

REGISTRATION REPORT

Part B

Section 6

Mammalian Toxicology

Detailed summary of the risk assessment

Product code: GLOB2112dH

Product name: Walkover Trio

Chemical active substances:

Thiencarbazone-methyl, 75 g/L

Mesotrione, 375 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Update February 2025

Applicant: Globachem NV

Submission date: September 2024

zRMS Assessment : 31/03/2025

Version after commenting: 03/07/2025

List of references update: 10/07/2025

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Version history

When	What
September 2024	Initial dossier submission by applicant for approval of new product.
February 2025	Update by applicant to include report generated by the EFSA AOEM.
March 2025	zRMS assessment
July 2025	zRMS – after commenting period
July 2025	List of references update

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6 Mammalian Toxicology (KCP 7)

6.1 Summary

Table 6.1-1: Information on GLOB2112dH *

Product name and code	GLOB2112dH/Walkover Trio
Formulation type	Suspension concentrate [SC]
Active substance(s) (incl. content)	Mesotrione; 375 g/L Thiencarbazone-methyl; 75 g/L
Function	Herbicide
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 GLOB2112dH 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 GLOB2112dH according to Regulation (EC) No 1272/2008

Hazard class(es), categories	Repr. 2, STOT RE2
Hazard pictograms or Code(s) for hazard pictogram(s)	GHS08
Signal word	Warning
Hazard statement(s)	H361d ₇ - Suspected of damaging the unborn child. H373 - May cause damage to organs (eyes, nervous system) through prolonged or repeated exposure.
Precautionary statement(s)	P201 ₇ - Obtain special instructions before use. P202 ₇ - Do not handle until all safety precautions have been read and understood. P260 ₇ - Do not breathe spray. P284 ₀ - Wear protective gloves, protective clothing, eye protection or face protection. P308+P313 ₇ - IF exposed or concerned: Get medical advice/attention. P314 ₇ - Get medical advice/attention if you feel unwell. P405 ₇ - Store locked up. P501 - Dispose of contents/container to...
Additional labelling phrases	To avoid risks to man and the environment, comply with the instructions for use. [EUH401]
	Contains 1,2-benzisothiazol-3(2H)-one (CAS No. 2634-33-5); 2-methyl 4-isothiazolin 3-one (CAS No. 2682-20-14) and a mixture of 5-chloro 2-methylisothiazol-3(2H)-one and 2-methylisothiazol-3(2H)-one (CAS No. 55965-84-9). May produce an allergic reaction. [EUH208]

Table 6.1-3: Summary of risk assessment for operators, workers, residents and bystanders for GLOB2112dH

	Result	PPE / Risk mitigation measures
Operators	Acceptable	Gloves during mixing/loading (resulting from exposure assessment), Workwear, gloves and protective goggles or face protection during mixing/loading due to the fact that the product is classified as Repr. 2 H361d and STOT RE2 H373 (eyes, nervous system)
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 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) mesotrione b) thiencarba- zone-methyl	Water L/ha min / max			Operator	Worker	Residents	Bystander
1, 3	Maize (BBCH 10-18)	F	Spraying, LCTM	1 ; 1	a) 0.075 b) 0.015	100-300	NA	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 2022;20(1):7032				

* 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 substances

	Mesotrione	Thien carbazone-methyl
Common Name	Mesotrione	Thien carbazone-methyl

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	Mesotrione	Thiencarbazone-methyl
CAS-No.	104206-82-8	317815-83-1
Classification and proposed labelling		
With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended)	Hazard classes (s), categories: Repr 2, STOT RE2 Code(s) for hazard pictogram(s): GHS08 Signal word: Warning Hazard statement(s): H361d, H373 Precautionary statement(s): P201, P202, P308 + P313, P405, P501, P260, P314	Hazard classes (s), categories: none Code(s) for hazard pictogram(s): none Signal word: none Hazard statement(s): none Precautionary statement(s): none
Additional C&L proposal	None	None
Agreed EU endpoints		
AOEL systemic	0.005 mg/kg bw/d (corrected for 50 % oral absorption)	0.12 mg/kg bw/d (corrected for 50% oral absorption)
Reference	EFSA Scientific Report Journal (2016); 14 (3):4419	EFSA Conclusion (EFSA, 2013) EFSA Journal 2013;11(7):3270
Conditions to take into account/critical areas of concern with regard to toxicology		
According to Review Report/EFSA Conclusion	None	None

6.3 Toxicological Evaluation of Plant Protection Product

A summary of the toxicological evaluation for GLOB2112dH 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.

