REGISTRATION REPORT

Part B

Section 6

Mammalian Toxicology

Detailed summary of the risk assessment

Product code: AG-E1-500 SC1

Product name(s): see Part A

Chemical active substances:

Ethofumesate, 500 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Sponsor: ADAMA Agan Ltd.
Applicant: Country organisation / representative of ADAMA, as given in Part A

Submission date: March 2021

MS Finalisation date: January 2022 (initial Core Assessment)

June 2022 (final Core Assessment)

Version history

When	What
March 2021	dRR version 1 submitted by applicant
January 2022	Initial assessment by the zRMS. The report in the dRR format has been prepared by the Applicant, therefore all comments, additional evaluations and conclusions of the zRMS are presented in grey commenting boxes. Minor changes are introduced directly in the text and highlighted in grey. Not agreed or not relevant information are ~~struck through and shaded for transparency~~.
June 2022	Final report (Core Assessment updated following the commenting period). Additional information/assessments included by the zRMS in the report in response to comments received from the cMS and the Applicant are highlighted in yellow. Information no longer relevant ~~is struck through and shaded~~.

STATEMENT ON OWNERSHIP

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DATA PROTECTION CLAIM

Under Article 59, Regulation 1107/2009/EC, on behalf of the Sponsor Company the applicant claims data protection for these studies. The data protection status and corresponding justification as valid for the respective country will be confirmed in the respective PART A.

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Reviewer comments:

This part of dossier summarizes data related to the toxicological assessment and exposure data for the plant protection product AG-E1-500 SC1/Ethosat 500 SC and has been submitted to support registration according art. art. 33 of 1107/2009 in Poland.
Product was not a representative formulation reviewed during the Annex I inclusion/renewal of active substance(s) and has not been previously evaluated in any EU countries according to the Uniform Principles.
For the current product registration, Applicant provided an *in vivo* toxicity studies which were performed using previous composition of AG-E1-500 SC1. Comparison of both formulations are presented in the confidential Part C of this dossier. Difference in the composition has been considered as admissible, thus studies has been accepted as relevant data to prediction of toxicological potential of the product AG-E1-500 SC1/Ethosat 500 SC.
The testing strategy takes into account methods compliant with the 3R concept for refinement, reduction and replacement of animal testing where applicable and acceptable (please refer Appendix 2 to this dossier).
ZRMS accepted already existing *in vivo* studies and do not request for the new one. Since there are *in vivo* tests already exist the information gained on animal studies are more than just a classification. Existing animal studies allow to identify of effects following a single exposure to the plant protection product can be established. The data is sufficient to indicate the time course and characteristics of the effect with full details of behavioral changes and possible gross pathological findings at post-mortem. These studies are valid for hazard classification and toxicological risk assessment.
NDE assessment and combined exposure calculations provided for operator, workers and B&R resulting from use of AG-E1-500 SC1/Ethosat 500 SC (*SC formulation, containing 500 g/L ethofumesate for use as a herbicide; refer dRR part B0*) considering critical use(s), identify safe applications of the product AG-E1-500 SC1/Ethosat 500 SC.

6 Mammalian Toxicology (KCP 7)

6.1 Summary

Table 6.1-1: Information on AG-E1-500 SC1 *

Product name and code	AG-E1-500 SC1
Formulation type	Suspension concentrate [Code: SC]
Active substance(s) (incl. content)	Ethofumesate, 500 g/L
Function	Herbicide
Product already evaluated as the ‘representative formulation’ during the approval of the active substance(s)	No
Product previously evaluated in another MS according to Uniform Principles	No

* Information on the detailed composition of AG-E1-500 SC1 can be found in the confidential dRR Part C.

Justified proposals for classification and labelling

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

Table 6.1-2: Justified proposals for classification and labelling for AG-E1-500 SC1 according to Regulation (EC) No 1272/2008

Hazard class(es), categories:	Not classified
Hazard pictograms or Code(s) for hazard pictogram(s):	n.a.
Signal word:	n.a.
Hazard statement(s):	n.a.
Precautionary statement(s):	n.a.
Additional labelling phrases:	[EUH401] To avoid risks to man and the environment, comply with the instructions for use. [EUH208] "Contains 1,2-Benzisothiazol-3(2H)-one. May produce an allergic reaction."

Table 6.1-3: Summary of risk assessment for operators, workers, bystanders and residents for AG-E1-500 SC1

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

No unacceptable risk for operators, workers, bystanders and residents was identified when the product is used as intended.
A summary of the critical uses and the overall conclusion regarding exposure for operators, workers and bystanders/residents is presented in the following table.

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

1	2	3	4	5	6	7	8	9	10			
Use-No.*	**Crops and situation (e.g. growth stage of crop)**	**F, Fn, Fpn G, Gn, Gpn or I ****	**Application**		**Application rate**		**PHI (d)**	**Remarks:** **(e.g. safener/synergist (L/ha))** **critical gap for operator, worker, bystander or resident exposure based on [Exposure model]**	**Acceptability of exposure assessment**			
			Method / Kind **(incl. application technique *****	**Max. number (min. interval between applications)**	**Max. application rate kg as/ha** **a) a.s. 1** **b) a.s. 2** **a) per use** **b) per crop/ season**	**Water L/ha** **min / max**			**Operator**	**Worker**	**Bystander**	**Residents**
1,2	Sugar beet Fodder beet	F	Spraying, LC, TM	2 (5)	a) 0.5 b) 1.0	100 - 400	n.a.				#	

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1
** F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application
*** e.g. LC: low crops, HC: high crop, TM: tractor-mounted, HH: hand-held
# In case when AAOEL has not been set residents exposure also covers bystander exposure. EFSA Journal 2014;12(10):3874, 55 pp., point 4.1 (..) 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. (..)
Explanation for column 10 "Acceptability of exposure assessment"

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

Data gaps

Noticed data gaps are: none.

