios GLP Unpublished	N	Globachem NV
KCP 7.1.6	██████████	2022d	LOCAL LYMPH NODE ASSAY (LLNA): BRDU-ELISA FOR SKIN SENSITIZATION BY GLOB2011I ██████████ GLP Unpublished	Y	Globachem NV

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

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

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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
			Source GLP/non GLP/GEP/non GEP Published/Unpublished		

Appendix 2 Detailed evaluation of the studies relied upon

Comments on zRMS:	<p>For the acute toxicity including irritancy and skin sensitisation the assessments have been conducted by the applicant based on the calculation method according to the Regulation (EC) 1272/2008. Proposed classification based on calculation method according to Regulation (EC) 1272/2008 is acceptable by the zRMS. In addition to the calculation method, the applicant submitted toxicology studies (in vitro and in vivo), that were performed to obtain the registration in Brazil. Results of studies match with classification results from calculation approach. zRMS do not accept those in vivo studies within EU region as there was no justified reason to perform those studies, while there is sufficient data on individual ingredients and calculation method is reliably applicable.</p> <p>zRMS accepts skin irritation and skin corrosion in-vitro studies submitted by the applicant. The submitted studies are considered by zRMS in addition to the calculation method in order to support proposed classification.</p> <p>According to the Regulation (EC) 1272/2008 possible skin corrosion has to be evaluated prior to consideration of any testing for serious eye damage/eye irritation in order to avoid testing for local effects on eyes with skin corrosive substances. Skin corrosive substances shall be considered as leading to serious eye damage (Category 1) as well. Eye irritation in-vitro test was not required.</p>
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A 2.1 Statement on bridging possibilities

No bridging was necessary.

Comments of zRMS:	Acceptable.
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A 2.2 Acute oral toxicity (KCP 7.1.1)

No study has been performed for Europe for GLOB2011I as it is possible to extrapolate toxicity from data available on active substance and co-formulants. The assessments have been conducted according to Regulation (EC) 1107/2009 (amended by Commission Regulation (EU) No 286/2011).

Nevertheless, a GLP study was performed to obtain the registration in Brazil and is provided for the sake of completeness in addition to the calculation method.

Comments of zRMS:	See above Appendix 2 – grey box.
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A 2.2.1 Study 1

Reference

KCP 7.1.1

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Report	ACUTE ORAL TOXICITY STUDY IN RATS AFTER THE ADMINISTRATION OF GLOB2011I, [REDACTED] 2022a, [REDACTED]
Guideline(s)	Yes – OECD 423 (2001)
Deviations	No
GLP	Yes
Acceptability	Yes/No/Supplementary
Duplication (if vertebrate study)	No – Study done for Brazil registration and provided for the sake of completeness in Europe. In Europe, classification by calculation can be done based on data available on the active substance and co-formulants.

Materials and methods

Test material (Lot/Batch No.)	GLOB2011I (Batch No. GLOB2011I03H18M21)
Species	Wistar (albino) rats (<i>Rattus norvegicus</i>)
No. of animals (group size)	3 female rats/group (2 groups for the study)
Dose(s)	2000 mg/kg bw
Exposure	Once by gavage
Vehicle/Dilution	None
Post exposure observation period	14 days
Remarks	None

Results and discussions

Table A 1: Results of acute oral toxicity study in rats of GLOB2011I

Dose (mg/kg bw)	Toxicological results *	Duration of signs	Time of death	LD ₅₀ (mg/kg bw) (14 days)
Female rats (group 1)				
2000	0/3/3	2-3 hours	-	> 2000
Female rats (group 2)				
2000	0/0/3	-	-	> 2000

* Number of animals which died/number of animals with clinical signs/number of animals used

Table A 2: Summary of findings of acute oral toxicity study in rats of GLOB2011I

Mortality	No mortality occurred.
Clinical signs	Yes. Piloerection was observed in animals 1 (from 0.5 hour to 1 hour), 2 (from 0.5 hour to 2 hours), and 3 (from 0.5 hour to 3 hours), soon after these times the clinical sign ceased and remained so until the end of the test period.
Body weight	Body weight gain was considered to be normal.
Macroscopic examination	The necropsies performed at the end of the study revealed no apparent findings.