The plant protection product GLOB2112dH is a mixture containing two active substances. The combined toxicological effect of these active substances has not been investigated with regard to repeated dose toxicity. Therefore, combined toxicity with dose additivity is assumed as worst case. Reference is made to point 6.6.5 for the calculation of the combined exposure whereby as a worst case approach, combined exposure is calculated as the sum of the component exposures without regard to the mode of action or mechanism/target of toxicity. 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. The Hazard Index (HI) is the sum of the individual HQs.

Comments of zRMS:	GLOB2112dH/Walkover Trio was not a representative formulation reviewed during the Annex I inclusion/active substances renewal and was not previously evaluated in any EU countries. For the product registration no experimental acute toxicity data are available. An assessment of acute toxicity including irritancy and skin sensitisation properties of GLOB2112dH/Walkover Trio has been conducted by the applicant based on the alternative method (calculation) according to the Regulation (EC) 1272/2008. Classification of all relevant ingredients were considered by the applicant. zRMS noted that outcome of calculation for eye irritation is close to the concentration limit but still below 10%. For reprotoxicity and specific target organ toxicity the alternative method (calculation) according to the Regulation (EC) 1272/2008 was applied. Details of the calculation can be found in Part C.
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	In order to avoid tests on animals, the use of alternative method for the purposes of hazard classification is preferred. GLOB2112dH/Walkover Trio contains safener, but currently, according to the approach agreed in Poland, safeners are evaluated the same way as co-formulants. Proposed classification based on alternative method according to Regulation (EC) 1272/2008 is acceptable by the zRMS.
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Table 6.3-1: Summary of evaluation of the studies on acute toxicity including irritancy and skin sensitisation for GLOB2112dH

Type of test, species, model system (Guideline)	Result	Acceptability	Classification (acc. to the criteria in Reg. 1272/2008)	Reference
LD ₅₀ oral,	Study not necessary.	Yes /No/ Supplementary	None	Calculation method (Part C)
LD ₅₀ dermal	Study not necessary.	Yes /No/ Supplementary	None	Calculation method (Part C)
LC ₅₀ inhalation	Study not necessary.	Yes /No/ Supplementary	None	Calculation method (Part C)
Skin irritation	Study not necessary.	Yes /No/ Supplementary	None	Calculation method (Part C)
Eye irritation	Study not necessary.	Yes /No/ Supplementary	None	Calculation method (Part C)
Skin sensitisation	Study not necessary.	Yes /No/ Supplementary	None	Calculation method (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 GLOB2112dH

	Substance (concentration in product, % w/w)	Classification of the substance (acc. to the criteria in Reg. 1272/2008)	Reference	Classification and labelling of product (acc. to the criteria in Reg. 1272/2008)
Toxicological properties of active substance(s) (relevant for classification of product)	Thiencarbazone-methyl (6.17% (w/w))	None	Reg. 1272/2008 / MSDS**	None
	Mesotrione (30.86% (w/w))	Repr. 2, H361d (≥ 3%)	Commission Delegated Regulation (EU) 2020/1182 amending Reg.	Repr. 2, H361d
		STOT RE2, H373 (≥ 10%)		STOT RE2, H373

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	Substance (concentration in product, % w/w)	Classification of the substance (acc. to the criteria in Reg. 1272/2008)	Reference	Classification and label- ling of product (acc. to the criteria in Reg. 1272/2008)
			1272/2008	
Toxicological properties of safener (relevant for classification of product)	Cyprosulfamide (9.22% (w/w))	None	Reg. 1272/2008 / MSDS**	None
Toxicological properties of non- active substance(s) (relevant for classification of product)	-1,2- benzisothiazol- 3(2H)-one (<0.036%)	- Skin Sens. 1A, H317 (SCL ≥0.036%)	-	- EUH208
Further toxicological information	No data – not required			

* 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 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 BYH 18636-carboxylic acid