6.2 Toxicological Information on Active Substance(s)

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

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

Common Name	Ethofumesate
CAS-No.	26225-79-6
Classification and proposed labelling	
With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended)	None
Additional C&L proposal	None
Agreed EU endpoints	
AOEL systemic	2.5 mg/kg bw/day
AAOEL	Not derived, not necessary
Reference	Peer review of the pesticide risk assessment of the active substance ethofumesate, EFSA Journal 2016;14(1):4374
Conditions to take into account/critical areas of concern with regard to toxicology	
	The toxicity studies were not representative of the proposed technical specification for the active substance and associated impurities
Reference	Peer review of the pesticide risk assessment of the active substance ethofumesate, EFSA Journal 2016;14(1):4374

6.3 Toxicological Evaluation of Plant Protection Product

Toxicological studies were performed with a previous composition of AG-E1-500 SC1. The results of these studies can be taken into account for AG-E1-500 SC1 as the difference in the composition can be regarded as minor. Details of both compositions are presented in the confidential Part C of this dossier.
A summary of the toxicological evaluation for AG-E1-500 SC1 is given in the following table. Full summaries of the studies are described in detail in Appendix 2. Studies on the product have not been previously considered within an EU peer review process.

Table 6.3-1: Summary of evaluation of the studies on acute toxicity including irritancy and skin sensitisation for AG-E1-500 SC1*

Type of test, species, model system (Guideline)	Result	Acceptability	Classification (acc. To the criteria in Reg. 1272/2008)	Reference
LD_{50} oral, rat (OECD 423)	> 2000 mg/kg bw	Yes	None	xxxxxxxxxxx 1999a
LD_{50} dermal, rat (OECD 402)	> 4000 mg/kg bw	Yes	None	xxxxxxxxxxx 1999b
LC_{50} inhalation, rat (OECD 403)	> 4.29 mg/L air	Yes	None	xxxxxxxxxxxxx 1999
Skin irritation, rabbit (OECD 404)	Mild irritant (Draize)	Yes	None	xxxxxxxxxxxx 1999c
Eye irritation, rabbit	Minimal irritant (Kay	Yes	None	xxxxxxxx

(OECD 405)	and Calandra)			
Skin sensitisation, Guinea pig (OECD 406)	Mild sensitising (93/21/EEC)	Yes	None	xxxxxxxxxx 1999e
Supplementary studies for combinations of plant protection products	No data – not required	-	-	-

*studies were conducted with the previous composition of AG-E1-500 SC1

Table 6.3-2: Additional toxicological information relevant for classification/labelling of AG-E1-500 SC1

	Substance (Concentration in product, % w/w)	**Classification of the substance (acc. to the criteria in Reg. 1272/2008)**	**Reference**	**Classification of product (acc. to the criteria in Reg. 1272/2008)**
Toxicological properties of non-active substance(s) (relevant for classification of product)*	n.a.	n.a.	Reg. 1272/2008 / MSDSs*	No classification triggered
Further toxicological information	No data – not required			

* Material safety data sheet by the applicant

None of the ingredients of AG-E1-500 SC1 triggers further classification, in accordance with Regulation (EC) 1272/2008. For further information on the co-formulants please refer to the Confidential Part (Part C).

6.4 Toxicological Evaluation of Groundwater Metabolites

Reference is made to Part B section 10.

6.5 Dermal Absorption (KCP 7.3)

No dermal absorption studies were performed with the formulation AG-E1-500 SC1. Default values for water-based formulations defined in the EFSA Guidance document on dermal absorption (EFSA Journal 2017;15(6):4873_2017) of 10% for the concentrate and 50% for the dilution are considered.

Reviewer comment:

Table 6.5-1: Default dermal absorption rates for AG-E1-500 SC1 (ethofumesate)

	Value	**Justification for value**	**Acceptability of justification**
Concentrate	10 %	Default values for water-based formulations defined in the EFSA Guidance document on dermal absorption (EFSA Journal 2017;15(6))	Justification accepted. Endpoint can be used for current product.
Dilution	50 %	Default values for water-based formulations defined in the EFSA Guidance document on dermal absorption (EFSA Journal 2017;15(6))	Justification accepted. Endpoint can be used for current product.

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	AG-E1-500 SC1
Formulation type	Suspension concentrate [SC]
Category	Herbicide
Container size(s), short description	1 L, 5 L, 10 L and 20 L HDPE; for more details refer to packaging description in Section 4.
Active substance(s) (incl. content)	Ethofumesate, 500 g/L
AOEL systemic	2.5 mg/kg bw/d
AAOEL	Not derived, not necessary
Inhalation absorption	100 %
Oral absorption	>80 %
Dermal absorption (EFSA default values 2017)	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 Table 6.1-4. A list of all intended uses within the zone is given in Part B, Section 0.

Justification

AG-E1-500 SC1 is applied in sugar beets (BBCH 10 – 18). The critical GAP has been defined following evaluation of the individual GAPs for each scenario in each relevant Member State.

Critical GAP identified: use n°1 and 2

- The maximum application rate per growth season/year is 1 kg a.s/ha, with 2 applications per year at a use rate of 0.5 kg a.s./ha/application.
  (This covers the scenario of 3 applications/year at a use rate of 0. 3 kg a.s./ha/application leading to an annual application rate of 0.9 kg a.s./ha)
- The minimum water volume relevant for this zone is 100 L/ha
- The minimum spray interval is 5 days

6.6.2 Operator exposure (KCP 7.2.1)

6.6.2.1 Estimation of operator exposure

A summary of the exposure model used for estimation of operator exposure to the active substances during application of according to the critical use(s) of AG-E1-500 SC1 is presented in Table 6.6-2. Outcome of the estimation is presented in Table 6.6-3. Detailed calculations are in Appendix 3.

Table 6.6-2: Exposure model for intended uses

Critical use(s)	Sugar- and Fodder beets 2x 0.5 kg a.s./ha, Spray volume 100L/ha, minimum spray interval 5 days.

Model(s)	EFSA-OPEX [EFSA, guidance document on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products (EFSA Journal 2014;12(10):3874] latest version March 30, 2015

Table 6.6-3: Estimated operator exposure to ethofumesate

Model data	Level of PPE	Total absorbed dose (mg/kg/day)	% of systemic AOEL (2.5 mg/kg b.w./d)
Outdoor downward spraying, vehicle mounted to root and tuber vegetables, 50 ha/day 2 applications with 0.5 kg a.s. /ha each and spray interval of 5 days, minimum spray volume 100L/ha Low volatility, standard assumptions for dermal absorption			
EFSA AOEM	Work wear – arms, body and legs covered (no gloves)	0.1318	5.27%

Results
The estimated operator exposure wearing normal work clothing - but no gloves during mixing/loading or application - accounts for about 5% of the established AOEL.