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Conclusion

Under the experimental conditions, the oral LD₅₀ of GLOB2011I is higher than 2000 mg/kg bw in rats. Thus, no classification is required according to Regulation (EC) No. 1272/2008.

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

No study has been performed for Europe for GLOB2011I as it is possible to extrapolate toxicity from data available on active substance and co-formulants. The assessments have been conducted according to Regulation (EC) 1107/2009 (amended by Commission Regulation (EU) No 286/2011).

Nevertheless, a GLP study was performed to obtain the registration in Brazil and is provided for the sake of completeness in addition to the calculation method.

Comments of zRMS: See above Appendix 2 – grey box.

A 2.3.1 Study 1

Reference	KCP 7.1.2
Report	ACUTE DERMAL TOXICITY STUDY IN RATS AFTER THE ADMINISTRATION OF GLOB2011I, 2022b,
Guideline(s)	Yes – OECD 402 (2017)
Deviations	No
GLP	Yes
Acceptability	Yes/No/Supplementary
Duplication (if vertebrate study)	No – Study done for Brazil registration and provided for the sake of completeness in Europe. In Europe, classification by calculation can be done based on data available on the active substance and co-formulants.

Materials and methods

Test material (Lot/Batch No.)	GLOB2011I (Batch No. GLOB2011I03H18M21)
Species	Wistar (albino) rats (<i>Rattus norvegicus</i>)
No. of animals (group size)	1 female rat for group 1 2 female rats for group 2
Dose(s)	2000 mg/kg bw
Exposure	24 hours (dermal, semi-occlusive)
Vehicle/Dilution	None
Post exposure observation period	14 days
Remarks	None

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Results and discussions

Table A 3: Results of acute dermal toxicity study in rats of GLOB2011I

Dose (mg/kg bw)	Toxicological results *	Duration of signs	Time of death	LD ₅₀ (mg/kg bw) (14 days)
Female rat (group 1)				
2000	0/0/1	-	-	> 2000
Female rats (group 2)				
2000	0/2/2	2-3 days	-	> 2000

* Number of animals which died/number of animals with clinical signs/number of animals used

Table A 4: Summary of findings of acute dermal toxicity study in rats of GLOB2011I

Mortality	No mortality occurred.
Clinical signs	Yes. In group # 2, animal 2 had erythema between days 1 and 3 and animal 3 had erythema between days 1 and 2.
Body weight	Body weight gain was considered to be normal.
Macroscopic examination	The necropsies performed at the end of the study revealed no apparent findings.

Conclusion

Under the experimental conditions, the dermal LD₅₀ of GLOB2011I is higher than 2000 mg/kg bw in rats. Thus, no classification is required according to Regulation (EC) No. 1272/2008.

A 2.4 Acute inhalation toxicity (KCP 7.1.3)

No study has been performed for Europe for GLOB2011I as it is possible to extrapolate toxicity from data available on active substance and co-formulants. The assessments have been conducted according to Regulation (EC) 1107/2009 (amended by Commission Regulation (EU) No 286/2011).

Nevertheless, a GLP study was performed to obtain the registration in Brazil and is provided for the sake of completeness in addition to the calculation method.

Comments of zRMS:	See above Appendix 2 – grey box.
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A 2.4.1 Study 1

Reference	KCP 7.1.3
Report	ACUTE INHALATION TOXICITY STUDY IN RATS AFTER THE ADMINISTRATION OF GLOB2011I, Pampoloni J., 2022c, Study No. TX 2284 089 21 B
Guideline(s)	Yes – OECD 403 (2009)
Deviations	No

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GLP	Yes
Acceptability	Yes/No/Supplementary
Duplication (if vertebrate study)	No – Study done for Brazil registration and provided for the sake of completeness in Europe. In Europe, classification by calculation can be done based on data available on the active substance and co-formulants.

