FINAL REGISTRATION REPORT

Part B

Section 6

Mammalian Toxicology

Detailed summary of the risk assessment

Product code: GLOB289H / SAP63H

Product name(s): Zeppos

Chemical active substances:

Iodosulfuron-methyl-sodium, 6 g/kg
Mesosulfuron-methyl, 30 g/kg

Safener: Mefenpyr-diethyl, 90 g/kg

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: Globachem N.V. / Ascenza Agro S.A.

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08/ 2021	Assessment by expert
08/2021	Updated by Applicant
01/2022	Final version of the RR after Commenting period
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6 Mammalian Toxicology (KCP 7)

This document summarises the information related to the analytical methods for the plant protection product Iodosulfuron-methyl-sodium + Mesosulfuron-methyl + Mefenpyr-diethyl (0.6+3+9)%WG (also referred to as SAP63H, GLOB289H, Iodosulfuron + Mesosulfuron (0.6% + 3%) WG and Zeppos in this dossier). The product contains two active substances iodosulfuron-methyl-sodium and mesosulfuron-methyl-sodium, and safener mefenpyr-diethyl.
The product can be mixed in the tank with a non-ionic surfactant or a non-esterified rapeseed oil. In order to address the effect on operator, worker, bystander and resident, the combination of the plant protection product with a non-ionic surfactant (Pottok) was also considered in the risk assessment. Acute toxicity studies for Pottok are available and summarised in this document. No studies were done on Actirob. This adjuvant is on the market already for many years. The product is not classified and no endpoints are identified. A risk assessment is therefore not considered necessary.

A full risk assessment according to uniform principles is provided, which demonstrates that the product is safe for the environment.

Where appropriate, this document refers to the conclusions of the EU reviews of the active substances. This will be where:

- The active substance data is relied upon in the risk assessment of the formulation; or
- The EU review concluded that additional data/information should be considered at national registration.

Note: This Part B document only reviews data (Annex II and/or Annex III) and additional information that has not previously been considered within the EU review process, as part of the Annex I inclusion decision. New Annex II or Annex III data were included if they are considered essential for the evaluation and in this case a full study summary is provided. In the case where studies have been previously evaluated at European level, detailed summaries have not been provided.

The product Iodosulfuron-methyl-sodium + Mesosulfuron-methyl + Mefenpyr-diethyl (0.6% + 3% + 9%) WG was not the representative formulation during the Annex I inclusion of Iodosulfuron-methyl-sodium or Mesosulfuron-methyl and has thus not yet been evaluated.

Iodosulfuron-methyl-sodium
Iodosulfuron-methyl-sodium was included into Annex I of Directive 91/414/EEC in 2003 (Directive 2003/84/EC) and re-evaluated in accordance with Regulation (EC) No 1107/2009 and Commission Implementing Regulation (EU) No 844/2012, leading to the renewal of the approval of the active substance iodosulfuron-methyl-sodium (Commission Implementing Regulation (EU) 2017/407 of 8 March 2017, entry into force 1st of April 2017).

For the implementation of the Uniform Principles of Annex VI, the conclusions of the Renewal Report on iodosulfuron-methyl-sodium, as finalised in the Standing Committee on Plants, Animals, Food and Feed at its meeting on 7 December 2016 shall be taken into account.

In this overall assessment Member States should pay attention to:

- The protection of consumers,
- The protection of non-target terrestrial plants,
- The protection of aquatic plants

The Renewal Report (SANTE/2016/11167 Rev 3, 7/12/2016) for iodosulfuron-methyl-sodium provides a summary of the relevant scientific information from the EU review.

Mesosulfuron-methyl
Mesosulfuron-methyl was included in Annex I of Directive 91/414/EEC in 2003 (Directive 2003/119/EEC) and re-evaluated in accordance with Regulation (EC) No 1107/2009 and Commission Implementing Regulation (EU) No 844/2012, leading to the renewal of the approval of the active substance mesosulfuron-methyl (Commission Implementing Regulation (EU) 2017/755 of 28 April 2017,

entry into force 1st of July 2017).

For the implementation of the Uniform Principles of Annex VI, the conclusions of the Renewal Report on mesosulfuron-methyl, as finalised in the Standing Committee on Plants, Animals, Food and Feed at is meeting on 23 March 2017 shall be taken into account.

In this overall assessment Member States should pay attention to:

- The protection of aquatic organisms and non-target terrestrial plants;
- The protection of groundwater

The Renewal Report (SANTE/11827/2016 Rev 2, 23/03/2017) for mesosulfuron-methyl provides a summary of the relevant scientific information from the EU review.

Safener mefenpyr-diethyl
Mefenpyr-diethyl is a safener used in combination with herbicides and was not reviewed under Directive 91/414/EEC or Regulation (EC) No 1107/2009. In order to facilitate the assessment of products containing mefenpyr-diethyl, France and Austria in a work-sharing project prepared an assessment report for this substance in the format of a DAR. France was responsible for the sections "Phys-Chem Properties" (B.1-B.5), Environmental Fate and Ecotoxicology (B.8-B.9) and Austria for sections Toxicology and Residue Data (B.6-B.7). A bilateral peer-review in the form of comments took place between the two rapporteurs; the respective reporting tables were made available to all MS. In September 2011 the assessment report was "peer-reviewed" (in an unscheduled procedure on voluntary basis) by all MS. The revised assessment report can be found on CIRCA (Archive individual substances – Mefenpyr-diethyl (safener)).
All exposure and risk assessments presented will be based on agreed endpoints, if not otherwise stated.

6.1 Summary

Table 6.1-1: Information on GLOB289H *

Product name and code	GLOB289H	POTTOK
Formulation type	Water-dispersable granule (WG)	-
Active substance(s) (incl. content)	Iodosulfuron-methyl sodium: 6 g/kg Mesosulfuron-methyl: 30 g/kg Mefenpyr-diethyl: 90 g/kg	Effective adjuvant component of POTTOK, is fatty alcohol alkoxylate. Fatty alcohol alkoxylate: 985.2 g/kg**
Function	Herbicide	Tank Mix Adjuvant
Product already evaluated as the 'representative formulation' during the approval of the active substance(s)	No	No
Product previously evaluated in another MS according to Uniform Principles	No	No

* Information on the detailed composition of GLOB289H can be found in the confidential dRR Part C.
** Based on POTTOK's density of 1.013 g/cm^3. For details see certificate of analysis **(Nº0432/F).**

Justified proposals for classification and labelling

According to the criteria given in Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008, the following classification and labelling with regard to toxicological data is proposed for the preparation:

Table 6.1-2: Justified proposals for classification and labelling for GLOB289H according to Regulation (EC) No 1272/2008

Hazard class(es), categories	~~Eye Irrit.~~ 1 Eye Dam.1 Aquatic Acute 1
Hazard pictograms or Code(s) for hazard pictogram(s)	GHS05 GHS09
Signal word	Danger
Hazard statement(s)	H318 H410
Precautionary statement(s)	P280 P305 + P351 + P338 P310 P273 P391 P501
Additional labelling phrases	To avoid risks to man and the environment, comply with the instructions for use. [EUH401]

Table 6.1-3: Summary of risk assessment for operators, workers, residents and bystanders for GLOB289H

	Result	PPE / Risk mitigation measures
Operators	Acceptable	None
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. No specific PPE is necessary.

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

1	2	3	4	5	6	7	8	9	10			
Use-No.*	Crops and situation (e.g. growth stage of crop)	F, Fn, Fpn G, Gn, Gpn or I **	Application		Application rate		PHI (d)	Remarks: (e.g. safener/synergist (L/ha)) critical gap for operator, worker, resident or bystander exposure based on [Exposure model]	Acceptability of exposure assessment			
			Method / Kind (incl. application technique ***	Max. number (min. interval between applications) a) per use b) per crop/ season	Max. application rate kg as/ha a) iodosulfuron b) mesosulfuron	Water L/ha min / max			Operator	Worker	Residents	Bystander
7	Cereals BBCH 21-32	F	Downwards spraying LC TM	a) 1 b) 1	a) 0.003 b) 0.015	100/400	NA	Mefenpyr (safener): 45 g/ha Applied with 1 L/ha oil/wetting agent				

* 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

ACCEPTABLE

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) + POTTOK (Fatty alcohol alkoxylate)

	Iodosulfuron-methyl-sodium	**Mesosulfuron-methyl**	**Mefenpyr-diethyl**	**POTTOK (Fatty alcohol alkoxylate)**
Common Name	Iodosulfuron-methyl-sodium	Mesosulfuron-methyl	Mefenpyr-diethyl	Pottok Adjuvant
CAS-No.	144550-36-7	208465-21-8	135590-91-9	103818-93-5
Classification and proposed labelling				
With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended)	Hazard classes (s), categories: aqautic acute 1: H400 'very toxic to aquatic life' aquatic chronic 1: H410 'very toxic to aquatic life with long lasting effects' Code for hazard pictogram: GHS09 Signal word: warning Precautionary statement: P273, P391, P501	Hazard classes (s), categories: aqautic acute 1: H400 'very toxic to aquatic life' aquatic chronic 1: H410 'very toxic to aquatic life with long lasting effects' Code for hazard pictogram: GHS09 Signal word: warning Precautionary statement: P273, P391, P501	Hazard classe (s), categories: Aquatic chronic 2: H411 'Toxic to aquatic life with long lasting effects' GHS09 Precautionary statement: P273, P391, P501	Hazard classe (s), categories: Aquatic Chronic 3: H412 - Harmful to aquatic life with long lasting effects; Eye Irrit. 2: H319 - Causes serious eye irritation. Code for hazard pictogram: GHS07 Signal word: warning Precautionary statement: P102, P273, P280, P337+P313, P501
Additional C&L proposal	-	-	-	-
Agreed EU endpoints				
AOEL systemic	0.05 mg/kg bw/d (corrected for 70% oral absorption	0.13 mg/kg bw/d (corrected for 2% oral absorption	0.1 mg/kg bw/day	~~1.2~~ . 0.2026 kg fatty alcohol alkoxylate/ha)* = (max. 0.2 L fatty alcohol alkoxylate/ha)
Reference	EFSA Conclusion	EFSA Conclusion	DAR	AOEL based on combined repeated dose toxicity study with the

	Iodosulfuron-methyl-sodium	Mesosulfuron-methyl	Mefenpyr-diethyl	POTTOK (Fatty alcohol alkoxylate)
				reproduction/developmental toxicity screening test (OECD 422, 1996)
Conditions to take into account/critical areas of concern with regard to toxicology				
According to EFSA Conclusion for active substance	None	• The toxicological relevance of low levels of an unidentified unique human peak metabolite M-2 seen in an *in vitro* metabolism study conld not be finalised • The immunotoxicity potential of mesosulfuron-methyl could not be finalised • The consumer risk assessmen from the consumption of water could not be finalised, while satisfactory infirmation was not available to address the effect of water treatment processes on the nature of the residues that might be present in surface water and groundwater, when surface water or groundwater are abstracted for drinking water	None	None

6.3 Toxicological Evaluation of Plant Protection Product

A summary of the toxicological evaluation for GLOB289H is given in the following tables. No new studies on the product are submitted.

Acute toxicity studies for GLOB289H were not evaluated as part of the EU review of iodosulfuron-methyl-sodium or mesosulfuron-methyl. Therefore, all relevant data were provided here and considered adequate.
No tests were performed on GLOB289H. For the acute oral, dermal and inhalation toxicity, skin and eye irritation and skin sensitisation, the assessment has been conducted according Regulation EC 1272/2008.

Full details on composition, the classification of formulants and calculations are provided in part C of this registration report.
In other hand, a summary of the toxicological evaluation for POTTOK is given in the following tables. All the studies are summarized in Table 6.3-2. For study details please see point 0.

Table 6.3-1 shows the classification of the product based on theoretical calculation and toxicity data for ingredients of GLOB289H.

Table 6.3-1: Summary of evaluation of the studies on acute toxicity including irritancy and skin sensitisation for GLOB289H

Type of test, species, model system (Guideline)	Result	Acceptability	Classification (acc. to the criteria in Reg. 1272/2008)	Reference
LD_{50} oral, rat	Study not necessary	Yes	None	Theoretical calculation (seer Part C)
LD_{50} dermal, rat	Study not necessary	Yes	None	Theoretical calculation (seer Part C)
LC_{50} inhalation, rat	Study not necessary	Yes	None	Theoretical calculation (seer Part C)
Skin irritation	Study not necessary	Yes	None	Theoretical calculation (seer Part C)
Eye irritation	Study not necessary, Cat. 1 (based on calculations)	Yes	H318	Theoretical calculation (seer Part C)
Skin sensitisation	Study not necessary	Yes	None	Theoretical calculation (seer Part C)
Supplementary studies for combinations of plant protection products	Study not necessary			

Table 6.3-2: Summary of evaluation of the studies on acute toxicity including irritancy and skin sensitisation for POTTOK

Type of test, species, model system (Guideline)	Result	Acceptability	Classification (acc. to the criteria in Reg. 1272/2008)	Reference
LD_{50} oral, rat (OECD No. 423, EC method B1 tris and OPPTS 870.1100)	LD50 > 2000 mg/kg b.w.	Yes	None	xxx (2013a)
LD_{50} dermal, rat	LD50 > 2000 mg/kg b.w.	Yes	None	Xxx (2013b)
LC_{50} inhalation, rat	Study not necessary since no significant	Yes	-	-

	exposure is expected			
Skin irritation	Not irritating	Yes	None	xxx (2013a)
Eye irritation	Irritating	Yes	H319/Eye Irrit.2	xxx (2013b)
Skin sensitisation	Not sensitising	Yes	None	xxx. (2013c)
Mutagenicity study in Salmonella typhimurium reverse mutation assay (in vitro) (OECD Guideline 471, EC method B.13/14 and 870.5100)	No mutagenic effect	Yes	-	xxx (2013)
Combined repeated dose toxicity study (reproduction/developmental toxicity screening test (OECD 422, 1996).)	NOAEL = 300 mg/kg b.w./d*	Yes	-	US-EPA memorandum on alkyl alcohol alkoxylates (2009)

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.