An overview of the results of the accepted toxicological studies for groundwater metabolite BYH 18636-carboxylic acid 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 BYH 18636-carboxylic acid

Type of test, species (Guideline)	Result	Acceptability	Reference*
In vitro genotoxicity – Bacterial assay for gene mutation (OECD 471)	Non-mutagenic with or without S9 mix	Yes / No / Supplementary	Wirnitzer U., 2004*
In vitro genotoxicity – Test for clastogenicity in mammalian cells (OECD 473)	Not clastogenic for mammalian cells <i>in vitro</i>	Yes / No / Supplementary	Herbold B., 2005*
In vitro genotoxicity – Test for gene mutation in mammalian cells (OECD 476)	Non-mutagenic in the V79/HPRT forward mutation assay, both with and without metabolic activation	Yes / No / Supplementary	Herbold B., 2005*
Acute oral toxicity in the rat	LD ₅₀ > 2000 mg/kg bw	Yes / No / Supplementary	Anonymous, 2006*

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Type of test, species (Guideline)	Result	Acceptability	Reference*
90-day toxicity study in the rat (OECD 408)	The NOEL = 972 and 1170 mg/kg/day in males and females respectively	Yes / No / Supplementary	Anonymous, 2007*

* indicates that a study was reviewed at EU level

Metabolite BYH 18636-carboxylic acid has already been assessed for groundwater relevance as part of the EU review for Annex I inclusion of the active substance thien carbazone-methyl, and was considered to be non-relevant. Detailed data and assessments are found in the EU DAR (2012) of thien carbazone-methyl, and the corresponding EFSA peer review conclusion (EFSA Journal 2013; 11(7):3270). All toxicological studies on this metabolite have previously been considered within an EU peer review process. No studies are therefore summarised in detail in Appendix 2.

6.5 Dermal Absorption (KCP 7.3)

Comments by zRMS:	<p>Dermal absorption assessment provided by the applicant is based on the current version of EFSA Guidance document on dermal absorption (2017) and is acceptable. Data from in-vitro absorption study on dilution of formulation identical to GLOB2112dH/Walkover were provided for dermal absorption value for mesotrione from dilution. The target concentration was approximately 0.16 g/L, representing a 2310-fold dilution of the concentrate SC formulation (<i>i.e.</i> 0.13 L product in 300 L water). The highest in-use dilution suggested for extended use on the label of GLOB2112dH/Walkover is 1:2310 (0.13 L of product, 375 g of mesotrione in 300 L of water). The study is acceptable for evaluation of dermal absorption of mesotrione from in-use dilution of GLOB2112dH/Walkover. No pro rata correction is needed.</p> <p>Default dermal absorption values for products that are water-based/dispersed are acceptable for mesotrione in concentrate and for thien carbazone-methyl in concentrate and dilution of GLOB2112dH/Walkover.</p>
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A summary of the dermal absorption rates for the active substances in GLOB2112dH are presented in the following table.

Table 6.5-1: Dermal absorption rates for active substances in GLOB2112dH

	Mesotrione		Thien carbazone-methyl	
	Value	Reference	Value	Reference
Concentrate	10%	Default value EFSA Journal 2017;15(6):4873	10%	Default value EFSA Journal 2017;15(6):4873
Dilution (1:2310)	0.28 %	New study reported in Appendix 2	50%	Default value EFSA Journal 2017;15(6):4873

6.5.1 Justification for proposed values – mesotrione

Proposed dermal absorption rate for concentrate product containing mesotrione is the default value in line

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with the current EFSA Guidance document on dermal absorption (EFSA Journal 2017; 15(6):4873). Proposed dermal absorption rates for dilution of product containing mesotrione are based on dermal absorption studies on a formulation identical to GLOB2112dH. The study results are summarized in the following table. Full summaries of studies on the dermal absorption of mesotrione/GLOB2112dH that have not previously been evaluated within an EU peer review process are described in detail in Appendix 2.

