

European Commission



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ETHOFUMESATE

Volume 3 – B.6 (PPP) – Ethofol 500 SC

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B.6. TOXICOLOGY AND METABOLISM DATA AND ASSESSMENT OF RISKS FOR HUMANS

Search in the scientific peer reviewed open literature was conducted, covering a period from 2003 to 2013. The notifier stated that their literature search was conducted according to EFSA Guidance “Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009” (EFSA Journal 2011;9(2):2092. [49 pp.]).

The UPL included in the search only the active substance name combined by Boolean operators with some toxicological keywords which they considered relevant to address data requirements. Regarding the inclusion of the trade names in the search it is considered that this should be done case by case (if it is known that the formulation has a higher toxicity than the active substance) since trade names might tremendously increase the “background noise” (amount of information not related to the topic) in the search.

After the rapid and the full-text assessment the UPL concluded that none of the articles retrieved was relevant regarding the properties of the formulations containing ethofumesate. After detailed assessment of the chosen approaches for the literature search, the RMS concluded that the UPL appropriately addressed the scientific peer reviewed open literature.

B.6.1. ACUTE TOXICITY OF PLANT PROTECTION PRODUCT

The representative formulation Ethofol 500 SC was submitted by UPL. None of the studies with representative formulation have been previously evaluated in the European peer review since UPL was not the notifier for the first approval of ethofumesate.

The notifier submitted acute oral, acute dermal, skin irritation, eye irritation and skin sensitisation study (M&K) with Ethofol 500 SC. Additionally, a LLNA test was conducted with the comparable formulation Ethofumesate 500 SC (for comparison please see Volume 4).

No acute inhalation toxicity study was submitted/evaluated in the original DAR (1998). Based on the new data requirements (Commission regulation (EU) No 284/2013) where it is stated that an acute inhalation toxicity study is required if *(i) PPP is to be applied by spraying*, the UPL was asked to provide arguments why no acute inhalation study with Ethofol 500 SC is necessary. Upon this request the UPL submitted a rationale (for details see below under B.6.1.3 and in Volume 4) justifying the non-submission of the study.

B.6.1.1. Oral

Reference:	AD 496: ACUTE ORAL TOXICITY (LIMIT TEST) IN THE RAT
Author(s), year:	██████████ 1996
Report/Doc. number::	665/058 / KCP 7.1.1/01
Guideline(s):	OECD 401 (1987)
GLP:	Yes
Deviations from OECD 401 (1987):	No
Acceptability:	Yes

Materials and Methods

Ethofol 500 SC (=AD 496) was administered by gavage to five male and five female fasted Sprague-Dawley rats which were 5-8 weeks old. The test material (1.8 ml/kg bw) was administered undiluted at the dose level of 2000 mg/kg bw. The observation period was 14 days. Gross pathological examination (external examination and necropsy) was performed in all animals that died during study procedure or were sacrificed at study termination.

Results

No mortalities and no clinical signs were observed during the study. The oral LD₅₀ for male and female rats is concluded to be > 2000 mg/kg. All animals gained weight during the study. No treatment related macroscopic pathological changes were noted at necropsy.

Conclusions

Under the conditions of the study and based on the information given in the study report, the oral LD₅₀ of Ethofol 500 SC is greater than 2000 mg/kg bw in rats. Thus, no classification is required according to the classification criteria of Directive 67/548/EEC and subsequent regulations as well as according to Regulation (EC) No. 1272/2008.