6.4.1 AE F160459

Metabolite AE F160459 was not tested for genotoxicity. AE F160459 is an intermediate metabolite found in the rat metabolic pathway of mesosulfuron-methyl at trace amounts in the bile, urine and faeces of the low and high dose rats. This metabolite has a close structure similarity with the parent compound, the only difference between AE F160459 and mesosulfuron-methyl is due to a methyl group which is not present in the metabolite. It is structurally also very similar to AE F160460.
Mesosulfuron-methyl was negative in 5 genotoxicity studies. The *in vitro* testing comprised investigations for gene mutation in bacterial and mammalian cells, examination of chromosomal aberration Chinese Hamster cells and testing for unscheduled DNA-synthesis in primary rate hepatocytes. The *in vivo* test consisted a mouse micronucleus assay. AE F160460 was also negative in the AMES, chromosomal aberration and gene mutation (HPRT) assays when tested both with and without the metabolic activation mix S9.
Additionally a Derek QSAR has been performed by the RMS with mesosulfuron-methyl and its metabolites AE F160459 and AE F160460. The results show similar alerts between parent compound and its metabolites (alpha-2-mu-Globulin nephropathy, bladder urothelial hyperplasia, carcinogenicity, photo allergenicity, skin sensitization and phototoxicity). It can be concluded that also AE F160459 is devoid of mutagenic potential.

The parent compound mesosulfuron-methyl is not classified as toxic or very toxic and has no classification for reproductive toxicity or carcinogenic properties. Consequently, according to Guidance Document Sanco/221/2000, rev.10-final, 25/02/2003, further toxicity testing with the metabolites is not required based on these criteria.

6.4.2 AE F160460

An overview of the results of the accepted toxicological studies for groundwater metabolite AE F160460 is given in the following table.

Table 6.4-1: Summary of the results of toxicity studies for AE F160460

Type of test, species (Guideline)	Result	Acceptability	Reference*
Ames test on *Salmonella Typhimurium*	Negative	Acceptable	EFSA Conclusion 2016; 14(10):4584
Chromosomal aberrations in Chinece Hamster V79 cells	Negative	Acceptable	EFSA Conclusion 2016; 14(10):4584
Gene mutation (HPRT) in Chinese Hamster V79 cells	Negative	Acceptable	EFSA Conclusion 2016; 14(10):4584

* indicates that a study was reviewed at EU level

Parent compound mesosulfuron-methyl is not classified as toxic or very toxic, and has no classification for reproductive toxicity or carcinogenic properties. Consequently, according to Guidance Document Sanco/221/2000, rev.10-final, 25/02/2003, further toxicity testing with the metabolites is not required based on these criteria.

6.4.3 AE F147447

An overview of the results of the accepted toxicological studies for groundwater metabolite AE F147447 is given in the following table.

Table 6.4-2: Summary of the results of toxicity studies for AE F147447

Type of test, species (Guideline)	Result	Acceptability	Reference*
Ames test on *Salmonella Typhimurium*	Negative	Acceptable	EFSA Conclusion 2016; 14(10):4584
Chromosomal aberrations in Chinece Hamster V79 cells	Negative	Acceptable	EFSA Conclusion 2016; 14(10):4584
Gene mutation (HPRT) in Chinese Hamster V79 cells	Negative	Acceptable	EFSA Conclusion 2016; 14(10):4584

* indicates that a study was reviewed at EU level

Parent compound mesosulfuron-methyl is not classified as toxic or very toxic, and has no classification for
reproductive toxicity or carcinogenic properties. Consequently, according to Guidance Document Sanco/221/2000, rev.10-final, 25/02/2003, further toxicity testing with the metabolites is not required based on these criteria.

6.4.4 BCS-CV14885

An overview of the results of the accepted toxicological studies for groundwater metabolite BCS-CV14885 is given in the following table.

Table 6.4-3: Summary of the results of toxicity studies for BCS-CV14885

Type of test, species (Guideline)	Result	Acceptability	Reference*
Ames test on *Salmonella Typhimurium*	Negative	Acceptable	EFSA Conclusion 2016; 14(10):4584
Chromosomal aberrations in Chinece Hamster V79 cells	Negative	Acceptable	EFSA Conclusion 2016; 14(10):4584
Gene mutation (HPRT) in Chinese Hamster V79 cells	Negative	Acceptable	EFSA Conclusion 2016; 14(10):4584

* indicates that a study was reviewed at EU level

Parent compound mesosulfuron-methyl is not classified as toxic or very toxic, and has no classification for
reproductive toxicity or carcinogenic properties. Consequently, according to Guidance Document Sanco/221/2000, rev.10-final, 25/02/2003, further toxicity testing with the metabolites is not required based on these criteria.

6.5 Dermal Absorption (KCP 7.3)

A summary of the dermal absorption rates for the active substances in GLOB289H + POTTOK are presented in the following table.

Table 6.5-1: Dermal absorption rates for active substances in GLOB289H + POTTOK

	GLOB289H						POTTOK	
	Iodosulfuron-methyl sodium		Mesosulfuron-methyl		Mefenpyr-diethyl		Fatty alcohol alkoxylate	
	Value	Reference	Value*	Reference	Value	Reference	Value	Reference
Concentrate	50%	Guidance on dermal absorption, EFSA 2017	50%	Guidance on dermal absorption, EFSA 2017	10%	Guidance on dermal absorption, EFSA 2017	10%	Guidance on dermal absorption, EFSA 2017
Dilution (dilution factor)	50%		50%		50%		50%	

*According to EFSA 2017 (pag.20): "In exceptional cases, if oral absorption is less than 70% for organic solvent-based or other formulations or less than 50% for water-based/dispersed or solid formulations, this can be used as a surrogate dermal absorption value for (in-use) dilutions. If oral absorption is less than 25% for organic solvent-based or other formulations or less than 10% for water-based/dispersed or solid formulations, it can be used instead of the default value for concentrated products." **However, the worst-case values of 50% for concentrate and diluted will be considered for risk assessment.**

6.5.1 Justification for proposed values - Iodosulfuron-methyl sodium

No data on dermal absorption for Iodosulfuron-methyl sodium in GLOB289H is available. Justifications for default values according to Guidance on Dermal Absorption (EFSA Journal 2017; 15(5):4873) are presented in the following table.

Table 6.5-2: Default dermal absorption rates for Iodosulfuron-methyl sodium

	Value	Justification for value	Acceptability of justification
Concentrate	50%	Default value (0.6% ≤ 5% a.s.)	Acceptable

	Value	Justification for value	Acceptability of justification
Dilution	50%	Default value (≤ 5% a.s.)	Acceptable

6.5.2 Justification for proposed values - Mesosulfuron-methyl

No data on dermal absorption for Mesosulfuron-methyl in GLOB289H is available. Justifications for default values according to Guidance on Dermal Absorption (EFSA Journal 2017; 15(5):4873) are presented in the following table.

Table 6.5-3: Default dermal absorption rates for Mesosulfuron-methyl

	Value	Justification for value	Acceptability of justification
Concentrate	50%	Default value (3% ≤ 5% a.s.)	Acceptable
Dilution	50%	Default value (≤ 5% a.s.)	Acceptable

6.5.3 Justification for proposed values - Mefenpyr-diethyl

No data on dermal absorption for mefenpyr-diethyl in GLOB289H is available. Justifications for default values according to Guidance on Dermal Absorption (EFSA Journal 2017; 15(5):4873) are presented in the following table.

Table 6.5-4: Default dermal absorption rates for Mefenpyr-diethyl

	Value	Justification for value	Acceptability of justification
Concentrate	10%	Default value (9% > 5% a.s.)	Acceptable
Dilution	50%	Default value (≤ 5% a.s.)	Acceptable

6.5.4 Justification for proposed values - POTTOK (Fatty alcohol alkoxylate)

No data on dermal absorption for POTTOK is available. Justifications for default values according to Guidance on Dermal Absorption (EFSA Journal 2017; 15(5):4873) are presented in the following table.

Table 6.5-5: Default dermal absorption rates for Fatty alcohol poly-alkoxyklate

	Value	Justification for value	Acceptability of justification
Concentrate	10%	Default value (99.8% > 5% a.s.)	Acceptable
Dilution	50%	Default value (≤ 5% a.s.)	Acceptable

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	GLOB289H	POTTOK

Formulation type	WG			It will be used in a WG formulation
Category	Herbicide			Adjuvant used in herbicides
Active substance(s) (incl. content)	**Iodosulfuron-methyl sodium** 6 g/kg	**Mesosulfuron-methyl** 30 g/kg	**Mefenpyr** 90 g/kg	**Fatty alcohol alkoxylate** (998 g/L = 985.2 g/Kg)* * Based on POTTOK's density of = 1.013 g/cm3. For details see certificate of analysis **(Nº0432/F)**
AOEL systemic	0.05 mg/kg bw/d	0.13 mg/kg bw/d	0.1 mg/kg bw/day	1.2 mg/kg bw/day
Inhalation absorption	100%	100%	100%	100%
Oral absorption	~~100%~~ 70%	~~100%~~ 2%	~~100%~~ 73%	100%
Dermal absorption	Concentrate: 50% Dilution: 50%	Concentrate: 50% Dilution: 50%	Concentrate: 10% Dilution: 50%	Concentrate: 10% Dilution: 50%

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 **Błąd! Nie można odnaleźć źródła odwołania.**. A list of all intended uses within the zone is given in Part B, Section 0.

Justification

There is only 1 intended use, that is cereals. The highest application rate was used as worst-case scenario.

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 GLOB289H + POTTOK 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. Detailed calculations are in Appendix 3.

Table 6.6-2: Exposure models for intended uses

Critical use(s)	Cereals (max. 0.5 kg 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 2014;12(10):3874 calculator version: 30/03/2015
Critical use(s)	Cereals (max. 0.2026 kg fatty alcohol alkoxylate/ha)* = (max. 0.2 L fatty alcohol alkoxylate/ha)
Model(s)	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015

* Based on POTTOK's density of = 1.013 g/cm^3. For details see certificate of analysis **(Nº0432/F).**

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

		Iodosulfuron-methyl sodium		Mesosulfuron-methyl		Mefenpyr-diethyl		Fatty alcohol alkoxylate	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg/day**	**% of systemic AOEL**
Tractor mounted boom spray application outdoors to low crops									
Application rate		0.003 kg a.s./ha		0.015 kg a.s./ha		~~0.45~~ ~~0~~,045 kg a.s./ha		0.1996 kg EAC/ha	
Spray application outdoor (AOEM**;** 75th percentile) Body weight: 60 kg	No PPE (work wear during M/L and A)	0.0031	**6.25**	0.0105	**8.05**	0.0079	**7.88**	0.0273	**2.28**

The operator exposure estimates performed have shown that the acceptable operator exposure level (AOEL) will not be exceeded under the conditions of the intended use including workwear during M / L and A.

6.6.2.2 Measurement of operator exposure

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

6.6.3 Worker exposure (KCP 7.2.3)

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 GLOB289H and POTTOK according to the critical use(s). Outcome of the estimation is presented in Table 6.6-5 (longer term exposure). Detailed calculations are in Appendix 3.

Table 6.6-4: Exposure models for intended uses

Critical use(s)	Cereals (max. 1 x 0.5 kg product/ha)
Model	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015
Critical use(s)	Cereals (max. 0.2026 kg fatty alcohol alkoxylate/ha)* = (max. 0.2 L fatty alcohol alkoxylate/ha)
Model(s)	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015

* Based on POTTOK's density of = 1.013 g/cm^3. For details see certificate of analysis **(N°0432/F).**

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

		Iodosulfuron-methyl sodium		**Mesosulfuron-methyl**		**Mefenpyr-diethyl**		**Fatty alcohol alkoxylate**	
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**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
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 0.003 kg a.s./ha		1 x 0.015 kg a.s./ha		1 x 0.045 kg a.s./ha		1 x 0.1996 kg EAC/ha	
Body weight: 60 kg	Potential	0.0019	3.75	0.0094	7.21	0.0281	28.13	0.1248	10.40
	Work wear (arms, body and legs covered)	0.0002	**0.42**	0.0011	**0.81**	0.0032	**3.15**	0.0140	**1.16**

The worker exposure estimates performed have shown that the exposure limit (AOEL) will not be exceeded under the conditions of the intended uses

6.6.3.2 Refinement of generic DFR value (KCP 7.2)

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

6.6.3.3 Measurement of worker exposure

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

6.6.4 Resident and bystander exposure (KCP 7.2.2)

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 Iodosulfuron-methyl-sodium, Mesosulfuron-methyl and Mefenpyr-diethyl. The outcome of the estimation is presented in Table 6.6-7. Detailed calculations are in Appendix 3.