It is concluded that there is no undue risk to operators when handling AG-E1-500 SC1 according to label instructions for safe use.

6.6.3 Measurement of operator exposure

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

6.6.4 Worker exposure (KCP 7.2.3)

6.6.4.1 Estimation of worker exposure

~~**Błąd! Nie można odnaleźć źródła odwołania.**~~ 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 AG-E1-500 SC1 according to the critical use(s). Outcome of the estimation is presented in Table 6.6-5. Detailed calculations are in Appendix 3.

Table 6.6-4: Exposure models for intended uses

Critical use(s)	Sugar- and Fodder beets 2 x 0.5 kg a.s./ha, Spray volume 100L/ha, minimum spray interval 5 days, DFR DT50 30 days.
Model	EFSA-OPEX [EFSA, guidance document on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products (EFSA Journal 2014;12(10):3874] latest version March 30, 2015

Table 6.6-5 Estimated worker exposure

		Ethofumesate	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
Number of applications and application rate: 2 x 0.5 kg a.s./ha, Spray volume 100L/ha, minimum spray interval 5 days. DFR DT50 30 days			
2 hours/day. inspection irrigation, TC: 1 400 cm^2/person/h when arms, body and legs covered Body weight: 60 kg	Work clothing i.e. wearing long sleeved shirt, long trousers ("permeable") but no gloves	0.0662	2.65%

Results
The exposure of the worker with work wear (arms, body and legs covered, no gloves) accounts for about 3% of the established AOEL.

It is concluded that there is no unacceptable risk anticipated when re-entering crops treated with AG-E1-500 SC1. As a standard rule, it should be mentioned on the label that treated crops should not be re-entered before spray deposits on leaf surfaces have completely dried**.**

6.6.4.2 Refinement of generic DFR value (KCP 7.2)

Since the worker exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) will not be exceeded under conditions of intended uses and considering above mentioned PPE, exposure estimates using dislodgeable residue data are considered to be not necessary.

6.6.4.3 Measurement of worker exposure

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

6.6.5 Bystander and resident exposure (KCP 7.2.2)

6.6.5.1 Estimation of bystander and resident exposure

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

- the European Food Safety Authority , and
- the European Commission Standing Committee.

Therefore, this waiver is presented in line with the Guidance of the European Commission.

According to EFSA longer term exposure of bystanders is covered by the resident scenario.

Table 6.6-6 shows the exposure model used for estimation of resident exposure to ethofumesate. 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)	Sugar- and Fodder beets 2x 0.5 kg a.s./ha, Spray volume 100L/ha, minimum spray interval 5 days. DFR DT50 30 days
Model (resident)	EFSA-OPEX [EFSA, guidance document on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products (EFSA Journal 2014;12(10):3874] latest version March 30, 2015

Table 6.6-7: Estimated bystander and resident exposure

	Ethofumesate	
Model data: EFSA	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
All pathways: (mean values)		
Residents child	0.1071	4.29%
Residents adults	0.0456	1.82%

Results
The exposure estimates for residents result in values accounting for about 4% and 2% of the AOEL for the child and adult scenario respectively.

It is concluded that there is no undue risk to residents upon the application of AG-E1-500 SC1.

6.6.5.2 Measurement of bystander and/or resident exposure

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

6.6.6 Combined exposure

Not relevant.

Appendix 1 Lists of data considered in support of the evaluation

List of data submitted by the applicant and relied on

Data point	Author(s)	Year	**Title** **Company Report No.** **Source (where different from company)** **GLP or GEP status** **Published or not**	**Vertebrate study Y/N**	**Owner**
KCP 7.1.1/01	xxxxxxxxxx	1999a	Ethosat 500: Acute oral toxicity study in the rat – acute toxic class method Report nº. 644/040 xxxxxxxxxxxxxxxxxxxxx GLP Unpublished	Y	ADM*
KCP 7.1.2/01	xxxxxxxxxxxxxxx	1999b	Ethosat 500: Acute dermal toxicity (limit test) in the rat Report nº. 644/041 xxxxxxxxxxxxxxxxxxxxx GLP Unpublished	Y	ADM*
KCP 7.1.3/01	xxxxxxxxxxxx	1999	Ethosat 500: Acute inhalation toxicity (nose only) study in the rat Report nº. 644/042 xxxxxxxxxxxxxxxxxxxxx GLP Unpublished	Y	ADM*
KCP 7.1.4/01	xxxxxxxxxxxx	1999c	Ethosat 500: Acute dermal irritation test in the rabbit Report nº. 644/043 GLP Unpublished	Y	ADM*
KCP 7.1.5/01	xxxxxxxxxxxxxx	1999d	Ethosat 500: Acute eye irritation test in the rabbit Report nº. 644/044 xxxxxxxxxxxxxxxxxxxxxxxx GLP Unpublished	Y	ADM*
KCP 7.1.6/01	xxxxxxxxxxxxx	1999e	Ethosat 500: Magnusson & Kligman Maximisation study in the guinea pig Report nº. 644/045 xxxxxxxxxxxxxxxxxxxxxxx	Y	ADM*

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

*The original sponsor company Feinchemie Schwebda GmbH was re-named to ADAMA Agan Ltd. (ADM), which is a member of ADAMA Agricultural Solutions.
Under Article 59, Regulation 1107/2009/EC, the sponsor company claims data protection for these studies. For details on country specific data protection, refer to Part A

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

None.

List of data submitted by the applicant and not relied on

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

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

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

Appendix 2 Detailed evaluation of the studies relied upon

A 2.1 Statement on bridging possibilities

Acute toxicity
The acute toxicity studies were performed with the previous formulation of AG-E1-500 SC1, which is very similar to AG-E1-500 SC1. The results of the studies can be taken into account for AG-E1-500 SC1 as the difference in composition can be regarded as minor (addressed in Part C).

Dermal absorption
No dermal absorption studies were performed with the formulation AG-E1-500 SC1. Default values defined in the EFSA Guidance document on dermal absorption (EFSA Journal 2017;15(6):48732017) of 10% for the concentrate and 50% for the dilution are considered.

Comments of zRMS:	Accepted. Comparison of both formulations are presented in the confidential Part C of this dossier. Difference in the composition has been considered as admissible, thus studies has been considered as relevant data to prediction of toxicological potential of the product AG-E1-500 SC1/Ethosat 500 SC.