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

Test	Concentrate	Spray dilution (1:2310)	Formulation in study	Acceptability of study	Justification provided on representativity of study formulation for current product	Acceptability of justification	Reference*
In vitro (human)	10% (default value)	0.28 %	GLOB2112dH	Acceptable Yes / No / Supplementary	Not required	Not required Justification accepted. Endpoint can be used for current product / Justification not accepted. Endpoint cannot be used for current product.	Spa S., 2023

* indicates that a study was reviewed at EU level

Table 6.5-3: Default dermal absorption rates for mesotrione

	Value	Justification for value	Acceptability of justification
Concentrate	10%	Default value	Acceptable

6.5.2 Justification for proposed values – thienencarbazone-methyl

No data on dermal absorption for thienencarbazone-methyl in GLOB2112dH 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 6.5-34: Default dermal absorption rates for thienencarbazone-methyl

	Value	Justification for value	Acceptability of justification
Concentrate	10%	Default value	Acceptable
Dilution	50%	Default value	Acceptable

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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	GLOB2112dH/Walkover Trio	
Formulation type	SC	
Category	Herbicide	
Container size(s), short description	0.1-20 L, HDPE; HDPE-F; HDPE/PA; HDPE-EVOH, 39-63 mm opening	
Active substance(s) (incl. content)	Mesotrione 375 g/L	Thiencarbazone-methyl 75 g/L
AOEL systemic	0.005 mg/kg bw/d	0.12 mg/kg bw/d
Inhalation absorption	100 %	100%
Oral absorption	70 %	50%
Dermal absorption	Concentrate: 10 % (Default) Dilution: 0.28 % (Dilution rate: 1:2310) (Based on product GLOB2112dH)	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 highest application rate was selected as critical GAP.

6.6.2 Operator exposure (KCP 7.2.1)

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 GLOB2112dH 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)	Maize (max. 0.2 L product/ha)
Model(s)	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2022;20(1):7032 calculator version: 1.0.2

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

		Mesotrione		Thiencarbazone-methyl	
Model data	Level of PPE	Total absorbed dose (mg/kg/day)	% of systemic AOEL	Total absorbed dose (mg/kg/day)	% of systemic AOEL
Tractor mounted boom spray application outdoors to low crops					
Application rate		0.075 kg a.s./ha		0.015 kg a.s./ha	
Spray application (AOEM; 75 th percentile) Body weight: 60 kg	Work wear (arms, body and legs covered) M/L and A	0.03	646	0.01	10.4
	Work wear (arms, body and legs covered) M/L and A + gloves M/L	0.0009	18.4	0.001	1.1

6.6.2.2 Measurement of operator exposure

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

Comments of zRMS study comment 6.6.2	The applicant presented calculations for operator exposure during application of GLOB2112dH/Walkover on maize: max. 1x 0.2 L product/ha using the tractor-mounted (field). The exposure calculations were conducted by the applicant using the EFSA online calculator OPEX v 1.0.2. The calculations provided by the applicant were done correctly.
agreed endpoints 6.6.2	According to EFSA OPEX calculations, it can be concluded that the risk of operator exposure during mixing & loading and application of GLOB2112dH/Walkover using the tractor-mounted on field is acceptable under conditions of intended use when workwear (arms, body and legs covered) and protective gloves are worn during mixing, loading and workwear is worn during application. Due to the fact that the product is classified as Repr. 2 H361d and STOT RE2 H373 (eyes, nervous system) the operator should wear workwear, gloves and protective goggles or face protection during mixing/loading.

6.6.3 Worker exposure (KCP 7.2.3)

6.6.3.1 Estimation of worker exposure

Table 6.6-4 shows the exposure model(s) used for estimation of worker exposure after entry into a previously treated area or handling a crop treated with GLOB2112dH according to the critical use(s). Outcome

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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)	Maize (max. 1 x 0.2 L product/ha)
Model	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2022;20(1):7032 calculator version: 1.0.2

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

		Mesotrione		Thiencarbazone-methyl	
Model data	Level of PPE	Total absorbed dose (mg/kg bw/day)	% of systemic AOEL	Total absorbed dose (mg/kg bw/day)	% of systemic AOEL
Inspection, irrigation Outdoor Work rate: 2 hours/day, DT ₅₀ : 30 days DFR: 3 µg/cm ² /kg a.s./ha Interval between treatments: 365 days					
Number of applications and application rate		1 x 0.075 kg a.s./ha		1 x 0.015 kg a.s./ha	
Body weight: 60 kg	Potential TC: 12500 cm ² /person/h	0.009	188	0.009	7.8
	Work wear (arms, body and legs covered) TC: 1400 cm ² /person/h	0.001	21	0.001	0.9

6.6.3.2 Refinement of generic DFR value (KCP 7.2)

Not required.