Table 6.6-6: Exposure models for intended uses

Critical use(s)	Cereals (max. 1 x 0.5 kg product/ha)
Model	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015
Critical use(s)	Cereals (max. 0.2026 kg fatty alcohol alkoxylate/ha)* = (max. 0.2 L fatty alcohol alkoxylate/ha)
Model(s)	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015

* Based on POTTOK's density of = 1.013 g/cm^3. For details see certificate of analysis **(N°0432/F).**

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

		Iodosulfuron-methyl sodium		**Mesosulfuron-methyl**		**Mefenpyr-diethyl**		**Fatty alcohol alkoxylate**	
Model data		**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**	**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 0.003 kg a.s./ha		1 x 0.015 kg a.s./ha		1 x 0.045 kg a.s./ha		1 x 0.1996 kg EAC/ha	
Resident child Body	Drift (75th perc.)	0.0004	0.81	0.0020	1.55	0.0060	6.04	0.0268	2.23
	Vapour (75th	0.0011	2.14	0.0011	0.82	0.0011	1.07	0.0011	0.09

weight: 10 kg	perc.)								
	Deposits (75th perc.)	2.35e-5	0.05	0.0001	0.09	0.0004	0.36	0.0016	0.13
	Re-entry (75th perc.)	0.0002	0.51	0.0013	0.97	0.0038	3.80	0.0168	1.40
	Sum (mean)	0.0015	**3.02**	0.0033	**2.52**	0.0077	**7.69**	0.0304	**2.53**
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0001	0.19	0.0005	0.37	0.0014	1.45	0.0064	0.53
	Vapour (75th perc.)	0.0002	0.46	0.0002	0.18	0.0002	0.23	0.0002	0.02
	Deposits (75th perc.)	1.02e-5	0.02	0.0001	0.04	0.0002	0.15	0.0007	0.06
	Re-entry (75th perc.)	0.0001	0.28	0.0007	0.54	0.0021	2.11	0.0094	0.78
	Sum (mean)	0.0004	**0.79**	0.0011	**0.81**	0.0027	**2.71**	0.0112	**0.94**

The resident and/or bystander exposure estimations carried out indicated that the acceptable exposure level (AOEL) for Iodosulfuron-methyl-sodium, Mesosulfuron-methyl and Mefenpyr-diethyl will not be exceeded under conditions of intended uses. Buffer zone 2-3 m

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 Iodosulfuron-methyl-sodium, Mesosulfuron-methyl and Mefenpyr-diethyl will not be exceeded under conditions of intended uses and considering above mentioned risk mitigation measures, a study to provide measurements of resident/bystander exposure was not necessary and was therefore not performed.

6.6.5 Combined exposure

The product is a mixture of two active substances and one safener, that is mixed with an adjuvant. In order to guarantee that mixing the adjuvant POTTOK with the plant protection product GLOB289H does not result in an unacceptable risk for human health, the combine exposure was considered. For details please see Table 6.6-8.Table 6.1-1

Note: The combined toxicological effect of these active substances has not been investigated with regard to repeated dose toxicity for GLOBB289H. However, the effects of fatty alcohol alkoxylate were investigated in a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD 422, 1996). This study is summarized in a US-EPA memorandum on alkyl alcohol alkoxylates (2009). The summary is presented in point **Błąd! Nie można odnaleźć źródła odwołania.**.

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

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

Application scenario	Active ingredient	Estimated exposure / AOEL (HQ)
Operators	*Iodosulfuron-methyl sodium*	0.063
	Mesosulfuron-methyl	0.081
	Mefenpyr-diethyl	0.079
	Fatty alcohol poly-alkoxyklate	0.023
	Cumulative risk operators (HI)	**0.256**
Workers	*Iodosulfuron-methyl sodium*	0.004
	Mesosulfuron-methyl	0.008
	Mefenpyr-diethyl	0.032
	Fatty alcohol poly-alkoxyklate	0.012
	Cumulative risk workers (HI)	**0.056**
Resident - child	*Iodosulfuron-methyl sodium*	
	Drift	0.008
	Vapour	0.021
	Deposits	0.001
	Re-entry	0.005
	Sum of all pathways	0.030
	Mesosulfuron-methyl	
	Drift	0.016
	Vapour	0.008
	Deposits	0.001
	Re-entry	0.010
	Sum of all pathways	0.025
	Mefenpyr-diethyl	
	Drift	0.060
	Vapour	0.011
	Deposits	0.004
	Re-entry	0.038
	Sum of all pathyways	0.077
	Fatty alcohol poly-alkoxyklate	
	Drift	0.022
	Vapour	0.001
	Deposits	0.001
	Re-entry	0.014
	Sum of all pathways	0.025
	Cumulative risk resident – child (HI)	
	Drift	0.106

Application scenario	Active ingredient	Estimated exposure / AOEL (HQ)
	Vapour	0.041
	Deposits	0.007
	Re-entry	0.067
	Sum of all pathways	**0.157**
Resident - adult	*Iodosulfuron-methyl sodium*	
	Drift	0.002
	Vapour	0.005
	Deposits	0.000
	Re-entry	0.003
	Sum of all pathways	0.008
	Mesosulfuron-methyl	
	Drift	0.004
	Vapour	0.002
	Deposits	0.000
	Re-entry	0.005
	Sum of all pathways	0.008
	Mefenpyr-diethyl	
	Drift	0.015
	Vapour	0.002
	Deposits	0.002
	Re-entry	0.021
	Sum of all pathways	0.027
	Fatty alcohol poly-alkoxyklate	
	Drift	0.005
	Vapour	0.000
	Deposits	0.001
	Re-entry	0.008
	Sum of all pathways	0.009
	Cumulative risk resident – adult (HI)	
	Drift	0.026
	Vapour	0.009
	Deposits	0.003
	Re-entry	0.037
	Sum of all pathways	**0.052**

The Hazard Index is < 1. Thus, combined exposure to all active substances in GLOB289H is not expected to present a risk for operators, workers, residents and bystanders. No further refinement of the assessment is required.

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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
-	-	-	-	-	-

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
KIIIA 7.1.1/01	xxx	2013a	Acute oral toxicity study of HAG 530 01 S study in rats xxx Report-no. 29035 GLP: yes Published: no		HELM AG BELCHIM SAPEC
KIIIA	xxx	2013b	Acute dermal toxicity study of HAG 530 01 S study in CD rats	Y	HELM AG

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**
7.1.2/01			xxx Report-no. 29034 GLP: yes Published: no		BELCHIM SAPEC
KIIIA 7.1.3/01	xxx	2013	EPI Suite Results For CAS 103818-93-5 xxx Report-no. n.a. GLP: n.a. Published: no	Y	HELM AG BELCHIM SAPEC
KIIIA 7.1.4/01	xxx	2013a	Acute dermal irritation/corrosion test (patch test) of HAG 530 01 S in rabbits xxx Report-no. 29031 GLP: yes Published: no	Y	HELM AG BELCHIM SAPEC
KIIIA 7.1.5/01	xxx	2013b	Acute eye irritation/corrosion test of HAG 530 01 S in rabbits xxx Report-no. 29033 GLP: yes Published: no	Y	HELM AG BELCHIM SAPEC
KIIIA 7.1.6/01	xxx	2013c	HAG 530 01 S Skin sensitisation: local lymph node assay in NMRI mice xxx Report-no. 29032 GLP: yes Published: no	Y	HELM AG BELCHIM SAPEC
KIIIA 7.2/01	xxx	2013	Mutagenicity study of HAG 530 01 S in the *Salmonella typhimurium* reverse mutation assay (*in vitro*) xxx Report-no. 29030 GLP: yes Published: no	N	HELM AG BELCHIM SAPEC

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
-	-	-	-	-	-

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

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

Appendix 2 Detailed evaluation of the studies relied upon

A 2.1 Data on co-formulants (KCP 7.4)

A 2.1.1 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 2.1.2 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.2.2Toxicological Evaluation of Plant Protection Product (GLOB289H)

No tests were performed on GLOB289H. For the acute oral toxicity, acute dermal toxicity, eye irritation, skin irritation and skin sensitisation the assessment has been conducted according to Directive 1999/45/EC by conventional method described in Annex II and according Regulation EC 1272/2008.

See below

Acute oral toxicity (KCP 7.1.1)

A study to assess the acute oral toxicity of the plant protection product GLOB289H was judged to be not necessary in the interest of animal welfare. The assessment has been conducted according to Regulation (EC) 1107/2009 requirements.

As GLOB289H does not contain any substance (active or formulant) classified for acute oral toxicity the preparation **is not classified** for acute oral toxicity according to Regulation EC 1272/2008

Conclusion

Following the assessment of the formulants properties, GLOB289H is not classified for acute oral toxicity according to Regulation EC 1272/2008 and Directive 1999/45/EC.

Acute percutaneous (dermal) toxicity (KCP 7.1.2)

A study to assess the acute dermal toxicity of the plant protection product GLOB289H was judged to be not necessary in the interest of animal welfare. The assessment has been conducted according to Regulation (EC) 1107/2009 requirements.

As GLOB289H does not contain any substance (active or formulant) classified for acute dermal toxicity the preparation **is not classified** for acute dermal toxicity according to Regulation EC 1272/2008.

Conclusion

Following the assessment of the formulants properties, GLOB289H is not classified for acute dermal toxicity according to Regulation EC 1272/2008 and Directive 1999/45/EC.

Acute inhalation toxicity (KCP 7.1.3)

A study to assess the acute inhalation toxicity of the plant protection product GLOB289H was judged to be not necessary in the interest of animal welfare. The assessment has been conducted according to Regulation (EC) 1107/2009 requirements.

As GLOB289H does not contain any substance (active or formulant) classified for acute inhalation toxicity the preparation **is not classified** for acute inhalation toxicity according to Regulation EC 1272/2008.

Conclusion

Following the assessment of the formulants properties, GLOB289H is not classified for acute inhalation toxicity according to Regulation EC 1272/2008 and Directive 1999/45/EC.

Skin irritation (KCP 7.1.4)

A study to assess the skin irritation of the plant protection product GLOB289H was judged to be not necessary in the interest of animal welfare. The assessment has been conducted according to Regulation (EC) 1107/2009 requirements.

The co-formulant Morwet EFW is classified as Category 2 for skin irritation; H315. None of the other ingredients attract skin irritation classifications.

According to Table 3.2.3 in Regulation EC 1272/2008, the ingredient concentration is compared to the generic concentration limits:

Skin irritant Category 2 = 3%

This is < 10 %, indicating that GLOB289H **is not classified** for skin irritation according to Regulation EC 1272/2008.

Conclusion

Following the assessment of the formulants properties, GLOB289 is not classified for skin irritation according to Regulation EC 1272/2008.

Eye irritation (KCP 7.1.5)

A study to assess the eye irritation of the plant protection product GLOB289H was judged to be not necessary in the interest of animal welfare. The assessment has been conducted according to Regulation (EC) 1107/2009 requirements.

The co-formulants Morwet D-425, Morwet EFW and Morwet D-500 are classified as Category 2 for eye irritation; H319, Category 1 for eye irritation; H318 and Category 2 for eye irritation; H319 respectively. None of the other ingredients attract eye irritation classifications.
Also the adjuvant Pottok that can be added in tank-mix is classified as Category 2 for eye irritation; H319. Although it is not part of the formulation, it is also considered for the calculation.

According to Table 3.3.3 in Regulation EC 1272/2008, the ingredient concentration is compared to the generic concentration limits:
Eye Effects Category 1 or Skin Corrosive Category 1A, 1B, 1C = 3%
This is ≥ 3%, indicating that GLOB289H **should be classified** for eye irritation according to Regulation EC 1272/2008 as Eye ~~**Irrit.**~~ **Dam.**1, H318.

Conclusion

Following the assessment of the formulants properties, GLOB289H is classified for eye irritation according to Regulation EC 1272/2008 as Eye ~~Irrit.~~ Dam.1; H318.

A 2.2 Acute studies – POTTOK

The following tests were performed with HAG 530 01 S = POTTOK. The individual study summaries are provided below (point A 2.2.1 to A 2.2.6). The studies below were already evaluated and accepted by France during POTTOK dossier authorisation **(No. 2014-2914)**.

A 2.2.1 Acute oral toxicity

The following tests were performed with HAG 530 01 S = POTTOK. The individual study summaries are provided below (point A 2.2.1 to A 2.2.6). The studies below were already evaluated and accepted by France during POTTOK dossier authorisation **(No. 2014-2914)**.

Comments of zRMS:	**The acute oral toxicity was estimated to be > 2000 mg/ kg mc. Therefore, according to the Regulation EC No. 1272/2008, HAG 530 01 S is not classified**

Report:	**IIIA 7.1.1/01** xxx (2013a)
Title:	Acute oral toxicity study of HAG 530 01 S study in rats
Document No:	29035
Guidelines:	OECD No. 423, EC method B1 tris and OPPTS 870.1100
GLP	Yes

Executive Summary

A group of 3 CD female rats was given a single oral dose of 2000 mg/kg b.w. of HAG 530 01 S (as such). There was no death at this dose level and an additional group of three animals (females) was given a single oral dose of 2000 mg/kg b.w. of HAG 530 01 S (as such). The animals were observed for fourteen days after the day of dosing and were then killed and subjected to gross necropsy.

- There were no deaths or clinical signs of toxicity.
- All animals showed expected gains in bodyweight during the 14-day study period.
- No abnormalities were noted at necropsy.
- The discriminatory dose was identified as 2000 mg/kg body weight.

The acute oral median lethal dose (LD_{50}) of the test material in the CD rat was estimated to be greater than 2000 mg/kg body weight. The test material was considered to have no significant acute toxic risk if swallowed and did not meet the criteria for classification under EC labelling regulations. No symbol or risk phrase are required.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Material:	HAG 530 01 S
Description:	Clear colourless liquid
Lot/Batch #:	ARK0712AD
EAC content (nominal):	Fatty alcohol alkoxylate 99.8% w/w
Stability of test compound:	Stable at room temperature Expiry date: 11/07/2014
2. Vehicle and/or positive control:	HAG 530 01 S was used as such
3. Test animals	
Species:	Rat
Sex:	Female
Strain:	CD *I* Crl: CD(SD)
Weight at dosing:	Minimum: 166 g, Maximum: 185 g
Age:	Approx. 8 weeks at the time of dosing
Source:	xxx
Acclimation period:	5 days minimum
Diet:	ssniff® R/M-H V1534, ssniff Spezialdiaten GmbH, 59494 Soest, Germany, *ad libitum*
Water:	Drinking water, *ad libitum*
Housing:	Makrolon rat cages covered with stainless steel grid top were used. Autoclaved granulated texture wood were used as bedding material.
4. Environmental conditions	
Temperature:	22 +/- 3°C
Humidity:	55 +/- 15% rH
Photoperiod:	The photoperiod was 12 h artificial light and 12 h darkness

B. STUDY DESIGN AND METHODS:

1. In life dates: 17/09/2012 – 10/10/2012

2. Animal assignment and treatment

All animals (6 females) were dosed once only by gavage using a metal cannula attached to a graduated syringe. The volume administered to each animal was calculated according to its bodyweight at the time of dosing, 1.98 mL/kg b.w. corresponding to 2000 mg/kg b.w.