A 2.2 Acute oral toxicity (KCP 7.1.1)

Comments of zRMS:	Data has been reviewed for compliance with the current guidelines, resulting from scientific progress. Study (xxxxxx 1999a) implements 3R rules minimizing the number of animals required to estimate the acute oral toxicity of a chemical. Method uses pre-defined doses and the results allow a substance to be ranked and classified according to the CLP for the classification of chemicals which cause acute toxicity Noted deviation has no critical impact on study outcome. Results of the study and conclusions are adequate for risk assessment and classification purpose. Study accepted.

Reference:	KCP 7.1.1/01
Report	Ethosat 500: Acute oral toxicity study in the rat – acute toxic class method, xxxxxxxxxxxxxx., 6 July 1999, xxxxxxxxxxxxxxxxxx, Report nº. 644/040
Guideline(s):	OECD 423
Deviations:	This study was performed before the revision of OECD TG 423 and the entry into force of Regulation (EC) 1107/2009 and CLP Regulation (EC) 1272/2008. Technical acceptability (acceptability of the technical performance and outcome of the study) and analytical acceptability (analytical method validation) were not provided in this study report. These deviations are not considered to influence the quality or integrity of the study.
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	No

Materials and methods

Test material (Lot/Batch No.)	AG-E1-500 SC1 (batch no. 00504209)
Species	Rat, Sprague-Dawley CD
No. of animals (group size)	3 males and 3 females
Dose(s)	2000 mg/kg bw
Exposure	Once by gavage
Vehicle/Dilution	None, liquid test material was used as supplied
Post exposure observation period	½, 1, 2, 4 hours and thereafter once daily for 14 days
Remarks	None

Results and discussions

Table A 1: Results of acute oral toxicity study in rats of AG-E1-500 SC1

Dose (mg/kg bw)	Toxicological results *	Duration of signs	Time of death	LD50 (mg/kg bw) (14 days)
Male rats				
2000	0/3/3	Day 1 only	scheduled sacrifice	> 2000
Female rats				
2000	0/0/3	n.a.	scheduled sacrifice	> 2000

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

Table A 2: Summary of findings of acute oral toxicity study in rats of AG-E1-500 SC1

Mortality:	No mortality occurred.
Clinical signs:	Hunched posture was noted in all males during the day of dosing and one day after dosing.
Body weight:	Throughout the 14-day observation period, the weight gain of the animals was within the normal range of variation for this strain.
Macroscopic examination:	At necropsy, no treatment-related macroscopic findings were noted.

Conclusion

Under the conditions of the study, the oral LD50 of AG-E1-500 SC1 is > 2000 mg/kg bw in rats. No classification is required according to Regulation (EC) No. 1272/2008.

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

Comments of zRMS:	Data has been reviewed for compliance with the current guidelines, resulting from scientific progress. In the study (xxxxxxxxxxxxxxxxxxx., 1999b) tested material has not been administered at doses which cause pain and distress due to potential corrosive or severely irritant actions (note: AG-E1-500 SC1 is not classified as skin irritant). Noted deviation has no critical impact on study outcome. Results of the study and conclusions are adequate for risk assessment and classification purpose. Study accepted.

Reference: KCP 7.1.2/01

Report: Ethosat 500: Acute dermal toxicity (limit test) in the ratxxxxxxxxxxxxx 8 July 1999, xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx Report nº. 644/041

Guideline(s): OECD 402

Deviations: This study was performed before the revision of OECD TG 402 and the entry into force of Regulation (EC) 1107/2009 and CLP Regulation (EC) 1272/2008.
Technical acceptability (acceptability of the technical performance and outcome of the study) and analytical acceptability (analytical method validation) were not provided in this study report.
These deviations are not considered to influence the quality or integrity of the study.

GLP: Yes

Acceptability: Yes

Duplication (if vertebrate study): No

Materials and methods

Test material (Lot/Batch No.)	AG-E1-500 SC1 (batch no. 00504209)
Species	Rat, Sprague-Dawley CD
No. of animals (group size)	5 rats/sex
Dose(s)	4000 mg/kg bw
Exposure	24 hours (dermal, semi-occlusive)
Vehicle/Dilution	None
Post exposure observation period	½, 1, 2, 4 hours and thereafter once daily for 14 days
Remarks	None

Results and discussions

Table A 3: Results of acute dermal toxicity study in rats of AG-E1-500 SC1

Dose (mg/kg bw)	Toxicological results *	Duration of signs	Time of death	LD50 (mg/kg bw) (14 days)
Male rats				
2000	0/0/5	n.a.	scheduled sacrifice	> 4000
Female rats				

Dose (mg/kg bw)	Toxicological results *	Duration of signs	Time of death	LD50 (mg/kg bw) (14 days)
2000	0/0/5	n.a.	scheduled sacrifice	> 4000

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

Table A 4: Summary of findings of acute dermal toxicity study in rats of AG-E1-500 SC1

Mortality:	No mortality occurred.
Clinical signs:	No clinical signs of toxicity were noted.
Dermal reactions:	Yellow-colored staining at the treatment sites of all animals. The staining did not affect the evaluation of the skin response. No signs of skin irritation were noted during the study.
Body weight:	Throughout the 14-day observation period, the weight gain of the animals was within the normal range of variation for this strain.
Macroscopic examination:	At necropsy, no treatment-related macroscopic findings were noted.

Conclusion

Under the experimental conditions, the dermal LD_{50} of AG-E1-500 SC1 is > 4000 mg/kg bw in rats. No classification is required according to Regulation (EC) No. 1272/2008.

A 2.4 Acute inhalation toxicity (KCP 7.1.3)

Comments of zRMS:	Data has been reviewed for compliance with the current guidelines, resulting from scientific progress. In the study (xxxxxxxxxxxxxx 1999) animals are exposed to one limit concentration for a predetermined duration (4 hours) and obtain sufficient information on the acute toxicity of test article to enable its classification and to provide lethality data (LC_{50}) for both sexes as needed for quantitative risk assessments. Noted deviation has no critical impact on study outcome. Results of the study and conclusions are adequate for risk assessment and classification purpose. Study accepted.