Materials and methods

Test material (Lot/Batch No.)	GLOB2011I (Batch No. GLOB2011I03H18M21)
Species	Wistar (albino) rats (<i>Rattus norvegicus</i>)
No. of animals (group size)	3 rats/sex/dose
Concentration(s)	5.212 mg/L air
Exposure	4 hours (nose only)
Vehicle/Dilution	None
Post exposure observation period	14 days
Remarks	None

Results and discussions

Table A 5: Concentration(s) and exposure conditions

Target conc. (mg/L air)	or	Nominal conc. (mg/L air)	Actual conc. (mg/L air)	MMAD * (µm)	GSD ** (µm)
-		5.96	5.212	1.73	2.79

* MMAD = Mass Median Aerodynamic Diameter

** GSD = Geometric Standard Deviation

Table A 6: Results of acute inhalation toxicity study in rats of GLOB2011I

Concentration (mg/L air)	Toxicological results *	Duration of signs	Time of death	LC ₅₀ (mg/L air) (14 days)
Male rats				
5.212	0/0/3	-	-	> 5.212
Female rats				
5.212	0/0/3	-	-	> 5.212

* Number of animals which died/number of animals with clinical signs/number of animals used

Table A 7: Summary of findings of acute inhalation toxicity study in rats of GLOB2011I

Mortality	No mortality occurred.
Clinical signs	No clinical signs of toxicity were observed.
Body weight	Body weight gain was considered to be normal.
Macroscopic examination	The necropsies performed at the end of the study revealed no apparent findings.

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Conclusion

Under the experimental conditions, the inhalation LC₅₀ of GLOB2011I is higher than 5.212 mg/L air in rats. Thus, no classification is required according to Regulation (EC) No. 1272/2008.

A 2.5 Skin irritation (KCP 7.1.4)

No study has been performed for Europe for GLOB2011I as it is possible to extrapolate toxicity from data available on active substance and co-formulants. The assessments have been conducted according to Regulation (EC) 1107/2009 (amended by Commission Regulation (EU) No 286/2011).

Nevertheless, a GLP study was performed to obtain the registration in Brazil and is provided for the sake of completeness in addition to the calculation method.

Comments of zRMS:	<p>Study 1 was performed according to OECD 439 and was GLP compliant. The study is acceptable. Under the experimental conditions, GLOB2011I is a skin irritant. OECD test guideline 439 cannot discriminate between skin irritation/corrosion categories 1 and 2, therefore study 2 (skin corrosion test) was performed.</p> <p>Study 2 was performed according to OECD 431 and was GLP compliant. The study is acceptable. Under the experimental conditions, GLOB2011I is corrosive to skin. Skin Corr. 1 classification is required according to Regulation 1272/2008.</p> <p>Based on calculation method GLOB2011I should be classified as Skin Corrosion Category 1, Sub-Category 1C according to Regulation 1272/2008. As a hazardous constituent contributing to classification, the labelling should include: contains 2-octadec-9-enoxyethanol;phosphoric acid. The submitted studies are considered in addition to the calculation method in order to support proposed classification.</p>
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A 2.5.1 Study 1

Reference	KCP 7.1.4
Report	IN VITRO SKIN IRRITATION TEST FOR GLOB2011I: RECONSTRUCTED HUMAN EPIDERMIS (RHE) TEST METHOD, Mecatti Elias L., 2022a, Study No. TX 2284 083 21 B
Guideline(s)	Yes – OECD 439 (2021)
Deviations	No
GLP	Yes
Acceptability	Yes/No/Supplementary
Duplication (if vertebrate study)	No

Materials and methods

Test material (Lot/Batch No.)	GLOB2011I (Batch No. GLOB2011I03H18M21)
Material used	Reconstructed human epidermis (RHE) from human keratinocytes cultured on an inert polycarbonate membrane at the air-liquid interface, in a chemically defined medium