Mortality and overt signs of toxicity were checked immediately and 5, 15, 30 and 60 minutes after treatment, then 3, 6 and 24 hours after dosing and subsequently once daily until day 14. Body weights were recorded before dosing, and after 8, and 14 days post dosing. On day 14, all animals were sacrificed and subjected to gross necropsy.

3. Statistics

The data did not warrant any statistical analysis.

II. RESULTS AND DISCUSSION

- There was no death or clinical sign of toxicity.
- All animals showed expected gains in bodyweight during the 14-day study period.
- No abnormalities were noted at necropsy.
- The discriminatory dose was identified as 2000 mg/kg bodyweight.

III. CONCLUSIONS

The acute oral median lethal dose (LD_{50}) of the test material in the CD female rats was estimated to be greater than 2000 mg/kg body weight. The test material was considered to have no significant acute toxic risk if swallowed and did not meet the criteria for classification under EC labelling regulations. No symbol or risk phrase are required.

A 2.2.2 Acute percutaneous (dermal) toxicity

Comments of zRMS:	**The acute dermal toxicity of HAG 530 01 S as estimated to be > 2000 mg/kg bw.** **Therefore, according to the Regulation EC No. 1272/2008, HAG 530 01 S is not classified.**

Report:	**IIIA 7.1.2/01** xxx (2013b)
Title:	Acute dermal toxicity study of HAG 530 01 S study in CD rats
Document No:	29034
Guidelines:	OECD No. 402 and EC method B.3 and OPPTS 870.1200
GLP	Yes

Executive Summary

Ten CD rats, 5 males and 5 females, were randomly selected for the study. Approximately, 10% of the body surface area was clipped 24 h prior to the dermal application of the test item. The rats were given a limit dose of 2000 mg/kg b.w. of HAG 530 01 S. A calculated dose quantity was applied over the clipped area (approximately 10% of body surface) by single dermal application and the rats were observed for a period of 14 days.

- No sign of toxicity and no mortality were observed in either rats treated with 2000 mg/kg b.w. of HAG 530 01 S.
- All animals showed expected gains in bodyweight during the 14-day study period.
- No dermal reaction was observed.
- No apparent abnormality was seen at necropsy in any animal.

The acute dermal median lethal dose (LD_{50}) of HAG 530 01 S in CD rats was found to be greater than 2000 mg/kg b.w. Therefore, no classification is needed.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Material: HAG 530 01 S
Description: Clear colourless liquid
Lot/Batch #: ARK0712AD
EAC content (nominal): Fatty alcohol alkoxylate 99.8% w/w
Stable at room temperature
Stability of test compound: Expiry date: 11/07/2014

2. Vehicle and/or positive control: HAG 530 01 S was used as such

3. Test animals
Species: Rat
Sex: 10 males and 10 female
Strain: CD I Crl: CD(SD)
Weight at dosing: Males: 210-230 g, females: 210-220 g
Age: Approx. 8 weeks at the time of dosing
Source: xxxx
Acclimation period: 5 days minimum
Diet: ssniff® R/M-H V1534, ssniff Spezialdiaten

xxx, ad libitum

Water: Drinking water, ad libitum
Housing: Makrolon rat cages covered with stainless steel grid top were used. Autoclaved granulated texture wood were used as bedding material.

4. Environmental conditions
Temperature: 22 +/- 3°C
Humidity: 55 +/- 15% rH
Photoperiod: The photoperiod was 12 h artificial light and 12 h darkness

B. STUDY DESIGN AND METHODS

1. In life dates: 17/09/2012-08/10/2012

2. Animal assignment, treatment and observations

HAG 530 01 S was used as supplied. The administration volume was 1.98 mL/kg b.w. based on a density of 1.01 g/mL.

The intact dorsal skin of the animals was shaved free of hair with a shaver 24 hours before application. The site was situated on the animals back between the fore and hind extremities and had an area of at least 5 cm x 6 cm (approx. 1/10 of body surface).

The test item was applied to 8 layers of gauze. The gauze was covered with a plastic sheet and secured with adhesive plaster on the application site. Exposure time was 24 hours. At the end of the exposure period no residual test item had to be removed.

Following administration, observations were made and recorded systematically with individual records being maintained for each animal. Observations were performed before and immediately, 5, 15, 30 and 60 min, as well as 3, 6 and 24 hours after administration. All animals were observed for a period of 14 days. During the follow-up period (two weeks), changes of skin and fur, eyes and mucous membranes, respiratory and circulatory function, autonomic and central nervous system and somatomotor activity as well as behaviour pattern, were observed at least once a day until all symptoms subsided, thereafter each working day. Attention was also paid to possible tremors, convulsions, salivation, diarrhoea, lethargy, sleep and coma. Observations on deaths were made at least once daily to minimize loss of animals during the study. Individual body weights were recorded before administration of the test item and thereafter in weekly intervals up to the end of the study. Changes in weight were calculated and recorded.

At the end of the experiments, all animals were sacrificed, dissected and inspected macroscopically. All gross pathological changes were recorded. No histopathology was carried out as no macroscopic findings were noted at autopsy.

3. Statistics

No LD_{50} was calculated due to lack of deaths at the applied dose level. Body weight data was statistically analysed by Student's "t" test.

II. RESULTS AND DISCUSSION

A. MORTALITY / CLINICAL OBSERVATIONS

No sign of toxicity and no mortality were observed in either rats treated with 2000 mg/kg b.w. of HAG 530 01 S.

B. DERMAL RESPONSES

No skin reaction at the application site was noted.

C. BODY WEIGHT

All animals showed expected gains in bodyweight during the 14-day study period.

D. NECROPSY

The test item did not produce any treatment-related effect at the dose level used in the present study.

III. CONCLUSIONS

The acute dermal median lethal dose (LD_{50}) of HAG 530 01 S in CD rats was found to be greater than 2000 mg/kg b.w. Therefore, no classification is needed.

A 2.2.3 Acute inhalation toxicity

Comments of zRMS:	**An exposure of the user (when HAG 530 01 S is applied as recommended) is unlikely to occur.** **Therefore, according to the Regulation EC No. 1272/2008, HAG 530 01 S is not classified**

Vapour pressure and Henry's law constant for HAG 530 01 S were determined with the EPI suite (version 4.11). The EPI suite report is presented in document IIIA 7.1.3/01.

The effective adjuvant component contains a considerable number of different molecules, all of them carrying a terminal OH group and different numbers of ethoxy and propoxy groups. The chain lengths of the alcohols show variation although C11 alcohol is dominant with a content of min. 90%. Chain lengths of >11 and of <11 appear at max. 5% each. Taking into consideration the manufacturing process of the product, the typical ratio ethoxylated/propoxylated groups is 3-5/1.

The modelling was run according to the following structure, an alkyl chain of 11 carbons, 5 ethylene oxide units and 1 propylene oxide unit. The following SMILES (Simplified Molecular-Input Line-Entry System) was used: C.

The results are shown in table 7.1.3-1.

Table A 2.2.3-1: results of the EPI suite (version 4.11).

Endpoint	Software (version)	Result
Vapour pressure (at 25°C)	MPBPVP (v1.43)	From 8.98 x 10^{-12} to 3.23 x 10^{-7} Pa depending on the method
Henry's Law constant (at 25°C)	HENRYWIN (v3.20)	8.67 x 10^{-11} Pa-m^3/mole

Therefore, any significant volatilisation is not expected.

In addition, an acute inhalation toxicity study is only required when the preparation, or the smoke it generates is:

- a gas or liquefied gas,

- a smoke generating formulation or fumigant,
- used with fogging equipment,
- a vapour releasing preparation,
- an aerosol,
- a powder containing a significant proportion of particles of diameter < 50 µm (> 1% on a weight basis),
- is to be applied from aircraft in cases where inhalation exposure is relevant,
- contains an effective adjuvant component with a vapour pressure > 1 x 10^{-2} Pa,
- to be included in enclosed spaces such as warehouses or glasshouses,
- to be applied in a manner which generates a significant proportion of particles or droplets of diameter < 50 µm (> 1% on a weight basis).

Therefore, an exposure of the user (when **HAG 530 01 S** is applied as recommended) is unlikely to occur. For these reasons, an acute inhalation toxicity in rats was not considered as needed.

A 2.2.4 Skin irritation

Comments of zRMS:	**Under the conditions of this study, no skin reaction was observed. According to the Regulation EC No. 1272/2008, HAG 530 01 S is not classified**

Report:	**KIIIA 7.1.4/01**, xxx (2013a)
Title:	Acute dermal irritation/corrosion test (patch test) of HAG 530 01 S in rabbits
Document No:	29031
Guidelines:	OECD Guideline 404, EC method B.4 and OPPTS 870.2500
GLP	Yes

Executive Summary

The test substance was applied for 4 hours to three female Himalayan white rabbits. A single dose of 0.5 mL of the test substance in its original form was applied to the closely-clipped skin of one flank. The test substance was held in contact with the skin by means of a semi-occlusive dressing. Cutaneous reactions were observed approximately 1 hour, 24, 48 and 72 hours after removal of the dressing. The mean values of the scores for erythema and oedema were calculated for each animal.

No cutaneous reactions were observed during the study.

Under the experimental conditions, the test substance HAG 530 01 S is non-irritant when applied topically to rabbits. According to the classification EC criteria, the test substance should not be classified as irritating to the skin.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Material: HAG 530 01 S
Description: Clear colourless liquid

Lot/Batch #:	ARK0712AD
EAC content (nominal):	Fatty alcohol alkoxylate 99.8% w/w Stable at room temperature Expiry date: 11/07/2014
Stability of test compound:	
2. Vehicle and/or positive control:	HAG 530 01 S was used as such
3. Test animals	
Species:	Rabbit
Sex:	3 females
Strain:	Himalayan white
Weight at dosing:	2.8 – 3.1 kg
Age:	14.5 to 19.5 months at the time of dosing
Source:	LPT Laboratory of Pharmacology and Toxicology GmbH Lohndorf/Post Wankendorf, Germany
Acclimation period:	20 days minimum
Diet:	ssniff® K-H V2333, (ssniff Spezialdiaten xxx,
Water:	*ad libitum* Drinking water, *ad libitum*
Housing:	Polyethylene cages.
4. Environmental conditions	
Temperature:	20 +/- 3°C
Humidity:	30-70% rH
Air changes:	Minimum 12 air changes/h
Photoperiod:	The photoperiod was 12 h artificial light and 12 h darkness

B. STUDY DESIGN AND METHODS

1. In life dates: 17/09/2012 – 19/11/2012

2. Animal assignment and treatment

Approximately 24 hours before the test, the fur was removed by closely clipping the dorsal area of the trunk of the animals. Care was taken to avoid abrading the skin. Only animals with healthy intact skin were used.

A dose of 0.5 ml of the test item was applied to the test site (area: approx. 6 cm^2). The test item was applied to the test site and then covered with a gauze patch. The patch was held in contact with the skin with non-irritating tape for the duration of the exposure period. The surrounding untreated skin served as a control. Exposure time was 4 hours. During the exposure the animals were kept in comfortable restrainers.

At the end of the exposure time no residual test item had to be removed.

The skin reactions were observed and scored at 1, 24, 48, 72 hours post patch removal.

II. RESULTS AND DISCUSSION

At 1, 24, 48 and 72 hours post patch removal the treated skin site of all the three rabbit appeared to be normal throughout the experimental period. The control skin site of all the three rabbits was normal throughout the experimental period.

Neither symptom of systemic toxicity nor mortality was reported.

The mean dermal irritation scores of erythema and oedema at 24, 48 and 72 h observation period were shown to be 0.

III. CONCLUSIONS

Under the conditions of this study, no skin reaction was observed. With regard to EU labelling regulations, the test item has not to be classified as "irritant" and no labelling is required.

A 2.2.5 Eye irritation

Comments of zRMS:	**Under the experimental conditions, the test substance HAG 530 01 S is irritant when administered by ocular route to rabbits. Classification as mildly irritant to the eyes.** **According to the Regulation EU No. 1272/2008, HAG 530 01 S is classified Eye Irrit.2/H319**

Report:	**KIIIA 7.1.5/01**, xxx (2013b)
Title:	Acute eye irritation/corrosion test of HAG 530 01 S in rabbits
Document No:	29033
Guidelines:	OECD Guideline 405, EC method B.5 and OPPTS 870.2400
GLP	Yes

Executive Summary

A single dose of 0.1 mL of the test substance in its original form was introduced into the conjunctival sac of the right eye of three male Himalayan white rabbits. The left eye was not treated and served as control. The eyes were not rinsed after administration of the test substance. Ocular reactions were observed approximately 1 hour, 24, 48 and 72 hours after the administration and then daily until reversibility of the ocular reactions (day 7). The mean values of the scores for chemosis, redness of the conjunctiva, iris lesions and corneal opacity were calculated for each animal.