Reference: KCP 7.1.3/01

Report: Ethosat 500: Acute inhalation toxicity (nose only) study in the rat xxxxxxxxxxx., 19 August 1999, xxxxxxxxxxxxxxxxxxxxx, Report nº. 644/042

Guideline(s): OECD 403

Deviations: This study was performed before the revision of OECD TG 403 and the entry into force of Regulation (EC) 1107/2009 and CLP Regulation (EC) 1272/2008.
Technical acceptability (acceptability of the technical performance and outcome of the study) and analytical acceptability (analytical method validation) were not provided in this study report.
These deviations are not considered to influence the quality or integrity of the study.

GLP: Yes

Acceptability: Yes

Duplication (if vertebrate study): No

Materials and methods

Test material (Lot/Batch No.)	AG-E1-500 SC1 (batch no. 00504209)
Species	Rat, Sprague-Dawley CD
No. of animals (group size)	5 rats/sex
Exposure Chamber Concentration	4.29 mg/L air (maximum attainable concentration)
Exposure	4 hours (nose only)
Vehicle	Distilled water
Post exposure observation period	14 days
Remarks	None

Results and discussions

Table A 5: Concentration(s) and exposure conditions

Nominal conc. (mg/L air)	Actual conc. (mg/L air) Maximum attainable	MMAD * (µm)	Inhalable fraction (% < 4 µM)	GSD ** (µm)
106.7	4.29	5.60	37.1	2.75

* MMAD = Mass Median Aerodynamic Diameter
** GSD = Geometric Standard Deviation

Table A 6: Results of acute inhalation toxicity study in rats of AG-E1-500 SC1

Concentration (mg/L air)	Toxicological results *	Duration of signs	Time of death	LC_{50} (mg/L air) (14 days)
Male rats				
4.29	0/3/3	up to day 2	scheduled sacrifice	> 4.29
Female rats				
4.29	0/3/3	up to day 2	scheduled sacrifice	> 4.29

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

Table A 7: Summary of findings of acute inhalation toxicity study in rats of AG-E1-500 SC1

Mortality:	No mortality occurred.
Clinical signs:	Wet fur, hunched posture, piloerection and increased respiratory rate were observed. One female female showed red/brown staining around the snout. This was not longer evident one hour after completion of exposure. By day 2 all animals had recovered.
Body weight:	All animals gained body weight during the course of the study.
Macroscopic examination:	At necropsy, dark foci in the lungs were observed in two males. Otherwise, no gross abnormalities were noted.

Conclusion

Under the experimental conditions, the inhalation LC_{50} of AG-E1-500 SC1 is > 4.29 mg/L air in rats. No classification is required according to Regulation (EC) No. 1272/2008.

A 2.5 Skin irritation (KCP 7.1.4)

A 2.5.1 Study 1

Comments of zRMS:	Study (xxxxxxxxx1999c) has been reviewed for compliance with the current guidelines, resulting from scientific progress. As we mentioned and explained in the our general comment (see p.5 to this dRR) already existed *in vivo* study has been accepted and considered by the ZRMS as reliable for the hazard assessment. Test product was applied in a single dose to the skin of an experimental animal; untreated skin areas of the test animal serve as the control. The degree of irritation/corrosion was read and scored at specified intervals in order to provide a complete evaluation of the effects. The duration of the study was sufficient to evaluate the reversibility or irreversibility of the effects observed. Noted deviation has no critical impact on study outcome. Results of the study and conclusions are adequate for risk assessment and classification purpose. Study accepted.

Reference:	KCP 7.1.4/01
Report	Ethosat 500: Acute dermal irritation test in the rabbit, xxxxxxxxxxx., 8 July 1999, xxxxxxxxxxxxx, Report nº. 644/043
Guideline(s):	OECD 404
Deviations:	This study was performed before the revision of OECD TG 404 and the entry into force of Regulation (EC) 1107/2009 and CLP Regulation (EC)

1272/2008.
Technical acceptability (acceptability of the technical performance and outcome of the study) and analytical acceptability (analytical method validation) were not provided in this study report.
These deviations are not considered to influence the quality or integrity of the study.

GLP: Yes

Acceptability: Yes

Duplication (if vertebrate study) No

Materials and methods

Test material (Lot/Batch No.)	AG-E1-500 SC1 (batch no. 00504209)
Species	Rabbit, New Zealand White
No. of animals (group size)	1 male, 2 females
Initial test using one animal	No
Exposure	0.5 mL per test site (undiluted), semi-occluded, 4 hours
Irrigation (time point)	None
Vehicle/Dilution	None
Post exposure observation period	24, 48, and 72 hours
Remarks	None

Results and discussions

Table A 11: Individual skin reactions - Draize classification scheme

	Observation time (hours)	Animal No. 186 Male	Animal No. 187 Female	Animal No. 188 Female	Total
Erythema Grade	1	1	1	1	(3)
	24	1	1	1	3
	48	0	0	0	(0)
	72	0	0	0	0
Oedema Grade	1	1	0	0	(1)
	24	1	0	0	1
	48	0	0	0	(0)
	72	0	0	0	0
Sum of 24 and 72 hours readings = 4 Primary irritation index 4/6 = 0.7 Classification: Mild irritant					

(): Total values not considered for primary irritation index

Table A 12: Individual skin reactions of AG-E1-500 SC1 and mean scores for labelling according to Regulation (EC) No. 1272/2008

	Observation time (hours)	Animal No. 186 Male	Animal No. 187 Female	Animal No. 188 Female
Erythema Grade	24	1	1	1
	48	0	0	0
	72	0	0	0
Total		1	1	1

Mean score		0.3	0.3	0.3
Oedema Grade	24 48 72	1 0 0	0 0 0	0 0 0
Total		1	0	0
Mean score		0.3	0	0

Mortality	No mortality occurred.
Clinical signs:	No clinical signs of systemic toxicity were observed during the entire study length for all animals.
Body weights	The body weight development of all animals was within the expected range.
Irritation, corrosion	No corrosive effects were noted. The test material caused very slight erythema and oedema to the intact skin of rabbits.

Conclusion

Under the conditions of the present study, the single dermal application of the test item AG-E1-500 SC1 to three rabbits at a dose of 0.5 mL caused a primary irritation index of 0.7. According to the Draize scheme AG-E1-500 SC1 was classified as mild irritant.
According to Regulation (EC) No. 1272/2008 no classification is required.