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No. of RHE (group size)	3 replicates per group (negative control, positive control, test item)
Initial test using one RHE	No
Exposure	16 ± 0.5 µL (42 minutes before washing)
Vehicle/Dilution	Tissues placed in plates with 300 µL of maintenance medium
Post exposure observation period	42 hours
Remarks	None

Results and discussions

Table A 8: Skin irritation of GLOB2011I

Treat-ment	Rep-li-cates	OD values (nm)			Individ-ual Mean (nm)	Cor-rected Mean (nm)	Stand-ard devia-tion (%)	Individ-ual Viabil-ity (%)	Total viability (%)
Negative control	1	2.324	2.118	1.945	2.0753	1.9727	10.18	105.20	100.00
	2	1.977	1.904	2.163	1.9610			99.41	
	3	1.953	1.924	1.929	1.8817			95.39	
Positive control	1	0.094	0.077	0.082	0.0307	0.0308	0.57	1.56	1.56
	2	0.077	0.086	0.087	0.0297			1.51	
	3	0.081	0.083	0.093	0.0320			1.62	
Test item	1	0.100	0.094	0.099	0.0440	0.0448	1.01	2.23	2.27
	2	0.094	0.086	0.100	0.0397			2.01	
	3	0.116	0.090	0.107	0.0507			2.57	
		Blank OD values (nm)			Blank Mean (nm)	Blank SD (%)			
Blank	1	0.049	0.058	0.054	0.0537	0.45			

Since the replicas were concordant, with deviation less than or equal to (\leq) 18%; mean percentage of cell viability outside the borderline range ($50 \pm 5\%$); negative control with mean OD within the acceptable range (≥ 0.8 and ≤ 3.0) and positive control with mean viability below 40%, with values within historically established limits; it is concluded that all the acceptability criteria were met.

With the acceptability criteria met, the test item is identified as requiring classification and labelling according to UN GHS (Category 2) if the mean percentage of tissue viability, after exposure and post-treatment incubation is less than or equal (\leq) to 50%. For regulatory bodies that do not adopt UN GHS Category 3 (moderate irritants), this assay can also identify non-skin irritant chemicals, which are not classified according to UN GHS (No Category), if tissue viability after exposure and post-treatment incubation is greater than ($>$) 50%.

Conclusion

Under the experimental conditions, GLOB2011I is a skin irritant. Thus, classification is required according to Regulation (EC) No. 1272/2008. GLOB2011I can be classified as UN GHS Category 2.

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A 2.5.2 Study 2

Reference	KCP 7.1.4
Report	IN VITRO SKIN CORROSION TEST FOR GLOB2011I: ASSAY WITH RECONSTRUCTED HUMAM EPIDERMIS (RHE), Ammirabile L., 2022, Study No. TX 2284 082 21 B
Guideline(s)	Yes – OECD 431 (2019)
Deviations	No
GLP	Yes
Acceptability	Yes/No/Supplementary
Duplication (if vertebrate study)	No

Materials and methods

Test material (Lot/Batch No.)	GLOB2011I (Batch No. GLOB2011I03H18M21)
Material used	Reconstructed human epidermis (RHE) from human keratinocytes cultured on an inert polycarbonate membrane at the air-liquid interface, in a chemically defined medium
No. of RHE (group size)	2 replicates per group (negative control, positive control, test item)
Initial test using one RHE	No
Exposure	40 ± 3 µL (3 and 60 minutes before washing, 2 different parts of the RHE exposed)
Vehicle/Dilution	Tissues placed in plates with 300 µL of maintenance medium
Post exposure observation period	180 ± 15 minutes
Remarks	None