The observed effects were as follows:

Corneal opacity was observed in all animals:

- animal no. 1: 24 hours (grade 2), 60 minutes, 48 and 72 hours (grade 1) after instillation;
- animal no. 2: 24 to 72 hours (grade 2), 60 minutes, 4 and 5 days (grade 1) after instillation;
- animal no. 3: 60 minutes to 72 hours (grade 1) after instillation.

The fluorescein test performed 24 hours after instillation revealed corneal staining in animal n° 1 and 3 (3/4 to whole surface) and animal n° 2 (1/2 to 3/4 of the surface).

Irritation of the **iris** (grade 1) was observed in all 3 animals 60 minutes after instillation.

Conjunctival redness (grade 1) was observed in all animals 60 minutes to 4 days, in animal n° 2 until 6 days after instillation.

Chemosis (grade 1) was observed in all animals 60 minutes to 72 hours after instillation, and in animal n°2 until 6 days after instillation.

There was no systemic intolerance reaction.

Under the experimental conditions, the test substance HAG 530 01 S is irritant when administered by ocular route to rabbits. Classification as mildly irritant to the eyes with H319 is needed.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Material:	HAG 530 01 S
Description:	Clear colourless liquid
Lot/Batch #:	ARK0712AD
EAC content (nominal):	Fatty alcohol alkoxylate 99.8% w/w
Stability of test compound:	Stable at room temperature Expiry date: 11/07/2014
2. Vehicle and/or positive control:	HAG 530 01 S was used as such
3. Test animals	
Species:	Rabbit
Sex:	3 females
Strain:	Himalayan white
Weight at dosing:	3.1 – 3.6 kg
Age:	7.5 to 9.5 months at the time of dosing
Source:	LPT Laboratory of Pharmacology and Toxicology GmbH Lohndorf/Post Wankendorf, Germany
Acclimation period:	20 days minimum
Diet:	ssniff® K-H V2333, (ssniff Spezialdiaten xxx, *ad libitum*
Water:	Drinking water, *ad libitum*
Housing:	Polyethylene cages.
4. Environmental conditions	
Temperature:	20 +/- 3°C
Humidity:	30-70% rH
Air changes:	Minimum 12 air changes/h
Photoperiod:	The photoperiod was 12 h artificial light and 12 h darkness

B. STUDY DESIGN AND METHODS

1. In life dates: 17/09/2012-27/12/2012

2. Animal assignment and treatment

The test substance (0.1 mL) was instilled into conjunctival sac of the eye of each animal and the eyelids were then gently held together for one second before releasing. The other eye remained untreated and served as the reference control.

The eyes were examined with a slit lamp prior to the administration and 1, 24, 48, 72 hours as well as 4 to 7 days after the administration. The eye reactions were observed and recorded Twenty-four hours after

administration, fluorescein was applied to the eyes before examination to aid evaluation of the cornea for possible lesions.

II. RESULTS AND DISCUSSION

The observed effects were as follows:

Corneal opacity was observed in all animals:

- animal n° 1: 24 hours (grade 2), 60 minutes, 48 and 72 hours (grade 1) after instillation;
- animal n° 2: 24 to 72 hours (grade 2), 60 minutes, 4 and 5 days (grade 1) after instillation;
- animal n° 3: 60 minutes to 72 hours (grade 1) after instillation.

The fluorescein test performed 24 hours after instillation revealed corneal staining in animal n° 1 and 3 (3/4 to whole surface) and animal n° 2 (1/2 to 3/4 of the surface).

Irritation of the **iris** (grade 1) was observed in all 3 animals 60 minutes after instillation.

Conjunctival redness (grade 1) was observed in all animals 60 minutes to 4 days, in animal n° 2 until 6 days after instillation.

Chemosis (grade 1) was observed in all animals 60 minutes to 72 hours after instillation and in animal n°2 until 6 days after instillation.

There was no systemic intolerance reaction.

III. CONCLUSIONS

Under the experimental conditions, the test substance HAG 530 01 S is irritant when administered by ocular route to rabbits. Classification as mildly irritant to the eyes with H319 is needed.

A 2.2.6 Skin sensitisation

Comments of zRMS:	**Under the present test conditions, HAG 530 01 S at concentrations of 25% or 50% (w/w) in acetone/olive oil (3 + 1 v/v) did not reveal any sensitising properties in the local lymph node assay.** **According to the Regulation EC No. 1272/2008, HAG 530 01 S is unclassified as skin sensitizer**

Report:	**KIIIA 7.1.6/01**, xxx (2013c)
Title:	HAG 530 01 S Skin sensitisation: local lymph node assay in NMRI mice
Document No:	29032
Guidelines:	OECD Guideline 429, EC method B.42 and 870.2600
GLP	Yes

Executive summary

The study was performed according to OECD 429, however not using radioactive labelling to measure cell proliferation, as the radioactive method proposed by the OECD guideline led to problems in various EU laboratories: such as (i) practical difficulties/complexity of the test, in particular the radiochemical

steps, which sometimes resulted in loss of specimen/activity; this in turn led to variability in the results and to a poor reproducibility and (ii) radiation protection issues.

However, the OECD guideline allows other endpoints for assessment of proliferation in form of lymph node cell counts and lymph node weights if justification and appropriate scientific support exist showing the validity of this method. The alternative method used for the study employing the lymph node weight and lymph node cell count to assess proliferation has been established by a European interlaboratory validation exercise, as described in the two publications by Fehling et al. 2005. This method has the advantage of (i) more simplistic experimental work, (ii) less variability, (iii) better reproducibility, (iv) faster results, (v) reduced costs.

In addition, the acute inflammatory skin reaction is measured by ear weight determination of circular biopsies of the ears and ear thickness measurements on test day 1 and test day 4 to identify skin irritation properties of the test item. It is important to determine if a positive test result is due to the skin irritation potential of the test item or due to its sensitising properties.

Stimulation indices were calculated for the lymph node cell count, lymph node weight, ear weight and ear thickness by dividing the average values per group of the test item treated animals by the vehicle treated ones. Values above 1.4 (lymph node cell count to identify sensitisation) or 1.1 (ear weight to identify irritation) are considered positive (these values were fixed empirically during the inter-laboratory validation of this method (Ehling et al. 2005a and 2005b)).

Three concentrations of HAG 530 01 S (25% and 50%, diluted with acetone/olive oil (3 + 1 v/v)) (w/w) or the undiluted test item (100%) were tested in six female NMRI mice per group and compared to a vehicle control group. In addition, a positive control group (25% solution (v/v) of α-hexyl cinnamic aldehyde in acetone/olive oil (3 + 1, v/v)) was employed.

Treatment with undiluted HAG 530 01 S revealed a concentration-related increased value for the lymph node cell count and a statistically significantly concentration-related increased value ($p \leq 0.01$) for the lymph node weight. The stimulation index of the lymph node cell count exceeded the threshold level of 1.4. However, ear weight was also significantly at $p \leq 0.01$ increased and exceeding the threshold level of 1.1 pointing to strongly irritating properties, hence, no valid information on possible sensitising properties can be obtained for the undiluted test item in the local lymph node assay in mice.

The positive control group caused the expected increases in lymph node cell count and lymph node weight (statistically significant at $p \leq 0.01$) and no increase in ear weight. Therefore, the study can be regarded as valid.

No signs of local or systemic intolerance were recorded. The animal body weight was not affected by the treatment.

In conclusion, under the present test conditions, HAG 530 01 S at concentrations of 25% or 50% (w/w) in acetone/olive oil (3 + 1 v/v) did not reveal any sensitising properties in the local lymph node assay. The undiluted test item shows strong irritating properties in this test system as evident from the increased ear weight, hence, no valid information on possible sensitising properties can be obtained for the undiluted test item in the local lymph node assay in mice.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Material:	HAG 530 01 S
Description:	Clear colourless liquid
Lot/Batch #:	ARK0712AD
EAC content (nominal):	Fatty alcohol alkoxylate 99.8% w/w
Stability of test compound:	Stable at room temperature Expiry date: 11/07/2014
2. Vehicle and/or positive control:	α-hexyl cinnamic aldehyde in acetone/olive oil (3 + 1, v/v)
3. Test animals	
Species:	NMRI mice
Sex:	30 females (5 groups of 6 animals)
Strain:	NMRI
Weight at dosing:	26-30 g
Age:	Approx. 7 weeks
Source:	xxx
Acclimation period:	5 days minimum
Diet:	ssniff® R/M-H V1534, ssniff Spezialdiaten xxx, *ad libitum*
Water:	Drinking water, *ad libitum*
Housing:	Makrolon cages.
4. Environmental conditions	
Temperature:	22 +/- 3°C
Humidity:	35-70% rH
Air changes:	Minimum 12 air changes/h
Photoperiod:	The photoperiod was 12 h artificial light and 12 h darkness.

B. STUDY DESIGN AND METHODS

1. In life dates: 25/10/2012-18/02/2013.

2. Animal assignment and treatment

A preliminary experiment was carried out in 3 animals to examine the irritating potential and handling/application of the test item in order to select the appropriate concentrations. Two concentrations of 25 and 50% of HAG 530 01 S in acetone/olive oil (3 + 1, v/v} and the undiluted test item were examined. Doses were selected according to OECD guideline from the concentration series 100%, 50%, 25%, 10%, 5%, 2.5%, 1%, 0.5% etc.

In the main study, 3 concentrations of HAG 530 01 S (25% and 50%, diluted with acetone/olive oil (3 + 1 v/v)) (w/w) or the undiluted test item (100%) were tested in six female NMRI mice per group and compared to a vehicle control group. In addition, a positive control group (25% solution (v/v) of α-hexyl cinnamic aldehyde in acetone/olive oil (3 + 1, v/v)) was employed.

The experimental schedule of the assay was as follows:

Day 1:

The weight of each animal was individually identified and recorded. In addition, ear swelling measurements were carried out at the helical edge of both ears using an Oditest micrometer. Open application of 25 µl of the appropriate dilution of the test item, the vehicle alone or the positive control (as appropriate) were administered to the dorsum of each ear.

Days 2 and 3:

The application procedure carried out on day 1 was repeated.

Day 4 (24 hours after the last application the animals were sacrificed under ether anaesthesia by cutting the aorta *abdominalis*):

Ear swelling measurements (immediately before sacrificing the mice) were carried out at the helical edge of both ears using an Oditest micrometer. Punch biopsies of 8 mm in diameter of the apical area of both ears were prepared and immediately weighed on an analytical balance. Lateral pairs of auricular lymph nodes draining the ear tissue were excised, carefully separated from remaining fatty tissue and weighed on an analytical balance immediately following preparation. The lymph nodes were then stored on ice in PBS / 0.5% BSA and subjected to the preparation of single cell suspensions by mechanical tissue disaggregation. The cells were counted automatically in a cell counter.

Animals were observed once daily for any clinical signs of local systemic irritation at the application site or of systemic toxicity. Observations were recorded for each individual animal. Cage side observations included skin/fur, eyes, mucous membranes, respiratory and circulatory systems, somatomotor activity and behaviour patterns. The onset, intensity and duration of any signs observed were recorded.

The weight of each mouse was recorded at the time of allocation of animals to groups (test day 1) and at the time of necropsy (test day 4).

Stimulation indices were calculated for the lymph node cell count, lymph node weight, ear weight and ear thickness by dividing the average values per group of the test item treated animals by the vehicle treated ones. Values above 1.4 (lymph node cell count to identify sensitisation) or 1.1 (ear weight to identify irritation) are considered positive (these values were fixed empirically during the inter-laboratory validation of this method (Ehling et al. 2005a and 2005b)).

In addition, the acute inflammatory skin reaction (irritating potential) was measured by ear weight determination of circular biopsies of the ears and ear thickness measurements on test day 1 and test day 4 to identify skin irritation properties of the test item employing the U-test according to MANN and WHITNEY by comparing the test groups to the vehicle control.

The stimulation indices were calculated by dividing the average ear weight and average ear thickness on test day 4 per group of the test item treated animals by the vehicle treated ones. The cut-off threshold value for ear weight was set at 1.1.

II. RESULTS AND DISCUSSION

Three concentrations of HAG 530 01 S (25% and 50%, diluted with acetone/olive oil (3 + 1 v/v)) (w/w) or the undiluted test item (100%) were tested in six female NMRI mice per group and compared to a vehicle control group. In addition, a positive control group (25% solution (v/v) of α-hexyl cinnamic aldehyde in acetone/olive oil (3 + 1, v/v)) was employed.

Results are shown in Table IIIA 7.1.6-1.

Table A 2.2.6-1: results of the main study.

	Control	**HAG 530 01 S (25%)**	**HAG 530 01 S (50%)**	**HAG 530 01 S (undiluted)**	**Positive control**
Lymph node cell count	1	1.206	1.324	1.695	1.926*****
Lymph node	1	1.209	1.256*****	1.535*****	1.814*****

weight					
Ear weight	1	1.095	1.071	1.124*****	1.036
Difference of ear thickness	1	1	1.035	1.009	1.122

*****: significantly different from control, $p \leq 0.01$

Treatment with undiluted HAG 530 01 S revealed a concentration-related increased value for the lymph node cell count and a statistically significantly concentration-related increased value ($p \leq 0.01$) for the lymph node weight. The stimulation index of the lymph node cell count exceeded the threshold level of 1.4. However, ear weight was also significantly at $p \leq 0.01$ increased and exceeding the threshold level of 1.1 pointing to strongly irritating properties, hence, no valid information on possible sensitising properties can be obtained for the undiluted test item in the local lymph node assay in mice.

The positive control group caused the expected increases in lymph node cell count and lymph node weight (statistically significant at $p \leq 0.01$) and no increase in ear weight. Therefore, the study can be regarded as valid.

No signs of local or systemic intolerance were recorded. The animal body weight was not affected by the treatment.