6.6.3.3 Measurement of worker exposure

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

Comments of zRMS study comment 6.6.3	<p>The applicant presented calculations for worker exposure after application of GLOB2112dH/Walkover on maize: : max. 1x 0.2 L product/ha using the tractor-mounted (field).</p> <p>The exposure calculations were conducted by the applicant using the EFSA online calculator OPEX v 1.0.2. The calculations provided by the applicant were done correctly.</p>
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agreed endpoints 6.6.3	According to EFSA OPEX calculations, it can be concluded that the risk of worker exposure to GLOB2112dH/Walkover is acceptable under conditions of intended use when workwear (arms, body and legs covered) is worn. As a standard rule, it should be mentioned on the label that treated crops should not be re-entered before spray deposits on leaf surfaces have completely dried.
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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 6.6-6 shows the exposure model(s) used for estimation of resident and bystander exposure to mesotrione and thiencazuron-methyl. 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)	Maize (max. 1 x 0.2 L product/ha)
Model	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2022;20(1):7032 calculator version: 1.0.2

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

		Mesotrione		Thiencazuron-methyl	
Model data		Total absorbed dose (mg/kg bw/day)	% of systemic AOEL	Total absorbed dose (mg/kg bw/day)	% of systemic AOEL
Tractor 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: 365 days					
Number of applications and application rate		1 x 0.075 kg a.s./ha		1 x 0.015 kg a.s./ha	
Resident child	Drift (75 th perc.)	0.00007	1.4	0.002	1.7
	Vapour (75 th perc.)	0.0006	12.7	0.0000000001	0.000000009

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Body weight: 10 kg	Deposits (75 th perc.)	0.0002	3	0.0001	0.1
	Re-entry (75 th perc.)	0.001	25.3	0.001	1.1
	Sum (mean)	0.002	35.9	0.002	1.8
Resident adult Body weight: 60 kg	Drift (75 th perc.)	0.00001	0.3	0.0005	0.4
	Vapour (75 th perc.)	0.0002	4.3	0.000000000004	0.000000003
	Deposits (75 th perc.)	0.00005	1	0.00005	0.04
	Re-entry (75 th perc.)	0.0007	14.1	0.0007	0.6
	Sum (mean)	0.0008	16.4	0.0008	0.7

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 mesotrione and thien carbazonemethyl 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.

Comments of zRMS study comment 6.6.4	The applicant presented calculations for resident exposure after application of GLOB2112dH/Walkover on maize: : max. 1x 0.2 L product/ha using the tractor-mounted (field). The exposure calculations were conducted by the applicant using the EFSA online calculator OPEX v 1.0.2. The calculations provided by the applicant were done correctly.
agreed endpoints 6.6.4	The exposure assessment for residents also covers bystander exposure. According to calculations, it can be concluded that there is no unacceptable risk to any resident (child and adult) and bystander after application of GLOB2112dH/Walkover.

6.6.5 Combined exposure

The product is a mixture of two active substances.

6.6.5.1 Exposure assessment of mesotrione and thien carbazonemethyl in GLOB2112dH

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

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

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Table 6.6-8: Risk assessment from combined exposure (longer term exposure)

Application scenario	Active ingredient	Estimated exposure / AOEL (HQ)
Operators – Tractor mounted boom spray application outdoors to low crops – gloves during M/L	Mesotrione	0.184
	Thiencarbazone-methyl	0.011
	Cumulative risk operators (HI)	0.2
Workers – inspection, irrigation	Mesotrione	0.21
	Thiencarbazone-methyl	0.009
	Cumulative risk workers (HI)	0.2
Resident - child	Mesotrione	
	Drift	0.014
	Vapour	0.127
	Deposits	0.03
	Re-entry	0.253
	Sum of all pathways	0.359
	Thiencarbazone-methyl	
	Drift	0.017
	Vapour	0.00000000009
	Deposits	0.001
	Re-entry	0.011
	Sum of all pathways	0.018
	Cumulative risk resident – child (HI)	
	Drift	0.03
	Vapour	0.1
	Deposits	0.03
	Re-entry	0.3
	Sum of all pathways	0.4
Resident - adult	Mesotrione	
	Drift	0.003
	Vapour	0.043
	Deposits	0.01
	Re-entry	0.141
	Sum of all pathways	0.164
	Thiencarbazone-methyl	
	Drift	0.004
	Vapour	0.00000000003
	Deposits	0.0004