Results and discussions

Table A 9: Skin corrosion of GLOB2011I after 3 minutes of exposition

Treat-ment	Rep-li-cates	OD values (nm)			Individ-ual Mean (nm)	Cor-rected Mean (nm)	Stand-ard devia-tion (%)	Individ-ual Viabil-ity (%)	Total viability (%)
Negative control	1	2.180	2.313	2.140	2.1530	2.0952	8.72	102.76	100.00
	2	2.106	2.088	2.092	2.0374			97.24	
Test item	1	1.345	1.341	1.354	1.2887	1.2552	5.28	61.51	59.91
	2	1.291	1.286	1.262	1.2217			58.31	
		Blank OD values (nm)			Blank Mean (nm)	Blank SD (%)			
Blank	1	0.049	0.059	0.057	0.0580	0.54			

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	2	0.056	0.064	0.063			
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Table A 10: Skin corrosion of GLOB2011I after 60 minutes of exposition

Treat-ment	Rep-li-cates	OD values (nm)			Individ-ual Mean (nm)	Cor-rected Mean (nm)	Stand-ard devia-tion (%)	Individ-ual Viabil-ity (%)	Total viability (%)
Negative control	1	2.427	2.552	2.532	2.4457	2.4431	0.92	100.11	100.00
	2	2.474	2.471	2.550	2.4404			99.89	
Positive control	1	0.089	0.077	0.086	0.0260	0.0222	1.08	1.06	0.91
	2	0.080	0.074	0.075	0.0184			0.75	
Test item	1	0.405	0.392	0.402	0.3417	0.2921	7.57	13.99	11.95
	2	0.303	0.310	0.288	0.2424			9.92	
		Blank OD values (nm)			Blank Mean (nm)	Blank SD (%)			
Blank	1	0.049	0.059	0.057	0.0580	0.54			
	2	0.056	0.064	0.063					

Under test conditions, the GLOB2011I showed 59.91% of cell viability in the 3 minutes exposition, and 11.95% of cell viability in the 60 minutes exposition, in relation to the negative control. According to UN GHS, a test item having $\geq 50\%$ after 3 min exposure and $< 15\%$ after 60 min exposure would need to be classified as corrosive. In addition, test item having a cell viability $\geq 18\%$ after 3 min exposure would need to be classified in subcategories 1B and 1C.

Conclusion

Under the experimental conditions, GLOB2011I is corrosive to skin. Thus, classification is required according to Regulation (EC) No. 1272/2008. GLOB2011I has to be classified as corrosive combination of Sub-categories 1B+1C to the skin according to UN GHS. Please note that the in-vitro test does not allow to differentiate between sub-categories 1B or 1C.

A 2.6 Eye irritation (KCP 7.1.5)

No study has been performed for Europe for GLOB2011I as it is possible to extrapolate toxicity from data available on active substance and co-formulants. The assessments have been conducted according to Regulation (EC) 1107/2009 (amended by Commission Regulation (EU) No 286/2011).

Nevertheless, a GLP study was performed to obtain the registration in Brazil and is provided for the sake of completeness in addition to the calculation method.

Comments of zRMS:	See above Appendix 2 – grey box.
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A 2.6.1 Study 1

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Reference	KCP 7.1.5
Report	BOVINE CORNEAL OPACITY AND PERMEABILITY TEST (BCOP) AFTER APPLICATION OF GLOB2011I, Mecatti Elias L., 2022b, Study No. TX 2284 013 21 B
Guideline(s)	Yes – OECD 437 (2020)
Deviations	No
GLP	Yes
Acceptability	Yes/No/Supplementary
Duplication (if vertebrate study)	No

Materials and methods

Test material (Lot/Batch No.)	GLOB2011I (Batch No. GLOB2011I03H18M21)
Species	Enucleated bovine eyes (from animals slaughtered for commercial purposes for use consumption) aged between 25 and 36 months.
No. of animals (group size)	3 replicates per group (negative control, positive control, test item) + 1 replicate for the blank.
Initial test using one animal	No
Exposure	750 µL (single instillation on the cornea followed by 10 minutes incubation time before washing)
Irrigation (time point)	No
Vehicle/Dilution	None
Post exposure observation period	2 hours
Remarks	None