III. CONCLUSIONS

In conclusion, under the present test conditions, HAG 530 01 S at concentrations of 25% or 50% (w/w) in acetone/olive oil (3 + 1 v/v) did not reveal any sensitising properties in the local lymph node assay. The undiluted test item shows strong irritating properties in this test system as evident from the increased ear weight, hence, no valid information on possible sensitising properties can be obtained for the undiluted test item in the local lymph node assay in mice.

A 2.3 Other studies – POTTOK

Comments of zRMS:	**Under the present test conditions HAG 530 01 S tested up to a concentration of 5000 µg/plate caused no mutagenic effect in the *Salmonella typhimurium* strains TA98, TA 100, TA 102, TA 1535 and TA 1537 either in the plate incorporation test or in the preincubation test each carried out without and with metabolic activation.**

Report:	**KIIIA 7.2/01**, xxx. (2013)
Title:	Mutagenicity study of HAG 530 01 S in the *Salmonella typhimurium* reverse mutation assay (*in vitro*)
Document No:	29030
Guidelines:	OECD Guideline 471, EC method B.13/14 and 870.5100
GLP	Yes

Executive summary

HAG 530 01 S was examined in the 5 *Salmonella typhimurium* strains TA98, TA 100, TA 102, TA 1535 and TA 1537 in two independent experiments, each carried out without and with metabolic activation (a

microsomal preparation derived from Aroclor 1254-induced rat liver). The first experiment was carried out as a plate incorporation test and the second as a preincubation test.

HAG 530 01 S was completely dissolved in *aqua ad iniectabilia.* The vehicle served as the negative control.

Preliminary test

HAG 530 01 S was examined in two preliminary cytotoxicity tests (plate incorporation test without and with metabolic activation) in test strain TA 100. Ten concentrations ranging from 0.316 to 5000 µg HAG 530 01 S/plate were tested. No sign of cytotoxicity was noted up to the greatest concentration of 5000 µg/plate. Hence, 5000 µg HAG 530 01 S/plate was selected as the highest concentration for the main study in the plate incorporation test and in the preincubation test.

Main study

Six concentrations ranging from 31.6 to 5000 µg HAG 530 01 S/plate were employed in the plate incorporation test and in the preincubation test, each carried out without and with metabolic activation.

In the plate incorporation test and in the preincubation test, each carried out without and with metabolic activation no sign of cytotoxicity was observed up to the highest concentration of 5000 µg/plate.

No increase in revertant colony numbers when compared to control counts was observed for HAG 530 01 S, tested up to a concentration of 5000 µg/plate, in any of the 5 test strains in two independent experiments without and with metabolic activation, respectively (plate incorporation and preincubation test). The positive control items showed a significant increase in the number of revertant colonies of the respective test strain and confirmed the validity of the test conditions and the sensitivity of the test system.

In conclusion, under the test conditions HAG 530 01 S tested up to a concentration of 5000 µg/plate caused no mutagenic effect in the *Salmonella typhimurium* strains TA98, TA 100, TA 102, TA 1535 and TA 1537 either in the plate incorporation test or in the preincubation test each carried out without and with metabolic activation.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Material:	HAG 530 01 S
Description:	Clear colourless liquid
Lot/Batch #:	ARK0712AD
EAC content (nominal):	Fatty alcohol alkoxylate 99.8% w/w
Stability of test compound:	Stable at room temperature Expiry date: 11/07/2014
2. Vehicle and/or positive control:	HAG 530 01 S was dissolved in *aqua ad iniectabilia*. Depending on the strain and the metabolic activation, sodium azide, 2-nitrofluorene, 9-aminoacridine, mitomycin C, benzo(a)pyrene and 2-amino-anthracene were used as positive control.
3. Test strain	
Strains:	*Salmonella typhimurium* strains TA98, TA 100, TA 102, TA 1535 and TA 1537

Source:	xxx, Germany
Plates:	3 per concentration and experiment
Experiment:	2 independent experiments, each with and without metabolic activation
Concentrations	31.6, 100, 316, 1000, 3160 and 5000 µg/plate

4. Environmental conditions

Growing conditions:	Test strains were kept as lyophilisate pellets. The permanent copies of the test strains were used to inoculate the overnight cultures. Overnight cultures were grown in a gyrorotary incubator (10 h/37°C) in Oxoid 24 nutrient broth. The final cell density was approximately 10^8 - 10^9 cells/mL.
Metabolic activation system:	Post-mitochondrial fraction (S9 fraction) from rats treated with Aroclor 1254 was prepared according to MARON and AMES (1983) at LPT. S9 was collected from 20 - 30 rats. The pooled fraction was tested for protein content, according to LOWRY et al. (1951) and P-450 content, according to MAZEL (1971). The protein content of the S9 fraction was 33.1 mg/mL S9, whilst the cytochrome P-450 content was 0.40 nmol/mg protein. The S9 fraction was stored in liquid nitrogen. The S9 mix was freshly prepared on the day of the test according to MARON and AMES (1983).

B. STUDY DESIGN AND METHODS

1. In life dates: 17/09/2012-10/01/2013.

2. Experimental design

Dose levels *I* Solvents *I* Reference items

The test item was completely dissolved *aqua ad iniectabilia.* The vehicle served as the negative control. Fresh preparations of the test item were used for the treatment in all experimental parts.

Prior to the main test two preliminary cytotoxicity tests (plate incorporation test, without and with metabolic activation) were carried out in test strain TA 100. Cytotoxicity is evidenced by a reduction in the number of spontaneous revertants, a clearing or diminution of the background lawn or by the degree of survival of the treated cultures. Insolubility could have been assessed as precipitation in the final mixture under the actual test conditions and evident to the unaided eye. In the main study 6 different concentrations of the test item were tested, with half-log intervals between plates (31.6, 100, 316, 1000, 3160 and 5000 µg per plate).

1st independent experiment - Plate Incorporation Method

Sterile top agar containing 0.6% agar and 0.5% NaCI was molten on the day of the test. Ten ml of a sterile solution of 0.5 mM L-histidine HCI/0.5 mM biotin were added to 100 mL of molten agar. Two mL of this top agar were distributed into culture tubes held at 45°C in a heating block. 0.1 mL of *Salmonella* cell suspension (containing approximately 10^8 viable cells in the late exponential or early stationary phase),

0.1 mL of test item solution (or 0.1 mL solvent or 0.1 mL positive control) and 0.5 mL of S9 mix were added to these culture tubes. In the assay without metabolic activation, the S9 mix was substituted with 0.5 mL phosphate buffer mentioned above. The test components were mixed by vortexing the soft agar for 3 sec at low speed and then poured onto a coded 27.5 mL minimal glucose agar plate (Minimal Glucose Agar medium E). To achieve a uniform distribution of the top agar on the surface of the plate, the uncovered plate was quickly tilted and rotated and then placed on a level surface with the cover on and finally allowed to harden. Immediately, the plates were inverted and placed in a dark 37°C incubator for 48 to 72 hours. The revertant colonies on the test plates and on the control plates were counted with a colony counter, and the presence of the background lawn on all plates was confirmed. A lawn that was thin compared with the lawn on the negative control plate was evidence of bacterial toxicity. Routine examination of the background lawn of bacterial growth resulting from the trace of histidine added to the top agar can be an aid in determining the presence of toxic effects. If massive cell death has occurred, the background lawn on the test plates will be sparse compared with control plates. In this case more histidine is available to the individual surviving bacteria and they undergo more cell divisions, consequently appearing as small colonies which can be mistaken for revertants if the absence of a normal background lawn is not noted.

2nd independent experiment - Preincubation Method

The test item/test solution was preincubated with the test strain (containing approximately 10^8 viable cells in the late exponential or early stationary phase) and sterile buffer (0.5 mL) or the metabolic activation system (0.5 mL) for 20 minutes at 37°C prior to mixing with the overlay agar and pouring onto the surface of a minimal agar plate. 0.1 mL of the test item (or 0.1 mL solvent or 0.1 mL positive control), 0.1 mL of bacteria, and 0.5 mL of S9 mix or sterile buffer, were mixed with 2 mL of overlay agar. Tubes were aerated during preincubation by using a shaker. The remaining steps were the same as described for the plate incorporation method.

I. RESULTS AND DISCUSSION

HAG 530 01 S was examined in the 5 *Salmonella typhimurium* strains TA98, TA 100, TA 102, TA 1535 and TA 1537 in two independent experiments, each carried out without and with metabolic activation (a microsomal preparation derived from Aroclor 1254-induced rat liver). The first experiment was carried out as a plate incorporation test and the second as a preincubation test.

HAG 530 01 S was completely dissolved in *aqua ad iniectabilia.* The vehicle served as the negative control.

Preliminary test

HAG 530 01 S was examined in two preliminary cytotoxicity tests (plate incorporation test without and with metabolic activation) in test strain TA 100. Ten concentrations ranging from 0.316 to 5000 µg HAG 530 01 S/plate were tested. No sign of cytotoxicity was noted up to the greatest concentration of 5000 µg/plate. Hence, 5000 µg HAG 530 01 S/plate was selected as the highest concentration for the main study in the plate incorporation test and in the preincubation test.

Main study

Six concentrations ranging from 31.6 to 5000 µg HAG 530 01 S/plate were employed in the plate incorporation test and in the preincubation test, each carried out without and with metabolic activation.

In the plate incorporation test and in the preincubation test, each carried out without and with metabolic activation no sign of cytotoxicity was observed up to the highest concentration of 5000 µg/plate.

No increase in revertant colony numbers when compared to control counts was observed for HAG 530 01 S, tested up to a concentration of 5000 µg/plate, in any of the 5 test strains in two independ-

ent experiments without and with metabolic activation, respectively (plate incorporation and preincubation test). The positive control items showed a significant increase in the number of revertant colonies of the respective test strain and confirmed the validity of the test conditions and the sensitivity of the test system.

III.CONCLUSIONS

In conclusion, under the present test conditions HAG 530 01 S tested up to a concentration of 5000 µg/plate caused no mutagenic effect in the *Salmonella typhimurium* strains TA98, TA 100, TA 102, TA 1535 and TA 1537 either in the plate incorporation test or in the preincubation test each carried out without and with metabolic activation.

Combined repeated dose toxicity study – POTTOK (fatty alcohol alkoxylate)

Fatty alcohol alkoxylate (99% EAC, batch n° 2110FD4449) was orally administered to ten Crl:CD(SD) rats/sex/dose by gavage at dose levels of 0, 48, 120 or 300 mg/kg b.w./day.

Parental animals were dosed with either the vehicle (controls) or the test substance for 2 weeks prior to the cohabitation period. The males received a total of at least 46 doses. The treatment of the females continued through the day of sacrifice, which was gestation day (GD) 4 for the animals not delivering a litter, lactation day (LD) 4 for the rats delivering a litter or study day (SD) 52 for the females with no confirmed day of mating. Overall, the female rats received between 38-52 doses. Five rats/sex/group were assigned for a functional observational battery (FOB) and motor activity assessment and the other five/sex/group were used for biochemical chemistry and histopathological examination.

There was no treatment-related effect in the parental animals when considering mortality, organ weight, fertility indices, FOB and motor activity assessment, haematology parameters or gross and histopathological examinations.

One female of the 300 mg/kg b.w. group died, but the lesions observed at necropsy indicated that death was caused by a gavage error.

Orange/red perioral staining and moderate salivation were observed in the males and females of the 300 mg/kg b.w. group.

During the pre-mating period (days 1-14), the total body weight gain of the males of the 300 mg/kg b.w. group was reduced by 33% when compared to controls. For the entire treatment period (days 1-46), body weight gain was decreased when compared to controls by 15% and 27% in the males of the groups 120 and 300 mg/kg b.w., respectively.

All treated females during pre-mating had decreased body weight and body weight gain, when compared to the controls, but the values were similar to each other and the controls appeared to be slightly higher than typical, indicating no dose-dependent decrease.

Food consumption was decreased in the males and females (within 10% of controls) during the premating period but the males were similar to controls by the time of their sacrifice.

Females during gestation and lactation had similar changes in body weight and body weight gain in all the treated groups when compared to controls.

Food consumption in the females during gestation and lactation was similar to controls.

No treatment-related effects in clinical chemistry were observed in the females.

The parental systemic NOAEL for fatty alcohol alkoxylate in rats was shown to be 120 mg/kg b.w./d. It was based on decreased body weight gain (males only) and clinical signs (orange/red perioral staining and moderate salivation in both sexes) resulting in a parental systemic LOAEL of 300 mg/kg b.w./d.

There was no treatment-related effect seen in any of the reproductive/developmental parameters measured. The number of implantations, corpora lutea, live births, gestation index, lactation index, fertility index and lactation index were all similar between the control and treated groups.

The reproductive/developmental NOAEL as well as the offspring toxicity NOAEL were shown to be 300 mg/kg b.w./d (the highest dose tested).

Based on this NOAEL in rats, an AOEL can be derived. It was considered that:

- The oral absorption of fatty alcohol alkoxylate was 100%;
- Fatty alcohol alkoxylate is of low acute toxicity (please refer to the acute toxicity studies performed with HAG 530 01 S, which contains 98% w:w of the effective adjuvant component);
- Fatty alcohol alkoxylate is not mutagenic;
- Fatty alcohol alkoxylate has neither neurotoxic nor reproductive effect.