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Application scenario	Active ingredient	Estimated exposure / AOEL (HQ)
	Re-entry	0.006
	Sum of all pathways	0.007
	Cumulative risk resident – adult (HI)	
	Drift	0.007
	Vapour	0.04
	Deposits	0.01
	Re-entry	0.1
	Sum of all pathways	0.2

The Hazard Index is < 1. Thus, combined exposure to all active substances in GLOB2112dH is not expected to present a risk for operators, workers, residents and bystanders. No further refinement of the assessment is required.

Comments of zRMS Study comment 6.6.5	The applicant presented the first tier, combined exposure calculation as the sum of the component exposures. The individual Hazard Quotients (HQ) were calculated and the Hazard Index (HI) as the sum of the individual HQs. The calculations were conducted by the applicant for operators, workers and residents using the EFSA online calculator OPEX v 1.0.2. The calculations provided by the applicant were done correctly.
zRMS agreed endpoints 6.6.5	According to EFSA OPEX calculations of combined exposure it can be concluded that the risk of operator exposure during mixing & loading is acceptable under conditions of intended use when the workwear and gloves are worn. Risk of operator exposure during application is acceptable under conditions of intended use when the workwear is worn. Due to the fact that GLOB2112dH/Walkover is classified as Repr. 2 H361d and STOT RE2 H373 (eyes, nervous system) the operator should wear workwear, gloves and protective goggles or face protection during mixing/loading. As regards risk of worker exposure during re-entry activities on area treated with GLOB2112dH/Walkover, according to EFSA OPEX calculations, it can be concluded that risk is acceptable under conditions of intended use when the workwear (long sleeved shirt, long trousers) is worn. As a standard rule, it should be mentioned on the label that treated crops should not be re-entered before spray deposits on leaf surfaces have completely dried. The exposure assessment for residents also covers bystander exposure. According to calculations, it can be concluded that there is no unacceptable risk to any resident (child and adult) and bystander after application of GLOB2112dH/Walkover.

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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 7.3	Spa S.	2023	The in vitro percutaneous absorption of radiolabelled mesotrione from an in-use dilution of GLOB2112dH through human split-thickness skin 20444571 Charles River Laboratories Den Bosch BV GLP Unpublished	N	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
KCA 5.8	Wirmitzer U.	2006	BYH 18636-carboxylic acid (project: BYH 18636) - Salmonella/microsome test - Plate incorporation and preincubation method - 1st amendment to toxicology report AT01522 of September 22, 2004 AT01522A GLP Unpublished	N	Bayer CropScience <i>Data out of protection</i>
KCA 5.8	Herbold B.	2005	BYH 18636-carboxylic acid (Project: BYH 18636) - In vitro chromosome aberration test with chinese hamster V79 cells M-250256-02-2 GLP Unpublished	N	Bayer CropScience <i>Data out of protection</i>
KCA 5.8	Herbold B.	2005	BYH 18636-carboxylic acid (Project: BYH 18636) - V79/HPRT-test in vitro for the detection of induced forward mutations AT02038 GLP Unpublished	N	Bayer CropScience <i>Data out of protection</i>
KCA 5.8	Anonymous	2006	BYH 18636-carboxylic acid (AE 1394083) - Acute toxicity in the rat after oral administration [REDACTED] GLP Unpublished	Y	Bayer CropScience <i>Data out of protection</i>
KCA 5.8	Anonymous	2007	BYH 18636-carboxylic acid - 90-day toxicity study in the rat by dietary administration [REDACTED] GLP Unpublished	Y	Bayer CropScience <i>Data out of protection</i>

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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 XX	Author	YYYY	Title Company Report N Source GLP/non GLP/GEP/non GEP Published/Unpublished	Y/N	Owner