B.6.1.2. Dermal

Reference:	AD 496:ACUTE DERMAL TOXICITY (LIMIT TEST) IN THE RAT
Author(s), year:	██████████ 1996
Report/Doc. number::	665/059 / KCP 7.1.2/01
Guideline(s):	OECD 402 (1987)
GLP:	Yes
Deviations from OECD 402 (1987):	No
Acceptability:	Yes

Material and Methods

Approximately 24 hours prior to the application of the test item Ethofol 500 SC (=AD 496), five Sprague-Dawley rats of each sex were shaven closely with veterinary clippers. Ethofol 500 SC was applied topically undiluted at the dose level of 4000 mg/kg. A piece of surgical gauze was placed over the treatment area (approximately 10% of the total body surface area). The test item remained in contact with the skin of each animal for 24 hours. After the treatment time the bandage and gauze were removed and the treated skin wiped with the cotton wool moistened with distilled water to remove residual test item. Gross pathological examination (external examination and necropsy) was performed in all animals that died during study procedure or were sacrificed at study termination.

Results

There were no mortalities and no treatment related clinical signs during the study. The dermal LD₅₀ for male and female rats is concluded to be > 4000 mg/kg. All animals gained weight during the study. No treatment related macroscopic pathological changes were noted at necropsy.

Conclusion

Under the conditions of the study and based on the information given in the study report, dermal LD₅₀ in male and female rats was above 4000 mg/kg bw. Thus, no classification is required according to the classification criteria of Directive 67/548/EEC and subsequent regulations as well as according to Regulation (EC) No. 1272/2008.

B.6.1.3. Inhalation

The UPL provided a rationale for not submitting an acute inhalation toxicity study with the representative formulation (or comparable formulation):

No acute inhalation toxicity study in rats for the formulated product is considered to be required based on the lack of acute inhalation hazard of the active substance and the components of the product Ethofol 500 SC. Furthermore, the vapour pressure of the active substance is very low (6.5×10^{-4} Pa) and the product is not foreseen to be applied by spraying but only as a 1% aqueous dilution. Intended uses are confined to arable crops such as sugar- and fodder beets thus application is done by downward spraying using tractor mounted boom sprayer equipment giving rise to droplet size $> 50 \mu\text{m}$ and minimum exposure by the inhalation route.

According to the safety data sheets for the components and the information retrieved from the ECHA database and other sources the components are either not classified for acute inhalation toxicity or constitute a proportion well below the trigger value of 1% (w/w) (for details please see Volume C) as indicated in Regulation (EC) No 1272/2008 Annex I, 3.13 and the relevant guidance documents. There is no indication that mixture effects will induce acute inhalation toxicity and, thus, this water based product does not require classification for acute inhalation toxicity or provision of the study.

The RMS considered the rationale justified – no acute inhalation toxicity study with representative formulation containing ethofumesate is required.

B.6.1.4. Skin irritation

Reference:	AD 496: ACUTE DERMAL IRRITATION TEST IN THE RABBIT
Author(s), year:	██████████ 1996
Report/Doc. number::	665/060 / KCP 7.1.4/01
Guideline(s):	OECD 404 (1992)
GLP:	Yes
Deviations from OECD (2002):	No
Acceptability:	Yes

Materials and Methods

One day prior to the application of Ethofol 500 SC (=AD 496), three male New Zealand White rabbits were clipped free of fur from the dorsal flank. 0.5 ml of the test item was applied under a cotton gauze patch. The patch was secured in position with surgical adhesive tape. The test substance remained in contact with the skin of each animal for 4 hours. Afterwards the patches were removed and any residual test material removed by gentle swabbing with cotton wool soaked in distilled water. Approximately one hour following the removal of the patches and 24, 48 and 72 hours later, the test sites were examined for evidence of primary irritation and scored.

Results

No symptoms of systemic toxicity and no mortality were reported. Body weight gain was unaffected. There were no corrosive effects.

Very slight erythema was found for one rabbit at 1 h after removal of the patch and in one rabbit after 24 h. For the third animal very slight erythema was observed at 1 h throughout to 72 h.

Desquamation was noted for two animals after 7 days. No oedema formation was noted.

The results of erythema and oedema scoring are summarized in Table 6.1.4-1.