Therefore, a margin of safety of 100 was regarded to be sufficient and an AOEL of 1.2 mg/kg b.w./day is proposed based on the NOAEL of 120 mg/kg b.w. determined in rats

Appendix 3 Exposure calculations

A 3.1 Operator exposure calculations (KCP 7.2.1.1)

A 3.1.1 Calculations for iodosulfuron-methyl-sodium

Table A 1.1: Estimation of operator exposure towards iodosulfuron-methyl-sodium using the AOEM model (including input parameters) without the use of PPE, according to EFSA guidance

Application rate of active substance	0,003	kg a.s./ha	*i_AppRate*
Assumed area treated	50	ha/day	*d_AreaTreated*
Amount of active substance applied	0,15	kg a.s./day	*i_AmoutAS*
Dermal absorption of the product	50,00%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	50,00%		*i_AbsorInuse*
Formulation type	Wettable granules, soluble granules		
Indoor or Outdoor application	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Season	not relevant		

OutdoorWettable granules, soluble granulesDownward sprayingVehicle-mounted

	Exposure values	µg exposure/day mixed and loaded 75th centile	95th centile	Reference	Comment
Mixing and loading	Hands	304	1427	AOEM	
	Body	325	9261	AOEM	
	Head	1	13	AOEM	
	Protected hands (gloves)	5	5	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	3	9	AOEM	
	Protected head (hood and face shield)	0	1	AOEM	
	Inhalation	21	248	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied 75th centile	95th centile	Reference	Comment
Application	Hands	22	571	AOEM	
	Body	12	64	AOEM	
	Head	1	2	AOEM	
	Protected hands (gloves)	15	2672	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	0	1	AOEM	
	Inhalation	0	1	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

1. Total

	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	0,3546564	0,1875915	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0,0059109	0,0031265	
% of RVNAS	11,82%	6,25%	

A 3.1.2 Calculations for mesosulfuron-methyl

Table A 1.2: Estimation of operator exposure towards mesosulfuron-methyl using the AOEM model (including input parameters) without the use of PPE, according to EFSA guidance

Application rate of active substance	0,015	kg a.s./ha	*i_AppRate*
Assumed area treated	50	ha/day	*d_AreaTreated*
Amount of active substance applied	0,75	kg a.s./day	*i_AmoutAS*
Dermal absorption of the product	50,00%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	50,00%		*i_AbsorInuse*
Formulation type	Wettable granules, soluble granules		
Indoor or Outdoor application	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Season	not relevant		

Database:Wettable granules, soluble granules;Downward spraying;Vehicle-mounted

	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75th centile	95th centile		
Mixing and loading	Hands	1051	4997	AOEM	
	Body	1009	14782	AOEM	
	Head	5	67	AOEM	
	Protected hands (gloves)	14	24	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	14	47	AOEM	
	Protected head (hood and face shield)	0	4	AOEM	
	Inhalation	34	258	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied		Reference	Comment
		75th centile	95th centile		
Application	Hands	111	1856	AOEM	
	Body	62	321	AOEM	
	Head	3	9	AOEM	
	Protected hands (gloves)	36	3223	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	2	4	AOEM	
	Inhalation	1	2	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

1. Total

	Without RPE/PPE	With RPE/PPE
Longer term		
Total systemic exposure from mixing, loading and application (mg a.s./day)	1,1555245	0,6280112
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0,0192587	0,0104669
% of RVNAS	14,81%	8,05%

A 3.1.3 Calculations for mesosulfuron-methyl

Table A 1.3: Estimation of operator exposure towards mefenpyr-diethyl using the AOEM model (including input parameters) without the use of PPE, according to EF-SA guidance

Application rate of active substance	0,045	kg a.s./ha	*i_AppRate*
Assumed area treated	50	ha/day	*d_AreaTreated*
Amount of active substance applied	2,25	kg a.s./day	*i_AmoutAS*
Dermal absorption of the product	10,00%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	50,00%		*i_AbsorInuse*
Formulation type	Wettable granules, soluble granules		
Indoor or Outdoor application	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Season	not relevant		

OutdoorWettable granules, soluble granulesDownward sprayingVehicle-mounted

	Exposure values	µg exposure/day mixed and loaded 75th centile	95th centile	Reference	Comment
Mixing and loading	Hands	2447	11755	AOEM	
	Body	2184	20340	AOEM	
	Head	15	201	AOEM	
	Protected hands (gloves)	28	71	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	38	140	AOEM	
	Protected head (hood and face shield)	0	11	AOEM	
	Inhalation	48	265	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied 75th centile	95th centile	Reference	Comment
Application	Hands	334	4150	AOEM	
	Body	187	962	AOEM	
	Head	9	27	AOEM	
	Protected hands (gloves)	66	3664	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	5	13	AOEM	
	Inhalation	2	5	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

1. Total

	Without RPE/PPE	With RPE/PPE
Longer term		
Total systemic exposure from mixing, loading and application (mg a.s./day)	0,7782579	0,4729352
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0,0129710	0,0078823
% of RVNAS	12,97%	7,88%

A 3.1.4 Calculations for POTTOK (fatty alcohol alkoxylate)

Table A 1.4: Estimation of operator exposure towards fatty alcohol alkoxylate using the AOEM model (including input parameters) without the use of PPE, according to EFSA guidance

Operator exposure for outdoor spray applications

Application rate of active substance	0,1996 kg a.s./ha	*i_AppRate*
Assumed area treated	50 ha/day	*d_AreaTreated*
Amount of active substance applied	9,98 kg a.s./day	*i_AmoutAS*
Dermal absorption of the product	10,00%	*i_AbsorpProduct*
Dermal absorption of in-use dilution	50,00%	*i_AbsorInuse*
Formulation type	Wettable granules, soluble granules	
Indoor or Outdoor application	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Season	not relevant	

	Exposure values	µg exposure/day mixed and loaded 75th centile	95th centile	Reference	Comment
Mixing and loading	Hands	7704	37496	AOEM	
	Body	6223	31355	AOEM	
	Head	65	16565	AOEM	
	Protected hands (gloves)	74	314	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	143	621	AOEM	
	Protected head (hood and face shield)	1	938	AOEM	
	Inhalation	74	274	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied 75th centile	95th centile	Reference	Comment
Application	Hands	1480	12358	AOEM	
	Body	828	4267	AOEM	
	Head	39	118	AOEM	
	Protected hands (gloves)	148	4359	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	23	56	AOEM	
	Inhalation	3	11	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

1. Total

	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	2,6500937	1,6395881	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0,0441682	0,0273265	
% of RVNAS	3,68%	2,28%	

A 3.2 Worker exposure calculations (KCP 7.2.3.1)

A 3.2.1 Calculations for iodosulfuron-methyl sodium

Table A 2.1: Estimation of worker exposure towards iodosulfuron-methyl-sodium using the AOEM model (including input parameters)

Crop type	Cereals		
Indoor or outdoor	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Worker's task	Inspection, irrigation		
Main body parts in contact with foliage	Hand and body		
Application rate of active substance	0,003	kg a.s./ha	*i_AppRate*
Number of applications	1		*i_AppNo*
Interval between multiple applications	365	days	*i_AppInt*
Half-life of active substance	30	days	*d_HalflifeAS*
Multiple application factor	1,0		*d_MAF*
Dermal absorption of the product	50,00%		*i_AbsorpProduct*
Dermal absorption of the in-use dilution	50,00%		*i_AbsorpInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	0,009	µg a.s./cm^2	*d_DFR*
Working hours	2	hr	*d_WorkHr*
Dermal transfer coefficient - Total potential exposure	12500	cm^2/hr	*d_DermTcUCV*
Dermal transfer coefficient - arms, body and legs covered	1400	cm^2/hr	*d_DermTcCV1*
Dermal transfer coefficient - hands, arms, body and legs covered	no TC available for this assessment	cm^2/hr	*d_DermTcCV2*
Inhalation transfer coefficient for automated applications	NA	ha/hr*10^(-3)	*d_InhalTcAut*
Inhalation transfer coefficient for cutting ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcCut*
Inhalation transfer coefficient for sorting / bundling ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcSort*

1. Total

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves	Comments
Total systemic exposure (mg a.s./day)	0,1125000	0,0126000	no TC available for this assessment	
Total systemic exposure per kg body weight (mg/kg bw/day)	0,0018750	0,0002100		
% of RVNAS	3,75%	0,42%		

A 3.2.2 Calculations for mesosulfuron-methyl

Table A 2.2: Estimation of worker exposure towards mesosulfuron-methyl using the AOEM model (including input parameters)

Crop type	Cereals		
Indoor or outdoor	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Worker's task	Inspection, irrigation		
Main body parts in contact with foliage	Hand and body		
Application rate of active substance	0,015	kg a.s./ha	*i_AppRate*
Number of applications	1		*i_AppNo*
Interval between multiple applications	365	days	*i_AppInt*
Half-life of active substance	30	days	*d_HalflifeAS*
Multiple application factor	1,0		*d_MAF*
Dermal absorption of the product	50,00%		*i_AbsorpProduct*
Dermal absorption of the in-use dilution	50,00%		*i_AbsorpInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	0,045	µg a.s./cm^2	*d_DFR*
Working hours	2	hr	*d_WorkHr*
Dermal transfer coefficient - Total potential exposure	12500	cm^2/hr	*d_DermTcUCV*
Dermal transfer coefficient - arms, body and legs covered	1400	cm^2/hr	*d_DermTcCV1*
Dermal transfer coefficient - hands, arms, body and legs covered	no TC available for this assessment	cm^2/hr	*d_DermTcCV2*
Inhalation transfer coefficient for automated applications	NA	ha/hr*10^(-3)	*d_InhalTcAut*
Inhalation transfer coefficient for cutting ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcCut*
Inhalation transfer coefficient for sorting / bundling ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcSort*

1. Total

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves	Comments
Total systemic exposure (mg a.s./day)	0,5625000	0,0630000	no TC available for this assessment	
Total systemic exposure per kg body weight (mg/kg bw/day)	0,0093750	0,0010500		
% of RVNAS	7,21%	0,81%		

A 3.2.3 Calculations for mefenpyr-diethyl

Table A 2.3: Estimation of worker exposure towards mefenpyr-diethyl using the AOEM model (including input parameters)

Crop type	Cereals		
Indoor or outdoor	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Worker's task	Inspection, irrigation		
Main body parts in contact with foliage	Hand and body		
Application rate of active substance	0,045	kg a.s./ha	*i_AppRate*
Number of applications	1		*i_AppNo*
Interval between multiple applications	365	days	*i_AppInt*
Half-life of active substance	2,4	days	*d_HalflifeAS*
Multiple application factor	1,0		*d_MAF*
Dermal absorption of the product	10,00%		*i_AbsorpProduct*
Dermal absorption of the in-use dilution	50,00%		*i_AbsorpInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	0,135	µg a.s./cm^2	*d_DFR*
Working hours	2	hr	*d_WorkHr*
Dermal transfer coefficient - Total potential exposure	12500	cm^2/hr	*d_DermTcUCV*
Dermal transfer coefficient - arms, body and legs covered	1400	cm^2/hr	*d_DermTcCV1*
Dermal transfer coefficient - hands, arms, body and legs covered	no TC available for this assessment	cm^2/hr	*d_DermTcCV2*
Inhalation transfer coefficient for automated applications	NA	ha/hr*10^(-3)	*d_InhalTcAut*
Inhalation transfer coefficient for cutting ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcCut*
Inhalation transfer coefficient for sorting / bundling ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcSort*

1. Total

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves	Comments
Total systemic exposure (mg a.s./day)	1,6875000	0,1890000	no TC available for this assessment	
Total systemic exposure per kg body weight (mg/kg bw/day)	0,0281250	0,0031500		
% of RVNAS	28,13%	3,15%		

A 3.2.4 Calculations for POTTOK (fatty alcohol alkoxylate)

Table A 2.4: Estimation of worker exposure towards fatty alcohol alkoxylate using the AOEM model (including input parameters)

Worker exposure from residues on foliage for

Crop type	Cereals		
Indoor or outdoor	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Worker's task	Inspection, irrigation		
Main body parts in contact with foliage	Hand and body		
Application rate of active substance	0,1996	kg a.s./ha	*i_AppRate*
Number of applications	1		*i_AppNo*
Interval between multiple applications	365	days	*i_AppInt*
Half-life of active substance	30	days	*d_HalflifeAS*
Multiple application factor	1,0		*d_MAF*
Dermal absorption of the product	10,00%		*i_AbsorpProduct*
Dermal absorption of the in-use dilution	50,00%		*i_AbsorpInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	0,5988	µg a.s./cm^2	*d_DFR*
Working hours	2	hr	*d_WorkHr*
Dermal transfer coefficient - Total potential exposure	12500	cm^2/hr	*d_DermTcUCV*
Dermal transfer coefficient - arms, body and legs covered	1400	cm^2/hr	*d_DermTcCV1*
Dermal transfer coefficient - hands, arms, body and legs covered	no TC available for this assessment	cm^2/hr	*d_DermTcCV2*
Inhalation transfer coefficient for automated applications	NA	ha/hr*10^(-3)	*d_InhalTcAut*
Inhalation transfer coefficient for cutting ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcCut*
Inhalation transfer coefficient for sorting / bundling ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcSort*

1. Total

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves	Comments
Total systemic exposure (mg a.s./day)	7,4850000	0,8383200	no TC available for this assessment	
Total systemic exposure per kg body weight (mg/kg bw/day)	0,1247500	0,0139720		
% of RVNAS	10,40%	1,16%		

A 3.3 Resident and bystander exposure calculations (KCP 7.2.2.1)

A 3.3.1 Calculations for iodosulfuron-methyl-sodium

Table A 3.1: Estimation of resident exposure towards iodosulfuron-methyl sodium using the AOEM model (including input parameters)