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

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

Appendix 2 Detailed evaluation of the studies relied upon

Comments of zRMS:	<p>GLOB2112dH/Walkover Trio was not a representative formulation reviewed during the Annex I inclusion/active substances renewal and was not previously evaluated in any EU countries. For the product registration no experimental acute toxicity data are available. An assessment of acute toxicity including irritancy and skin sensitisation properties of GLOB2112dH/Walkover Trio has been conducted by the applicant based on the alternative method (calculation) according to the Regulation (EC) 1272/2008. Classification of all relevant ingredients were considered by the applicant. For reprotoxicity and specific target organ toxicity the alternative method (calculation) according to the Regulation (EC) 1272/2008 was applied. Details of the calculation can be found in Part C.</p> <p>In order to avoid tests on animals, the use of alternative method for the purposes of hazard classification is preferred.</p> <p>GLOB2112dH/Walkover Trio contains safener, but currently, according to the approach agreed in Poland, safeners are evaluated the same way as co-formulants. Proposed classification based on alternative method according to Regulation (EC) 1272/2008 is acceptable by the zRMS.</p>
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A 2.1 Statement on bridging possibilities

Not necessary.

Comments of zRMS:	Comment on statement; acceptable or not not relevant
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A 2.2 Acute oral toxicity (KCP 7.1.1)

No tests were performed on GLOB2112dH in the interest of animal welfare. The assessments have been conducted according to Regulation (EC) 1107/2009 (amended by Commission Regulation (EU) No 286/2011).

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

No tests were performed on GLOB2112dH in the interest of animal welfare. The assessments have been conducted according to Regulation (EC) 1107/2009 (amended by Commission Regulation (EU) No 286/2011).

A 2.4 Acute inhalation toxicity (KCP 7.1.3)

No tests were performed on GLOB2112dH in the interest of animal welfare. The assessments have been conducted according to Regulation (EC) 1107/2009 (amended by Commission Regulation (EU) No 286/2011).

A 2.5 Skin irritation (KCP 7.1.4)

No tests were performed on GLOB2112dH in the interest of animal welfare. The assessments have been conducted according to Regulation (EC) 1107/2009 (amended by Commission Regulation (EU) No 286/2011).

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A 2.6 Eye irritation (KCP 7.1.5)

No tests were performed on GLOB2112dH in the interest of animal welfare. The assessments have been conducted according to Regulation (EC) 1107/2009 (amended by Commission Regulation (EU) No 286/2011).

A 2.7 Skin sensitisation (KCP 7.1.6)

No tests were performed on GLOB2112dH in the interest of animal welfare. The assessments have been conducted according to Regulation (EC) 1107/2009 (amended by Commission Regulation (EU) No 286/2011).

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

Not required.

A 2.9 Data on co-formulants (KCP 7.4)

A 2.9.1 Material safety data sheet for each co-formulant

Information regarding material safety data sheets of the co-formulants can be found in the confidential dossier of this submission (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)

A 2.10.1 Study 1 – Mesotrione in GLOB2112dH

Comments of zRMS:	Study 1 was performed according to OECD 428 and was GLP compliant. The study is acceptable. Dermal absorption assessment for mesotrione provided by the applicant is based on the current version of EFSA guidance document on dermal absorption (2017) and Excel template recommended in EFSA guidance and is acceptable.
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Reference	KCP 7.3
Report	The in vitro percutaneous absorption of radiolabelled mesotrione from an in-use dilution of GLOB2112dH through human split-thickness skin, Spa S., 2023, 20444571
Guideline(s)	Yes, OECD 428

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Deviations No
 GLP Yes
 Acceptability Yes/No/Supplementary
 Duplication /
 (if vertebrate study)

Materials and methods

Test material	Name (Lot/Batch No.)	Mesotrione (XXIII/38/E/3)
	Test preparation	radioformulation
	Specific activity	4.035 MBq/mg
	Radiochemical purity	98.86%
Product	Name (Lot/Batch No.)	-
	Company code	-
	Concentration a.s.	-
	Formulation type	-
Blank product	Name (Lot/Batch No.)	GLOB2112dH semi-blank (MAM 107689)
	Concentration a.s.	0 g/L mesotrione, 75 g/L thiencarbazone-methyl, 112 g/L cyprosulfamide