Table 6.1.4-1 Individual and mean skin irritation scores according to Draize method

Animal no.	Erythema			Oedema		
	1	2	3	1	2	3
1 h	1	1	0	0	0	0
24 h	1	0	1	0	0	0
48 h	1	0	0	0	0	0
72 h	1	0	0	0	0	0
7 days	0D	0	0D	0	0	0
Mean score 24 – 72 h	1	0	0.3	0	0	0

D desquamation

Conclusions

Under the conditions of the study and based on the information given in the study report, rabbits exposed dermally to Ethofol 500 SC for four hours developed only very slight signs of skin irritation. Thus, no classification is required according to the classification criteria of Directive 67/548/EEC and subsequent regulations as well as according to Regulation (EC) No. 1272/2008.

B.6.1.5. Eye irritation

Reference:	AD 496: ACUTE EYE IRRITATION TEST IN THE RABBIT
Author(s), year:	1996
Report/Doc. number::	665/061 / KCP 7.1.5/01
Guideline(s):	OECD 405 (1987)
GLP:	Yes
Deviations from OECD (2012):	- It is not reported in the study if the eyes were rinsed with saline or distilled water
Acceptability:	Yes

Materials and Methods

0.1 ml of Ethofol 500 SC (=AD 496) was applied into the conjunctival sac of the right eye of three New Zealand White rabbits (male and female). The eyelids were held together for about one second and then released. The left

eye of each rabbit was not treated and served as a control. It is not reported in the study if the eyes were rinsed with saline or distilled water after 24 hours. The cornea, iris, and conjunctiva of the treated and control eyes were examined with a standard ophthalmoscope prior to the test and at 1, 24, 48, and 72 hours after treatment.

Results

No signs of systemic toxicological symptoms were reported. No effects on cornea or iris were observed.

The test item produced minimal conjunctival redness (grade 1) in all treated eyes at 1 h and at 24h. Chemosis (grade 1) was noted in one animal at 1 h. From day 2 onwards all animals had recovered.

Individual results are summarized in Table 6.1.5-1.

Table 6.1.5-1: Individual eye irritation scores according to Draize

Time	Corneal opacity	Iris	Conjunctivae	
			Redness	Chemosis
1 h	0/0/0	0/0/0	1/1/1	1/0/0
24 h	0/0/0	0/0/0	1/1/1	0/0/0
48 h	0/0/0	0/0/0	0/0/0	0/0/0
72 h	0/0/0	0/0/0	0/0/0	0/0/0
Mean (24h-72h)	0/0/0	0/0/0	0.33/0.33/0.33	0/0/0

Individual scores for animals no 1/2/3

Conclusions

Under the conditions of the study and based on the information given in the study report, rabbit eyes exposed to Ethofol 500 SC developed only slight signs of eye irritation. Thus, no classification is required according to the classification criteria of Directive 67/548/EEC and subsequent regulations as well as according to Regulation (EC) No. 1272/2008.

B.6.1.6. Skin sensitization

B.6.1.6.1. Magnusson and Kligman maximisation test

Reference:	ETHOFOL 500 SC: SKIN SENSITISATION IN THE GUINEA PIG - MAGNUSSON AND KLIGMAN MAXIMISATION METHOD
Author(s), year:	2003
Report/Doc. number::	237/207 / KCP 7.1.6/02
Guideline(s):	OECD 406 (1992)
GLP:	Yes
Deviations from OECD 406 (1992):	Number of animals in the treated group lower than 10 and in control lower than 5 based on unexpected deaths
Acceptability:	Limited validity since unexpected deaths occurred (also in the control group) for which no reason was stated

Materials and Methods

Ethofol 500 SC was tested according to GPMT (Magnusson and Kligman) on male guinea pigs of the Dunkin-Hartley strain.

The experimental group consisted of 10 animals and a control group of 5 animals. For induction, on day 1, the scapular region was clipped and the following three pairs of intradermal injections (0.1 mL/site) were made:

- A 1:1 w/w mixture of Freund's Complete Adjuvant with aqua iniectionabilia
- Ethofol 500 SC in distilled water (5.0%)
- Ethofol 500 SC in a 1:1 (v/v) mixture of Freund's Complete Adjuvant and distilled water (5.0%)

Approximately 24, 48 and 72 h after intradermal injection the skin reactions were evaluated.