Results and discussions

Table A 11: Eye opacity after application of GLOB2011I

Treat-ment	Repe-titions	Initial Lux	Initial opacity	Final Lux	Final opacity	Pure opacity	Cor-rected pure opacity	Average	SD
Blank	1	1188	-	1191	-	-	-		
Negative control	1	1124	2.6908	1130	2.5730	-0.1178	-	-0.2782	0.2190
	2	1131	2.4302	1139	2.2412	-0.1890	-		
	3	1119	2.8790	1136	2.3512	-0.5278	-		
Positive control	1	1045	5.8742	378	86.1113	80.2371	80.5153	83.6126	3.5744
	2	1028	6.6232	356	93.8687	87.2456	87.5238		
	3	1051	5.6156	372	88.1360	82.5204	82.7986		
Test Item	1	1102	3.5315	497	56.0549	52.5234	52.8016	50.7822	2.0639
	2	1096	3.7666	506	54.3568	50.5902	50.8684		

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	3	1100	3.6096	519	52.0079	48.3983	48.6765		
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Table A 12: Eye permeability after application of GLOB2011I

Treat-ment	Repe-titions	Reading 1	Reading 2	Reading 2	Aveage	Corrected pure per-meability	Mean cor-rected pure per-meability	SD
Blank	1	0.074	0.084	0.089	0.0824	-	-	-
Negative control	1	0.093	0.095	0.091	0.0930	0.0106	0.0112	0.0005
	2	0.090	0.096	0.095	0.0937	0.0113		
	3	0.093	0.099	0.090	0.0940	0.0116		
Positive control	1	0.834	0.836	0.846	0.8387	0.8275	0.8583	0.0300
	2	0.875	0.859	0.879	0.8710	0.8598		
	3	0.896	0.896	0.904	0.8987	0.8875		
Test Item	1	1.435	1.313	1.353	1.3670	1.3558	1.4495	0.0830
	2	1.512	1.539	1.524	1.5250	1.5138		
	3	1.496	1.493	1.481	1.4900	1.4788		

Table A 13: IVIS calculation after application of GLOB2011I

Treatment	Opacity	Permeability	IVIS
Negative control	-0.2782	0.0112	-0.1102
Positive control	83.6126	0.8583	96.4871
Test Item	50.7822	1.4495	72.5247

GLOB2011I presented an IVIS equal to 72.5247 which do classify the test substance as eye irritant Category 1 according to technical proficiency of the lab which has validated the irritation scale using different 13 substances.

Conclusion

Under the experimental conditions, GLOB2011I is an eye irritant. Thus, classification is required according to Regulation (EC) No. 1272/2008. According to GHS, GLOB2011I has to be classified as eye irritant Category 1.

A 2.7 Skin sensitisation (KCP 7.1.6)

No study has been performed for Europe for GLOB2011I as it is possible to extrapolate toxicity from data available on active substance and co-formulants. The assessments have been conducted according to Regulation (EC) 1107/2009 (amended by Commission Regulation (EU) No 286/2011).

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Nevertheless, a GLP study was performed to obtain the registration in Brazil and is provided for the sake of completeness in addition to the calculation method.

Comments of zRMS: See above Appendix 2 – grey box.

A 2.7.1 Study 1

Reference	KCP 7.1.6
Report	LOCAL LYMPH NODE ASSAY (LLNA): BRDU-ELISA FOR SKIN SENSITIZATION BY GLOB2011I, [REDACTED], study # [REDACTED]
Guideline(s)	Yes – OECD 442B (2018)
Deviations	No
GLP	Yes
Acceptability	Yes/No/Supplementary
Duplication (if vertebrate study)	No – Study done for Brazil registration and provided for the sake of completeness in Europe. In Europe, classification by calculation can be done based on data available on the active substance and co-formulants.