Test system		
Diffusion cell	Cell type	dynamic
	(if dynamic) Flow rate	1.5 ml/h
	Exposed skin area	0.64 cm ²
	Cover	open
Membrane	Skin type	dermatomed
	Skin thickness range	200-400 µm
	Skin donors age	27-54
	Skin donors sex	f
	Location	abdomen / breast
	Source	ex vivo
	Integrity test	yes
Receptor	Receptor medium	Phosphate buffered saline (PBS) containing polyoxyethylene 20 oleyl ether (PEG; 6%, w/v), sodium azide (0.01%, w/v), streptomycin (0.1 mg/mL) and penicillin G (100 units/mL) with the pH adjusted to 7.4
	Solubility in receptor medium	y
Sample Time	Exposure time	8
	Observation time	24
Sampling	Sample intervals	hourly fractions from 0 to 2 h post dose, followed by 2-hourly fractions until 24 h post-dose
Washing		post exposure
Final Procedure	Tape stripping	y
	TS1-2 analysed separately	y
Remarks: -		

Tested doses	Spray dilution 1
Target concentration [mg/ml]	0.16
Area dose [µg/cm ²]	1.6
Total dose [µg/cell]	1.0

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Specific activity [kBq/ml]	62.3
No. of donors	4
No of cells used/valid cells*	8/8

* Justification for excluded cells, if applicable

Results and discussions

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

Dose group	Low dose (Spray dilution 1:2310)	
	Mean	S.D.
Target concentration [mg/mL]	0.16	
Target dose [$\mu\text{g}/\text{cm}^2$]	1.6	
Mean actual applied dose [$\mu\text{g}/\text{cm}^2$]	1.59	
	Recovery [%]	
	Mean	S.D.
Dislodgeable dose		
Skin washing after 8 h	97.63	3.78
Donor chamber wash	0.09	0.03
Dose associated to skin		
Tape strips: 1 st sample, strips 1 + 2	0.09	0.08
Tape strips: 2 nd sample; strips 3 - n	0.27	0.21
Skin preparation	0.09	0.05
Absorbed dose		
Receptor fluid	0.12	0.04
Receptor chamber wash	0.01	0.00
Total recovery¹	98.29	3.92
Absorption essentially complete at end of study (>75% absorption within half the study duration) [%Absorption at $t_{0.5}$]	Yes [76.66% \pm 4.12]	
If no: Absorption estimates = absorbed dose + skin preparation + tape strips sample 2) ²	-	-
If yes: Absorption estimates = absorbed dose + skin preparation	0.22	0.07
Absorption estimate normalised ³	0.22	
Relevant absorption estimate ⁴	0.279	
Absorption estimates used for risk assessment⁵	0.28	

¹ Values may not calculate exactly due to rounding of figures

² In accordance with the EFSA Guidance on Dermal Absorption (EFSA Journal 2017; 15(6):4873) the radioactivity in the second tape-strip pool (3rd to nth tape strip) is considered potentially absorbable if less than 75% of the

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absorption occurred in the first half of the study (see Table 7.6.2-1) Finally, the skin preparation is also considered potentially absorbable.

- ³ According to the EFSA Guidance on Dermal Absorption, cells with insufficient recovery (< 95%) can be corrected by normalisation of absorption estimate to 100% recovery; explanation should be included.
- ⁴ In accordance with the EFSA Guidance on Dermal Absorption, the standard deviation corrected for the number of replicates was added to the mean% dermal penetration.
- ⁵ Relevant absorption estimate was rounded to the required number of significant figures.

N/A: not applicable

Remarks

Justification for excluded cells / normalisation, if applicable

Conclusion/endpoint:

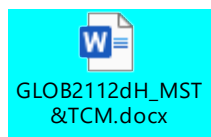
The dermal penetration of mesotrione formulated as GLOB2112dH through human dermatomed skin was determined in vitro. The amount of applied dose penetrating within 24 hours was determined to be 0.22 ± 0.07 (mean \pm standard deviation) for the 1:2310 spray dilution, respectively. The dermal penetration estimates to be used for risk assessment were set at 0.28% for the 1:2310 spray dilution based on the EFSA guidance criteria.

A 2.11 Other/Special Studies

No studies submitted.

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Appendix 3 Exposure calculations



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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 studies submitted.