One week after intradermal injection the shoulder region was treated topically using patches loaded with undiluted Ethofol 500 SC under occlusive conditions for 48 h. The application sites (2 × 4 cm) were shorn 24 hours before the treatment.

Two weeks after topical induction and three weeks after intradermal induction the flanks (shaved 24 h before treatment) of the guinea pigs were challenged topically using patches (2 × 2 cm) moistened with 75% aqueous solution (highest not irritant concentration) under occlusive conditions for 24 h. A further skin site was challenged similarly with 50% aqueous solution of Ethofol 500 SC.

At 24 and 48h after the removal of the occlusive dressing the skin reactions were observed and recorded using a scoring from 0 to 3 according to Magnusson and Kligman.

No concurrent positive control was run, but HCD of the laboratory with positive control 2-Mercaptobenzothiazole were included in the report.

Results

One animal of the test group was found dead on day 6. The cause of death was not determined and the absence of this animal was not considered to affect the integrity of the study. One further test group animal and one control group animal were killed for humane reasons on days 14 and 7, respectively.

No skin reactions were noted in control animals.

Following a challenge with 50% Ethofol 500 SC in distilled water positive skin responses (erythema grades 1 or 2) with or without slight or very slight oedema were noted for five animals at the 24 h observation and persisted in four test group animals at the 48h observation.

Following a challenge with 75% Ethofol 500 SC in distilled water positive skin responses (erythema grades 1 or 2) with or without slight or very slight oedema were noted for six animals at the 24 h observation and persisted in four test group animals at the 48h observation.

Individual scores are summarised in Table 6.1.6.1-1.

Table 6.1.6.1-1: Skin reaction induced by challenge with Ethofol 500 SC

Animal	Challenge with 50% Ethofol 500 SC		Challenge with 75% Ethofol 500 SC		Judgement
	24 h	48 h	24 h	48 h	
1	0/0	0/0	0/0	0/0	Negative
2	1/1	1/0	2/1	1/0	Positive
3	2/1	0/0	1/0	0/0	Negative
4	1/0	1/0	1/1	1/0	Positive
5	0/0	0/0	1/0	0/0	Negative
6	#	#	#	#	Animal died prematurely (day 4)
7	#	#	#	#	Animal killed for humane reasons (day 14)
8	0/0	0/0	0/0	0/0	Negative
9	2/2	2/1	2/2	2/1	Positive
10	2/2	1/0	1/1	1/0	Positive

No evidence of skin reaction was noted in the control group treated with distilled water during induction phase.

The positive control 2-Mercaptobenzothiazole induced skin sensitization proving the suitability of the test procedure.

Conclusion

Under the conditions of the study and based on the information given in the study report, 50% of the treated guinea pigs reacted upon dermal challenge. However, the number of surviving animals is lower than recommended in the Guideline OECD TG 426 and the deaths (one in the control group and two in the treatment group) were not explainable.

Under the conditions of the study and based on the information given in the study report, classification would be required according to the classification criteria of Directive 67/548/EEC and subsequent regulations as well as according to Regulation (EC) No. 1272/2008. However, the reliability if the study is questionable based on unexpected deaths. Thus, no conclusion on skin sensitisation of Ethofol 500 SC can be gained from this study.