A 2.6 Eye irritation (KCP 7.1.5)

A 2.6.1 Study 1

Comments of zRMS:	Study (xxxxxxxxxxxxx.1999d) has been reviewed for compliance with the current guidelines, resulting from scientific progress. As we mentioned and explained in the our general comment (see p.5 to this dRR) already existed *in vivo* study (note: AG-E1-500 SC1 is not classified as skin irritant) has been accepted and considered by the ZRMS as reliable for the hazard assessment. In the mentioned study degree of eye irritation/serious eye damage were evaluated by scoring lesions of conjunctiva, cornea, and iris, at specific intervals. Duration of the study was sufficient to evaluate the reversibility or irreversibility of the effects. Noted deviation has no critical impact on study outcome. Results of the study and conclusions are adequate for risk assessment and classification purpose. Study accepted.

Reference:	KCP 7.1.5/01
Report	Ethosat 500: Acute eye irritation test in the rabbit, xxxxxxxxxx 8 July 1999, xxxxxxxxxxxxxxxxxxxxxxxxxxxxx, Report nº. 644/044
Guideline(s):	OECD 405
Deviations:	This study was performed before the revision of OECD TG 405 and the entry into force of Regulation (EC) 1107/2009 and CLP Regulation (EC) 1272/2008. Technical acceptability (acceptability of the technical performance and outcome of the study) and analytical acceptability (analytical method validation) were not provided in this study report. These deviations are not considered to influence the quality or integrity of the study.
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	No

Materials and methods

Test material (Lot/Batch No.)	AG-E1-500 SC1 (batch no. 00504209)
Species	Rabbit, New Zealand White
No. of animals (group size)	3 males
Initial test using one animal	No
Exposure	0.1 mL (single instillation in conjunctival sac)
Irrigation (time point)	No
Vehicle/Dilution	None
Post exposure observation period	1, 24, 48, 72 hours
Remarks	None

Results and discussions

Table A 13: Individual eye reactions of AG-E1-500 SC1 and mean scores for labelling according to Regulation (EC) No. 1272/2008

Animal No.		Scores after treatment *				Mean scores (24-72 h)
		1h	24 h	48 h	72 h	
1	Corneal opacity	0	0	0	0	0
	Iritis	0	0	0	0	0
	Redness conjunctivae	1	0	0	0	0
	Chemosis conjunctivae	1	0	0	0	0
2	Corneal opacity	0	0	0	0	0
	Iritis	0	0	0	0	0
	Redness conjunctivae	1	0	0	0	0
	Chemosis conjunctivae	1	0	0	0	0
3	Corneal opacity	0	0	0	0	0
	Iritis	0	0	0	0	0
	Redness conjunctivae	1	0	0	0	0
	Chemosis conjunctivae	1	0	0	0	0

* scores in the range of 0 to 4 for cornea opacity and chemosis, 0 to 3 for redness of conjunctivae and 0 to 2 for iritis

Mortality	No mortality occurred.
Clinical signs:	No effects were observed on cornea and iris. Minimal conjunctival irritation was noted in all animals on hour after treatment. After 24 hours all eyes appeared normal.

Conclusion

Under the experimental conditions, a single ocular application of the test item AG-E1-500 SC1 to rabbits at a dose of 0.1 mL caused minimal conjunctival irritation in all animals one hour after treatment. After 24 hours all eyes appeared normal. According to the Kay and Calandra proposed classification scheme the test material was minimal irritant to the eye.
According to Regulation (EC) No. 1272/2008 no classification is required.

A 2.7 Skin sensitisation (KCP 7.1.6)

Comments of zRMS:	Study (xxxxxxxxxxxxxxxxx.1999c) has been reviewed for compliance with the current guidelines, resulting from scientific progress. As we mentioned and explained in the our general comment (see p.5 to this dRR) already existed *in vivo* study has been accepted and considered by the ZRMS as reliable for the hazard assessment. Additionally regarding following information available in the REACH Reg. 1907/2006, (..) *In vivo* skin sensitisation studies that were carried out or initiated before 10 May 2017, and that meet the requirements set out in Article 13(3), first subparagraph, and Article 13(4) shall be considered appropriate to address this standard information requirement. (..) (refer ANNEX VII, point 8.3.2. Skin sensitisation, *in vivo*) study (xxxxxxxxxxxx A.1999c) has been accepted. Test animals (Guinea pigs) has been exposed to the test material by intradermal injection and epidermal application (induction exposure). Following a rest period of the days, animals are exposed to a challenge dose. Skin reaction has been sufficiently assess in compared with that demonstrated by control animals. Noted deviation has no critical impact on study outcome. Results of the study and conclusions are adequate for risk assessment and classification purpose. Study accepted.

Reference:	KCP 7.1.6/01
Report	Ethosat 500: Magnusson & Kligman Maximisation study in the Guinea pig, xxxxxxxxxxxxxxxxx., 28 July 1999, xxxxxxxxxxxxxxxxxxxxxxxxxxxxxx, Report nº. 644/045
Guideline(s):	OECD 406
Deviations:	This study was performed before the entry into force of Regulation (EC) 1107/2009 and CLP Regulation (EC) 1272/2008. Technical acceptability (acceptability of the technical performance and outcome of the study) and analytical acceptability (analytical method validation) were not provided in this study report. These deviations are not considered to influence the quality or integrity of the study.
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	No

Materials and methods

Test material (Lot/Batch No.)	AG-E1-500 SC1 (batch no. 00504209)
Species	Guinea pig
No. of animals (group size)	Main study: 20 for the test and 10 for control
Selection of concentrations for intradermal induction	Four concentrations (1, 5, 10 and 25% in distilled water w/v). The amount of 0.1 ml was intradermally injected. Degree of erythema were assessed at 24, 48, 72 hours and 7 days after injection
Selection of concentrations for topical application	Two Guinea pigs (intradermally injected with Freud's adjuvant) were treated with the undiluted test material and three preparations of the test material (75, 50 , and 25% in distilled water). The degree of erythema and oedema were evaluated at 1, 24 and 48 hours. The highest concentration causing mild to moderate dermal irritation was selected for the topical induction in the main study.
Selection of concentrations for	Two Guinea pigs were treated with the undiluted test material and three preparations of