Materials and methods

Test material (Lot/Batch No.)	GLOB2011I (Batch No. GLOB2011I03H18M21)
Species	Mices (<i>Mus musculus</i>) from lineage CBA/J
No. of animals (group size)	Pre-test: 8 mice (2 per group) Main test: 20 mice (4 per group)
Range finding	A pre-test was done with 8 mice
Exposure (concentration(s), no. of applications)	Negative control, positive control, 25, 50 and 100%.
Vehicle	acetone:olive oil (AOO 4:1 v/v)
Pretreatment prior to topical application	No
Reliability check	α -hexylcinamaldehyde 25% diluted in acetone:olive oil (4:1, v/v) (The dose should not cause excessive irritation and its response, in relation to the negative control, should produce an IS \geq 1.6)
Remarks	None

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Results and discussions

Table A 14: Results of skin sensitisation study of product GLOB2011I

	No. of animals	Concentration (%)	BrdU / group	Stimulation index (SI)
GLOB2011I	4	25	1.571 ± 0.390	1.399
	4	50	1.572 ± 0.286	1.400
	4	75	1.704 ± 0.252	1.518
Test vehicle control group	4	-	1.123 ± 0.270	-
Positive control	4	-	2.329 ± 0.531	2.074

Clinical signs:	Yes. On day 1, all animals at all doses were free of erythema; On day 3, 2 animals of 25% had no erythema and 2 animals of 25%, 3 animals of 50 and 100% had very slight erythema (only 1 animal of 50% had no erythema); and on day 6, all 25% animals, 3 50% animals and 2 100% animals had mild erythema and 1 50% animal and 2 100% animals had well-defined erythema.
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Conclusion

Under the experimental conditions, product GLOB2011I is not a skin sensitiser. Thus, no classification is required according to Regulation (EC) No. 1272/2008.

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

No new study was 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)

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No study has been provided for GLOB2011I as default dermal absorption mentioned in Guidance on Dermal Absorption (EFSA Journal 2012; 10(4):2665–2017;15(6):4873) were sufficient to assess the risk to operator, worker, resident and bystander.

A 2.11 Other/Special Studies

None.

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Appendix 3 Exposure calculations

Table A 15: Information on product and active substance

Product name	Sankari
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.
Product category	Other
Name of active substance	Pelargonic acid
Concentration of active substance [g a.s./l or kg]	650
AOEL [mg/kg bw/day]	821
AAOEL [mg/kg bw]	
Inhalation absorption [%]	100
Oral absorption [%]	100
Dermal absorption [%] (concentrate)	25
Dermal absorption [%] (dilution) NA [g a.s./l or kg]	70

Table A 16: Assessed uses

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Use	Crops	Max. application rate of the product [l or kg/ha]	Unit	Max. no. of applica- tions	Interval between multiple applica- tions [days]	Min. volume water [l/ha]	Max. volume water [l/ha]	In- door/out door	Applica- tion method	Type of cultiva- tion	Applica- tion tech- nique	Buffer strip [m]	Drift re- duction [%]
Use 11	Field crops	3	l/ha	2	14	200	600	Outdoor	Down- ward spraying	Normal	Vehicle- mounted	2-3	0

A 3.1 Operator exposure calculations (KCP 7.2.1.1)

Table A 17: Input parameters for pelargonic acid considered for the estimation of operator exposure

Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	Name of active sub- stance	Pelargonic acid
Concentration of active substance [g a.s./l or kg]	650	Crops	Field crops
Area treated [ha/day]	50	Application method	Downward spraying
Dermal absorption [%] (concentrate)	25	Application technique	Vehicle-mounted
Dermal absorption [%] (dilution)	70	Indoor/outdoor	Outdoor
Oral absorption [%]	100	Drift reduction [%]	0

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Inhalation absorption [%]	100	Type of cultivation	Normal
Body weight (kg)	60		
AOEL [mg/kg bw/day]	821		
AAOEL [mg/kg bw]			