B.6.1.6.2. Local lymph node assay (LLNA)

Reference:	ETHOFUMESATE 500 G/L ASSESSMENT OF THE SKIN SENSITISATION POTENTIAL IN THE MOUSE USING THE LOCAL LYMPH NODE ASSAY (LLNA)
Author(s), year:	██████████ 2010
Report/Doc. number::	LLNA-PH-10/0154 / KCP 7.1.6/01
Guideline(s):	OECD 429 (2002)
GLP:	Yes
Deviations from OECD 429 (2010):	No
Acceptability:	Yes;

Materials and Methods

Groups of four female CBA/J mice were treated on three consecutive days by application of 25 µL to the dorsal surface of each ear with concentrations of 0 (negative control), 25% or 50% in propylene glycol and 100% (undiluted product). Based on the lack of irritancy in a preliminary study undiluted product was chosen as the highest concentration.

On day 6 the animals were sacrificed and the draining auricular lymph nodes from the four mice were excised and pooled for each experimental group. A single cell suspension of the lymph node cells of 4 mice of each group was prepared and the lymphocyte cells were counted using a cell counter. The stimulation index (SI) was determined as the number of lymphocytes per lymph node of the treated group divided by the number of cells per lymph node in the control group. 10% hexyl cinnamic aldehyde was validated as positive control, but was not co-run.

The adapted positive level (SI of 1.4) is used in the study. Such positive limits have to be calculated for each strain of mice individually. It is mentioned in the study report (and data presented in Appendix) that this SI for CBA/J was subject to in-house validation. The reasons for lower SI index for cell counting (SI = 1.4) than for 3H- thymidine incorporation (SI = 3) was stated to be based on lower individual variance compared to 3H- thymidine incorporation.

Results

No mortality and no signs of systemic toxicity were noted in the test and control animals during the test. Bodyweight changes of the test animals between Day 1 and Day 6 were comparable to those observed in the corresponding control group animals over the same period.

No significant increase in ear thickness and in ear weight was recorded at the concentrations of 25%, 50% and 100%. Therefore, the test item is considered "non irritant" at the three concentrations.

The Stimulation Index (SI) calculated by pooled approach was respectively 1.05, 1.22 and 0.95 for the treated group at 25%, 50% and 100%. The overview for laboratory positive control data showed consistent positive responses > 1.4 for 10% hexyl cinnamic aldehyde.

Scores are summarised in Table 6.1.6.2-1.

Table 6.1.6.2-1: Cell count, stimulation index after treatment with Ethofumesate 500

Group	Test item	Mean cell count / group (10 ⁶ cells/mL)	Stimulation index (cell count of treated group/cell count of control group)	Result
1	Propylene glycol	14.83	Not applicable	Not applicable
2	25%	15.51	1.05	Negative
3	50%	18.16	1.22	Negative
4	100%	14.04	0.95	Negative
5	10% hexyl cinnamic aldehyde*		>1.4	Positive

* not run concurrently

Conclusion

Under the conditions of the study and based on the information given in the study report, Ethofumesate 500 does not have skin sensitising properties. Thus, no classification is required for Ethofumesate 500 according to the classification criteria of Directive 67/548/EEC and subsequent regulations as well as according to Regulation (EC) No. 1272/2008.

B.6.1.7. Supplementary studies on the plant protection product

No supplementary studies on the representative formulations were submitted and not considered necessary.

B.6.1.8. Supplementary studies for combinations of plant protection products

Ethofol 500 SC is not used in association with other plant protection products. No supplementary study is required.

B.6.2. DERMAL ABSORPTION

The representative formulation Ethofol 500 SC was submitted by UPL. Submitted dermal absorption study with representative formulation has not been previously evaluated in the European peer review since UPL was not the notifier for the first approval of ethofumesate.

Reference:	ETHOFUMESATE - IN VITRO DERMAL ABSORPTION STUDY USING HUMAN SKIN
Author(s), year:	Dodd, E., 2012
Report/Doc. number::	YRK0017 / KCP 7.3/01
Guideline(s):	OECD 428 (2004)
GLP:	Yes
Deviations from OECD 428 (2004):	No
Acceptability:	Yes

Materials and Methods

In an *in vitro* percutaneous absorption study two test preparations containing [^{14}C]-Ethofumesate (concentrate (500 g/L) and dilution (0.17 g/L)) were prepared and applied, at an application volume of 10 $\mu\text{L}/\text{cm}^2$, to human dermatomed skin membranes (7 replicates from abdomen and back), 200 - 400 μm thick, mounted into flow-through diffusion cells *in vitro*.