topical challenge	the test material (75, 50 , and 25% in distilled water) for 24 hours. The degree of erythema and oedema were evaluated at 1, 24 and 48 hours. The highest non-irritant concentration and one lower concentration were selected for the topical challenge in the main study.
Main study - Induction of the test animals	3 injections were made: a) Freund's complete adjuvant plus distilled water (1:1) b) 5% w/v formulation in distilled water c) 5% w/v test material in a (1:1) preparation of Freund's complete adjuvant plus distilled water At 24 and 48 hours after intradermal injections the degree of erythema was evaluated. One week later the animals were treated with a topical application of undiluted test material. The degree of erythema and oedema were evaluted a 1 and 24 hours after application.
Main study - Induction of the control animals	In control animals 3 injections were made: a) Freund's complete adjuvant plus distilled water (1:1) b) 5% w/v distilled water c) 50% w/v formulation of distilled water in a 1:1 mixture of of Freund's complete adjuvant plus distilled water At 24 and 48 hours after intradermal injections the degree of erythema was evaluated. One week later the test material were treated with a topical application of filter paper without test material. The degree of erythema and oedema were evaluted at 1 and 24 hours after application.
Main study - Challenge	For the challenge the maximum non-irritant concentrations of 75% and 50% w/v in distilled water were applied at different sites for 24 hours. At 24 and 48 hours after challenge dressing removal the degree of erythema and oedema were evaluated.
Remarks	None

Results and discussions

Concentrations selected for the induction and challenge of the main study	Intradermal induction: • 5% w/v in distilled water Topical application • Undiluted Topical challenge • 75% and 50% w/v in distilled water
Skin reaction after intradermal induction	Intense erythema and swelling were noted at the intradermal induction site of all test animals at 24 and 48 hours.
Skin reaction after topical application	Erythema and oedema were noted in all test animals after 1 hour and in 17 out of 20 after 24 hours. Similar findings were noted in control animals.
Skin reactions after topical challenge	Four out of 20 animals tested with 75% and 50% w/v in distilled water showed slight skin reactions including erythema grade one and very slight oedema at 24 and 48 hours. Control animals showed no reactions.

Additional information/assessments has been included by the zRMS in response to comments received from the cMS and the Applicant

Table A2.7-1 Individual skin reactions in test animals at challenge (concentration75% and 50% v/v); vehicle distilled water.

Animal Number	Skin reaction (hours after removal of dressing)											
	24 hours						48 hours					
	50%			75%			50%			75%		
	Er	Oe	other	Er	Oe	other	Er	Oe	other	Er	Oe	other
1	0	0	-	0	0	-	0	0	-	0	0	-
2	1	1	-	1	0	-	1	1	-	1	0	-
3	0	0	-	0	0	-	0	0	-	0	0	-
4	1	0	-	1	1	-	1	0	D	1	0	D
5	0	0	-	0	0	-	0	0	-	0	0	-
6	0	0	-	0	0	-	0	0	-	0	0	-
7	0	0	-	1	0	-	1	0	-	1	0	-
8	0	0	-	0	0	-	0	0	-	0	0	-

9	0	0	-	0	0	-	0	0	-	0	0	-
10	0	0	-	0	0	-	0	0	-	0	0	-
11	0	0	-	0	0	-	0	0	-	0	0	-
12	0	0	-	0	0	-	0	0	-	0	0	-
13	1	0	-	1	0	-	1	0	-	1	0	-
14	0	0	-	0	0	-	0	0	-	0	0	-
15	0	0	-	0	0	-	0	0	-	0	0	-
16	0	0	-	0	0	-	0	0	-	0	0	-
17	0	0	-	0	0	-	0	0	-	0	0	-
18	0	0	-	0	0	-	0	0	-	0	0	-
19	0	0	-	0	0	-	0	0	-	0	0	-
20	0	0	-	0	0	-	0	0	-	0	0	-

Er-erythema; Oe-oedema; - no other reactions noted, D -desquamation

Table A2.7-2 Individual skin reactions in control animals at challenge (concentration75% and 50% v/v); vehicle distilled water.

Animal Number	Skin reaction (hours after removal of dressing)											
	24 hours						48 hours					
	50%			75%			50%			75%		
	Er	Oe	other	Er	Oe	other	Er	Oe	other	Er	Oe	other
21	0	0	-	0	0	-	0	0	-	0	0	-
22	0	0	-	0	0	-	0	0	-	0	0	-
23	0	0	-	0	0	-	0	0	-	0	0	-
24	0	0	-	0	0	-	0	0	-	0	0	-
25	0	0	-	0	0	-	0	0	-	0	0	-
26	0	0	-	0	0	-	0	0	-	0	0	-
27	0	0	-	0	0	-	0	0	-	0	0	-
28	0	0	-	0	0	-	0	0	-	0	0	-
29	0	0	-	0	0	-	0	0	-	0	0	-
30	0	0	-	0	0	-	0	0	-	0	0	-

Er-erythema; Oe- oedema; - no other reactions noted, D -desquamation

Conclusion

The test material AG-E1-500 SC1 caused a sensitization rate of 20% (4/20 test animals) under the experimental conditions. According to Regulation (EC) No. 1272/2008 no classification is required since less than 30 % of the animals were considered as positive in the adjuvant type guinea pig test method for skin sensitisation.

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

This is not applicable as only one active substance is contained in AG-E1-500 SC1.

Comments of zRMS:	Information accepted.

A 2.9 Data on co-formulants (KCP 7.4)

A 2.9.1 Material safety data sheet for each co- formulant

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

A 2.9.2 Available toxicological data for each co-formulant

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

A 2.10 Studies on dermal absorption (KCP 7.3)

No dermal absorption studies were performed with the formulation AG-E1-500 SC1. Default values as defined in the EFSA Guidance document on dermal absorption (EFSA Journal 2017;15(6):48732017) of 10% for the concentrate and 50% for the dilution are considered.

Comments of zRMS:	Justification accepted. Endpoints can be used for current product.

~~Reference:~~	~~KCP 7.3/01~~
~~Comments of zRMS:~~	

A 2.11 Other/Special Studies

None.