Croptype	Cereals		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		*i_AppEquip*
Formulation type	Wettable granules, soluble granules		*i_FormVal*
Buffer strip	2-3	m	*i_Buffer*
Application rate of the product	0,003	kg a.s./ha	*i_AppRate*
Concentration of active substance (in-use dilution for liquid applications)	0,03	g a.s./l	*d_ConcAS*
Dermal absorption of product	50,00%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	50,00%		*i_AbsorpInuse*
Oral absorption	100,00%		*i_AbsorpOralInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	0,009	µg a.s./cm^2	*d_DFR*
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa	*i_Volat*
Concentration in air	0,001	mg/m^3	*d_AirCon*
Resident dermal spray drift exposure 75th percentile - adult	0,47	ml spray dilution/person	
Resident dermal spray drift exposure 75th percentile - child	0,327	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - adult	0,00010	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - child	0,00022	ml spray dilution/person	
Resident dermal spray drift exposure mean - adult	0,22318	ml spray dilution/person	
Resident dermal spray drift exposure mean - child	0,18	ml spray dilution/person	
Resident inhal. spray drift exposure mean - adult	0,00009	ml spray dilution/person	
Resident inhal. spray drift exposure mean - child	0,00017	ml spray dilution/person	
Exposure duration dermal	2	hours	*d_ReExpDur*
Exposure duration inhalation	24	hours	*d_ReExpDurInhal*
Exposure duration entry into treated crops	0,25	hours	*d_ExpDurTreatCrop*
Light clothing adjustment factor	18,0%		*d_ClothAF*
Breathing rate adult	0,23	m^3/day/kg	*d_BreathRAd*
Breathing rate child (1-3 year old)	1,07	m^3/day/kg	*d_BreathRCh*
Drift percentage on surface (75th percentile)	5,60%		
Drift percentage on surface (mean)	4,10%		
Turf transferable residues percentage	5,00%		*d_Turf*
Transfer coeff. of surface deposits-adult	7300	cm^2/hour	*d_ReTCAd*
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm^2/hour	*d_ReTCCh*
Saliva extraction percentage	50,00%		*d_SalExt*
Surface area of hands mouthed	20	cm^2	*d_AreaHM*
Frequency of hand to mouth activity	9,5	events/hour	*d_ReFreqHM*
Ingestion rate for mouthing of grass per day	25	cm^2	*d_MouthGrass*
Dislodgeable residues percentage transferability for object to mouth	20,00%		*d_DRP*
Transfer coefficient for entry into treated crops (75th percentile) - adı	7500	cm^2/h	*d_TcEntryAd*
Transfer coefficient for entry into treated crops (75th percentile) - chi	2250	cm^2/h	*d_TcEntryCh*
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm^2/h	*d_TcEntryAd*
Transfer coefficient for entry into treated crops (mean) - child	1794	cm^2/h	*d_TcEntryCh*

1. Total

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0,0040287	0,0107000	0,0002428	0,0025313	0,0151151
Total systemic exposure per kg body weight (mg/kg bw/day)	0,0004029	0,0010700	0,0000243	0,0002531	0,0015115
% of RVNAS	0,81%	2,14%	0,05%	0,51%	3,02%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0,0057840	0,0138000	0,0006132	0,0084375	0,0237243
Total systemic exposure per kg body weight (mg/kg bw/day)	0,0000964	0,0002300	0,0000102	0,0001406	0,0003954
% of RVNAS	0,19%	0,46%	0,02%	0,28%	0,79%

A 3.3.2 Calculations for mesosulfuron-methyl

Table A 3.2: Estimation of resident exposure towards mesosulfuron-methyl using the AOEM model (including input parameters)

Croptype	Cereals		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		*i_AppEquip*
Formulation type	Wettable granules, soluble granules		*i_FormVal*
Buffer strip	2-3	m	*i_Buffer*
Application rate of the product	0,015	kg a.s./ha	*i_AppRate*
Concentration of active substance (in-use dilution for liquid applications)	0,15	g a.s./l	*d_ConcAS*
Dermal absorption of product	50,00%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	50,00%		*i_AbsorpInuse*
Oral absorption	100,00%		*i_AbsorpOralInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	0,045	µg a.s./cm^2	*d_DFR*
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa	*i_Volat*
Concentration in air	0,001	mg/m^3	*d_AirCon*
Resident dermal spray drift exposure 75th percentile - adult	0,47	ml spray dilution/person	
Resident dermal spray drift exposure 75th percentile - child	0,327	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - adult	0,00010	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - child	0,00022	ml spray dilution/person	
Resident dermal spray drift exposure mean - adult	0,22318	ml spray dilution/person	
Resident dermal spray drift exposure mean - child	0,18	ml spray dilution/person	
Resident inhal. spray drift exposure mean - adult	0,00009	ml spray dilution/person	
Resident inhal. spray drift exposure mean - child	0,00017	ml spray dilution/person	
Exposure duration dermal	2	hours	*d_ReExpDur*
Exposure duration inhalation	24	hours	*d_ReExpDurInhal*
Exposure duration entry into treated crops	0,25	hours	*d_ExpDurTreatCrop*
Light clothing adjustment factor	18,0%		*d_ClothAF*
Breathing rate adult	0,23	m^3/day/kg	*d_BreathRAd*
Breathing rate child (1-3 year old)	1,07	m^3/day/kg	*d_BreathRCh*
Drift percentage on surface (75th percentile)	5,60%		
Drift percentage on surface (mean)	4,10%		
Turf transferable residues percentage	5,00%		*d_Turf*
Transfer coeff. of surface deposits-adult	7300	cm^2/hour	*d_ReTCAd*
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm^2/hour	*d_ReTCCh*
Saliva extraction percentage	50,00%		*d_SalExt*
Surface area of hands mouthed	20	cm^2	*d_AreaHM*
Frequency of hand to mouth activity	9,5	events/hour	*d_ReFreqHM*
Ingestion rate for mouthing of grass per day	25	cm^2	*d_MouthGrass*
Dislodgeable residues percentage transferability for object to mouth	20,00%		*d_DRP*
Transfer coefficient for entry into treated crops (75th percentile) - ad	7500	cm^2/h	*d_TcEntryAd*
Transfer coefficient for entry into treated crops (75th percentile) - chi	2250	cm^2/h	*d_TcEntryCh*
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm^2/h	*d_TcEntryAd*
Transfer coefficient for entry into treated crops (mean) - child	1794	cm^2/h	*d_TcEntryCh*

1. Total

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0,0201435	0,0107000	0,0012138	0,0126563	0,0327754
Total systemic exposure per kg body weight (mg/kg bw/day)	0,0020144	0,0010700	0,0001214	0,0012656	0,0032775
% of RVNAS	1,55%	0,82%	0,09%	0,97%	2,52%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0,0289200	0,0138000	0,0030660	0,0421875	0,0634213
Total systemic exposure per kg body weight	0,0004820	0,0002300	0,0000511	0,0007031	0,0010570
% of RVNAS	0,37%	0,18%	0,04%	0,54%	0,81%

A 3.3.3 Calculations for mefenpyr-diethyl

Table A 3.3: Estimation of resident exposure towards mefenpyr-diethyl using the AOEM model (including input parameters)

Croptype	Cereals		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		*i_AppEquip*
Formulation type	Wettable granules, soluble granules		*i_FormVal*
Buffer strip	2-3	m	*i_Buffer*
Application rate of the product	0,045	kg a.s./ha	*i_AppRate*
Concentration of active substance (in-use dilution for liquid applications)	0,45	g a.s./l	*d_ConcAS*
Dermal absorption of product	10,00%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	50,00%		*i_AbsorpInuse*
Oral absorption	100,00%		*i_AbsorpOralInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	0,135	µg a.s./cm^2	*d_DFR*
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa	*i_Volat*
Concentration in air	0,001	mg/m^3	*d_AirCon*
Resident dermal spray drift exposure 75th percentile - adult	0,47	ml spray dilution/person	
Resident dermal spray drift exposure 75th percentile - child	0,327	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - adult	0,00010	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - child	0,00022	ml spray dilution/person	
Resident dermal spray drift exposure mean - adult	0,22318	ml spray dilution/person	
Resident dermal spray drift exposure mean - child	0,18	ml spray dilution/person	
Resident inhal. spray drift exposure mean - adult	0,00009	ml spray dilution/person	
Resident inhal. spray drift exposure mean - child	0,00017	ml spray dilution/person	
Exposure duration dermal	2	hours	*d_ReExpDur*
Exposure duration inhalation	24	hours	*d_ReExpDurInhal*
Exposure duration entry into treated crops	0,25	hours	*d_ExpDurTreatCrop*
Light clothing adjustment factor	18,0%		*d_ClothAF*
Breathing rate adult	0,23	m^3/day/kg	*d_BreathRAd*
Breathing rate child (1-3 year old)	1,07	m^3/day/kg	*d_BreathRCh*
Drift percentage on surface (75th percentile)	5,60%		
Drift percentage on surface (mean)	4,10%		
Turf transferable residues percentage	5,00%		*d_Turf*
Transfer coeff. of surface deposits-adult	7300	cm^2/hour	*d_ReTCAd*
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm^2/hour	*d_ReTCCh*
Saliva extraction percentage	50,00%		*d_SalExt*
Surface area of hands mouthed	20	cm^2	*d_AreaHM*
Frequency of hand to mouth activity	9,5	events/hour	*d_ReFreqHM*
Ingestion rate for mouthing of grass per day	25	cm^2	*d_MouthGrass*
Dislodgeable residues percentage transferability for object to mouth	20,00%		*d_DRP*
Transfer coefficient for entry into treated crops (75th percentile) - ad	7500	cm^2/h	*d_TcEntryAd*
Transfer coefficient for entry into treated crops (75th percentile) - chi	2250	cm^2/h	*d_TcEntryCh*
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm^2/h	*d_TcEntryAd*
Transfer coefficient for entry into treated crops (mean) - child	1794	cm^2/h	*d_TcEntryCh*

1. Total

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0,0604305	0,0107000	0,0036414	0,0379688	0,0769263
Total systemic exposure per kg body weight (mg/kg bw/day)	0,0060431	0,0010700	0,0003641	0,0037969	0,0076926
% of RVNAS	6,04%	1,07%	0,36%	3,80%	7,69%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0,0867600	0,0138000	0,0091980	0,1265625	0,1626640
Total systemic exposure per kg body weight	0,0014460	0,0002300	0,0001533	0,0021094	0,0027111
% of RVNAS	1,45%	0,23%	0,15%	2,11%	2,71%

A 3.3.4 Calculations for POTTOK (fatty alcohol alkoxylate)

Table A 3.4: Estimation of resident exposure towards fatty alcohol alkoxylate using the AOEM model (including input parameters)

Resident exposure for			
Croptype	Cereals		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		*i_AppEquip*
Formulation type	Wettable granules, soluble granules		*i_FormVal*
Buffer strip	2-3	m	*i_Buffer*
Application rate of the product	0,1996	kg a.s./ha	*i_AppRate*
Concentration of active substance (in-use dilution for liquid applications)	1,996	g a.s./l	*d_ConcAS*
Dermal absorption of product	10,00%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	50,00%		*i_AbsorpInuse*
Oral absorption	100,00%		*i_AbsorpOralInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	0,5988	µg a.s./cm^2	*d_DFR*
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa	*i_Volat*
Concentration in air	0,001	mg/m^3	*d_AirCon*
Resident dermal spray drift exposure 75th percentile - adult	0,47	ml spray dilution/person	
Resident dermal spray drift exposure 75th percentile - child	0,327	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - adult	0,00010	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - child	0,00022	ml spray dilution/person	
Resident dermal spray drift exposure mean - adult	0,22318	ml spray dilution/person	
Resident dermal spray drift exposure mean - child	0,18	ml spray dilution/person	
Resident inhal. spray drift exposure mean - adult	0,00009	ml spray dilution/person	
Resident inhal. spray drift exposure mean - child	0,00017	ml spray dilution/person	
Exposure duration dermal	2	hours	*d_ReExpDur*
Exposure duration inhalation	24	hours	*d_ReExpDurInhal*
Exposure duration entry into treated crops	0,25	hours	*d_ExpDurTreatCrop*
Light clothing adjustment factor	18,0%		*d_ClothAF*
Breathing rate adult	0,23	m^3/day/kg	*d_BreathRAd*
Breathing rate child (1-3 year old)	1,07	m^3/day/kg	*d_BreathRCh*
Drift percentage on surface (75th percentile)	5,60%		
Drift percentage on surface (mean)	4,10%		
Turf transferable residues percentage	5,00%		*d_Turf*
Transfer coeff. of surface deposits-adult	7300	cm^2/hour	*d_ReTCAd*
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm^2/hour	*d_ReTCCh*
Saliva extraction percentage	50,00%		*d_SalExt*
Surface area of hands mouthed	20	cm^2	*d_AreaHM*
Frequency of hand to mouth activity	9,5	events/hour	*d_ReFreqHM*
Ingestion rate for mouthing of grass per day	25	cm^2	*d_MouthGrass*
Dislodgeable residues percentage transferability for object to mouth	20,00%		*d_DRP*
Transfer coefficient for entry into treated crops (75th percentile) - ad	7500	cm^2/h	*d_TcEntryAd*
Transfer coefficient for entry into treated crops (75th percentile) - chi	2250	cm^2/h	*d_TcEntryCh*
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm^2/h	*d_TcEntryAd*
Transfer coefficient for entry into treated crops (mean) - child	1794	cm^2/h	*d_TcEntryCh*

1. Total

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0,2680428	0,0107000	0,0161516	0,1684125	0,3041110
Total systemic exposure per kg body weight	0,0268043	0,0010700	0,0016152	0,0168413	0,0304111
% of RVNAS	2,23%	0,09%	0,13%	1,40%	2,53%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0,3848288	0,0138000	0,0407982	0,5613750	0,6740944
Total systemic exposure per kg body weight	0,0064138	0,0002300	0,0006800	0,0093563	0,0112349
% of RVNAS	0,53%	0,02%	0,06%	0,78%	0,94%