Achieved dose levels were 4914 $\mu\text{g}/\text{cm}^2$ and 1.62 $\mu\text{g}/\text{cm}^2$, respectively.

The surface area of exposed skin within the cells was 0.64 cm^2 . Receptor fluid (5% w/v bovine serum albumin in 0.01 M phosphate buffered saline at pH 7.4), was pumped underneath the skin at a flow rate of approx. 1.5 mL/h. This receptor fluid was not rate limiting for solubility. The skin surface temperature was maintained at approximately 32°C throughout the experiment, relative humidity was 34.3% -48.9%.

A tritiated water barrier integrity test was performed.

Percutaneous absorption was assessed by collecting receptor fluid in hourly fractions from 0 to 24 h post application. At 8 h post application, exposure was terminated by swabbing the skin surface with 1% v/v Tween 80 in distilled water on cotton wool buds until no more radioactivity was recovered followed by drying the skin surface. At 24 h post application (i.e. after a 16 h post exposure monitoring period), the skin was removed from the flow-through diffusion cells, dried and the stratum corneum was removed with 23 successive tape strips (3 M Scotch 'Magic'). The remaining skin was divided into exposed and unexposed skin and solubilised. All samples were analysed by liquid scintillation counting.

Results

For [^{14}C]-Ethofumesate in test preparation 1 (concentrate: 500 g/L) applied to human skin *in vitro*, the majority of the applied dose (97%) was removed by washing at 8 h post application. At 24 h post application, the total non-absorbed dose was 99% of the applied dose. The *stratum corneum* retained 3% of the applied dose; 2% was removed with the first 2 tape strips. The total potentially absorbable dose (skin + receptor fluid + receptor chamber + stratum corneum (strips 3-23) was $2\% \pm 0.9\%$ of the applied dose. The mass balance was complete with 102% (SD = 4%) of the applied dose recovered.

For [^{14}C]-Ethofumesate in test preparation 2 (concentrate: 0.17 g/L) applied to human skin *in vitro*, the majority of the applied dose ($61\% \pm 10\%$) was removed by washing at 8 h post application. At 24 h post application, the total non-absorbed dose was $71\% \pm 8\%$ of the applied dose. The *stratum corneum* retained 19% of the applied dose; 7% was removed with the first 2 tape strips. The total potentially absorbable dose (skin + receptor fluid + receptor chamber + stratum corneum (strips 3-23) was $19\% \pm 4\%$ of the applied dose. The mass balance was 91% (SD = 6%) of the applied dose recovered.

Table 6.2-1: Dermal absorption of Ethofumesate through human skin in vitro (% of dose applied)

	Test preparation 1		Test preparation 2	
	(500 g/L)		(0.17 g/L)	
	Mean	SD	Mean	SD
Skin swab (8 h)	97	4	61	10
Tape surface (Stratum corneum strips 1 + 2)	1	0.6	7	3
Donor chamber	0.7	0.6	2	0.5
Non absorbed	99	4	71	8
Stratum Corneum (3-23)	2	1	12	4
Remaining Skin	0.06	0.06	2	1
Receptor Fluid	0.2	0.1	6	4
Receptor Chamber	nd	nd	nd	nd
Potentially Absorbable Dose	2	0.9	19	4
Total recovery	102	4	91	6

ns no further stratum corneum remaining
nd not detected

Conclusion

Following topical application of [¹⁴C]-Ethofumesate in test preparation 1 (concentrate: 500 g/L) and test preparation 2 (in-use spray dilution: 0.17 g/L) to human skin *in vitro*, the majority of the applied dose was removed by washing the skin (97% and 61% of the applied dose, respectively). The potentially absorbable dose (receptor fluid + tape stripes 3-23 + remaining skin) was 2% and 19% for the concentrate and the dilution, respectively.