Appendix 3 Exposure calculations

A 3.1 Operator exposure calculations (KCP 7.2.1.1)

A 3.1.1 Calculations for ethofumesate

Table A 14: Input parameters considered for the exposure estimation (EFSA-OPEX)

Substance	Ethofumesate	Formulation = Soluble concentrates, emulsifiable concentrate, etc.	Application rate-0.5 kg a.s. /ha	Spray dilution = 5 g a.s./l	Vapour pressure = low volatile substances having a vapour pressure of <5*10-3Pa
Scenario	Root and tuber vegetables / Outdoor / Downward spraying / Vehicle-mounted			Buffer = 2-3	Number applications = 2, Application interval = 5 days
Percentage Absoprtion	Dermal for product = 10	Dermal for in use diluation = 50	Oral = 80	Inhalation = 100	
RVNAS	2.5 mg/kg bw/day		RVAAS	Not acute toxic, thus not derived mg/kg bw/day	
DFR	3 µg a.s./cm2 per kg a.s./ha		DT50	30 days	

Table A 15: Estimation of operator exposure towards ethofumesate

Potential exposure	Longer term systemic exposure mg/kg bw/day		0.2050	% of RVNAS	8.20%
	Acute systemic exposure mg/kg bw/day		0.9755	% of RVAAS	#WERT!
Mixing and Loading		Gloves = No	Clothing = Work wear - arms, body and legs covered	RPE = None	Soluble bags = No
Application		Gloves = No	Clothing = Work wear - arms, body and legs covered	RPE = None	Closed cabin = No
Exposure (including PPE options above)	Longer term systemic exposure mg/kg bw/day		0.1318	% of RVNAS	5.27%
	Acute systemic exposure mg/kg bw/day		0.5878	% of RVAAS	#WERT!

A 3.2 Worker exposure calculations (KCP 7.2.3.1))

A 3.2.1 Calculations for ethofumesate

Table A 16 : Input parameters considered for the estimation of worker exposure

Crop type	Root and tuber vegetables	
Indoor or outdoor	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Worker's task	Inspection, irrigation	
Main body parts in contact with foliage	Hand and body	
Application rate of active substance	0.5	kg a.s./ha
Number of applications	2	
Interval between multiple applications	5	days
Half-life of active substance	30	days

Multiple application factor	1.9	
Dermal absorption of the product	10.00%	
Dermal absorption of the in-use dilution	50.00%	
Dislodgeable foliar residue (i_AppRate*i_DFR)	1.5	µg a.s./cm²
Working hours	2	hr
Dermal transfer coefficient - Total potential exposure	12500	cm²/hr
Dermal transfer coefficient - arms, body and legs covered	1400	cm²/hr
Dermal transfer coefficient - hands, arms, body and legs covered	no TC available for this assessment	cm²/hr

Table A 17 Estimation of worker exposure towards ethofumesate

Worker - Inspection, irrigation	Potential exposure mg/kg bw/day	0.5909	% of RVNAS	23.64%
	Working clothing mg/kg bw/day	0.0662	% of RVNAS	2.65%
	Working clothing and gloves mg/kg bw/day		% of RVNAS	

A 3.3 Bystander and resident exposure calculations (KCP 7.2.2.1)

Table A 18: Input parameters considered for the estimation of resident exposure

Croptype	Root and tuber vegetables	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Buffer strip	2-3	m
Application rate of the product	0.5	kg a.s./ha
Concentration of active substance (in-use dilution for liquid applications)	5	g a.s./l
Dermal absorption of product	10.00%	
Dermal absorption of in-use dilution	50.00%	
Oral absorption	80.00%	
Dislodgeable foliar residue (i_AppRate*i_DFR)	1.5	µg a.s./cm²
Vapour pressure of in-use dilution	low volatile substances	Pa
Concentration in air	0.001	mg/m³
Resident dermal spray drift exposure 75th percentile - adult	0.47	ml spray dilution/person
Resident dermal spray drift exposure 75th percentile - child	0.327	ml spray dilution/person
Resident inhal. spray drift exposure 75th percentile - adult	0.00010	ml spray dilution/person
Resident inhal. spray drift exposure 75th percentile - child	0.00022	ml spray dilution/person
Resident dermal spray drift exposure mean - adult	0.22318	ml spray dilution/person
Resident dermal spray drift exposure mean - child	0.18	ml spray dilution/person
Resident inhal. spray drift exposure mean - adult	0.00009	ml spray dilution/person
Resident inhal. spray drift exposure mean - child	0.00017	ml spray dilution/person
Exposure duration dermal	2	hours
Exposure duration inhalation	24	hours
Exposure duration entry into treated crops	0.25	hours
Light clothing adjustment factor	18.0%	
Breathing rate adult	0.23	m³/day/kg
Breathing rate child (1-3 year old)	1.07	m³/day/kg
Drift percentage on surface (75th percentile)	5.60%	
Drift percentage on surface (mean)	4.10%	
Turf transferable residues percentage	5.00%	
Transfer coeff. of surface deposits-adult	7300	cm²/hour
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm²/hour
Saliva extraction percentage	50.00%	
Surface area of hands mouthed	20	cm²
Frequency of hand to mouth activity	9.5	events/hour
Ingestion rate for mouthing of grass per day	25	cm²
Dislodgeable residues percentage transferability for object to mouth	20.00%	
Transfer coefficient for entry into treated crops (75th percentile) - adult	7500	cm²/h
Transfer coefficient for entry into treated crops (75th percentile) - child	2250	cm²/h
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm²/h
Transfer coefficient for entry into treated crops (mean) - child	1794	cm²/h

Table A 19: Estimation of resident exposure towards ethofumesate

Resident - child	Spray drift (75th percentile) mg/kg bw/day	0.0671	% of RVNAS	2.69%
	Vapour (75th percentile) mg/kg bw/day	0.0011	% of RVNAS	0.04%
	Surface deposits (75th percentile) mg/kg bw/day	0.0075	% of RVNAS	0.30%
	Entry into treated crops (75th percentile) mg/kg bw/day	0.0798	% of RVNAS	3.19%
	All pathways (mean) mg/kg bw/day	**0.1071**	**% of RVNAS**	**4.29%**
Resident - adult	Spray drift (75th percentile) mg/kg bw/day	0.0161	% of RVNAS	0.64%
	Vapour (75th percentile) mg/kg bw/day	0.0002	% of RVNAS	0.01%
	Surface deposits (75th percentile) mg/kg bw/day	0.0032	% of RVNAS	0.13%
	Entry into treated crops (75th percentile) mg/kg bw/day	0.0443	% of RVNAS	1.77%
	All pathways (mean) mg/kg bw/day	**0.0456**	**% of RVNAS**	**1.82%**

A 3.4 Combined exposure calculations for active substances

Not relevant.

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

Not relevant.