Table A 18: Estimation of longer term operator exposure towards pelargonic acid according to EFSA guidance for use 11 (field crops – scenario 1: Outdoor, normal, downward spraying, vehicle-mounted)

Activity	Systemic exposure per body part	With work-wear	With workwear + PPE/RPE
Mixing and loading (µg/kg bw per day)	<i>Hand protection</i>	None	None
	Hands exposure	635	635
	<i>Body protection</i>	Workwear	Workwear
	Body exposure	3.6	3.6
	<i>Head protection</i>	None	None
	Head exposure	25.6	25.6
	<i>Inhalation protection</i>	None	None
	Inhalation exposure	0.3	0.3
Application (µg/kg bw per day)	<i>Hand protection</i>	None	None
	Hands exposure	168	168
	<i>Body protection</i>	Workwear	Workwear
	Body exposure	2.5	2.5
	<i>Head protection</i>	None	None

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Activity	Systemic exposure per body part	With work-wear	With workwear + PPE/RPE
	Head exposure	4.4	4.4
	<i>Inhalation protection</i>	None	None
	Inhalation exposure	0.2	0.2
Total	Total systemic exposure [mg/kg bw per day]	0.8	0.8
	% of AOEL	0.1	0.1

A 3.2 Worker exposure calculations (KCP 7.2.3.1)

Table A 19: Input parameters for pelargonic acid considered for the estimation of worker exposure

Indoor/outdoor	Outdoor	AOEL [mg/kg bw/day]	821
Re-entry activity	Inspection, irrigation	Dermal transfer coefficient - Total potential exposure [cm²/h]	12500
Crops	Field crops	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	Dermal transfer coefficient - Hands covered, no workwear [cm²/h]	

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Max. application rate of the product [l or kg/ha]	3	DFR refined worker [µg/cm² foliage per kg a.s./ha]	3
Max. no. of applications	2	DT50 foliar worker [days]	30
Interval between multiple applications [days]	14		
Multiple application factor	1.72		
Body weight (kg)	60		
Name of active substance	Pelargonic acid		
Dermal absorption [%] (dilution)	70		
Inhalation absorption [%]	100		
Time [hours per day]	2		

Table A 20: Estimation of longer term worker exposure towards pelargonic acid according to EFSA guidance for use 11 (field crops – scenario 1: outdoor, normal)

Exposure route	Description	Potential	Workwear	Workwear and gloves	Gloves
Dermal	Systemic dermal exposure [mg a.s. per day]	176	19.7	17.6	NA
Inhalation	Systemic inhalation exposure [mg a.s. per day]				NA

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Exposure route	Description	Poten- tial	Work- wear	Workwear and gloves	Gloves
Total	Total systemic exposure [mg a.s. per day]	176	19.7	17.6	NA
	Total systemic exposure [mg/kg bw per day]	2.9	0.3	0.3	NA
	% of AOEL	0.4	0.04	0.04	NA

A 3.3 Resident and bystander exposure calculations (KCP 7.2.2.1)

Table A 21: Input parameters and estimation of longer term resident exposure towards pelargonic acid according to EFSA guidance for use 11 (field crops – scenario 1: outdoor, season not relevant)

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AA- OEL
Season: Not relevant Buffer zone: 2-3 m Drift reduction technology: 0 % Interval between treatments: 14 days Minimum volume of water: 200 l			
Number of applications and application rate: 2 x 1.95 kg a.s./ha Dermal absorption: 70 % DFR: 3 µg/cm ² foliage per kg a.s./ha DT50: 30 days			
Pelargonic acid			
Bystander child Body weight: 10 kg	Drift (95th perc.)		0.4
	Vapour (95th perc.)		0
	Deposits (95th perc.)		0.1
	Re-entry (95th perc.)		0.4
	Drift (95th perc.)		0.1

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Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AA- OEL
Bystander adult Body weight: 60 kg	Vapour (95th perc.)	0	
	Deposits (95th perc.)	0.05	
	Re-entry (95th perc.)	0.2	

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)

No new study submitted.