According to the new EFSA guidance¹ a standard deviation equal to or larger than 25% of the mean of the absorption requires the use of an alternative value or rejection of the study. The guidance prefers the approach of adding the standard deviation to the mean to cover the upper 84th percentile value of the results. Thus, the application of the guidance results in the following values for [¹⁴C]-ethofumesate in Ethofol 500 SC:

- 2.9% for the neat formulation (500 g/L)
- 19% for the dilution (0.17 g/L)

Additionally, since for the dilution the recovery was below 95%, dermal absorption for dilution is normalised and the values rounded, resulting in final dermal absorption values for Ethofol 500 SC:

¹ EFSA Panel on Plant Protection Products and their Residues (PPR); Guidance on Dermal Absorption. EFSA Journal 2012;10(4):2665. [30 pp.] doi:10.2903/j.efsa.2012.2665.

- 3% for the neat formulation (500 g/L)
- 20% for the dilution (0.17 g/L)

According to the GAP for representative uses, the highest dilution is 1.1 g/L (0.33 kg/ha ethofumesate in 300 L) and the lowest 3.3 g/l (1 kg/ha ethofumesate in 300 L). Both dilutions are covered by the calculated dermal absorption for 0.17 g/l dilution which is considered to be a worst case.

B.6.3. AVAILABLE TOXICOLOGICAL DATA RELATING TO CO-FORMULANTS

Available toxicological data for each co-formulant can be found in the confidential part of the dossier and in Volume 4.

B.6.4. EXPOSURE DATA

Ethofol 500 SC is a soluble concentrate formulation containing 500 g/L ethofumesate, intended as herbicide for weed control in sugar and fodder beets.

Ethofol 500 SC is applied either pre-emergence or during the early post-emergence growth stages. The product will be applied using tractor-mounted ground boom spray equipment. The maximum recommended application rate is 2.0 L Ethofol 500 SC per hectare corresponding to 1.0 kg a.s./ha.

Non-dietary risk assessment is made assuming exposure to total ethofumesate as a racemic mixture of both enantiomers and comparison with the ethofumesate AOEL (2.5 mg/kg bw/d). The AOEL is established from toxicological studies using the racemic mixture (50:50).

Operators, workers, bystanders and residents are expected to be always exposed to the racemate. The enantiomer ratio was shown to be stable in the environment (both the water/sediment study as well as the lysimeter study in soil) demonstrating that there is no enantio-selective microbial degradation or photolysis. Therefore, a change of the ratio is neither expected in the spray volume (relevant for the operator and the bystander) nor in leaf surface deposits (relevant for workers and residents).

As the enantiomeric ratio of ethofumesate isomers is stable in the environment additional safety factors for the AOEL are not necessary and the non-dietary risk assessment is considered to cover the worst case exposure scenario.

B.6.4.1. Operator exposure

The formulation is a suspension concentrate (SC) requiring dilution before application. Operator exposure may occur during mixing and loading and during application. Usage information identifying worst cases pertinent to operator exposure is summarised in Table 6.4.1-1.

Table 6.4.1-1 Summary of critical GAP for operator exposure evaluations

Crop/use	Spraying technique	Work rate (ha/d)	Application rate (L product/ha)	Application rate (kg as/ha)	Application volume (L/ha)	Step of work	Model	
Sugar/fodder beet	Field crop sprayer	20	2.0	1.0	300	Mix/load, application	German model	Field crop, SC liquid
		50					UK POEM	

Justification:

The product will be applied with tractor-mounted/-trailed field crop (boom) sprayers. The cGAP will result in the maximum exposure. Differences in the application rate are accounted for by using the maximum application rate (1.0 kg a.s./ha) when using the German Model. The critical GAP when using the UK-POEM results from a combination of highest dose rate with lowest water volume.

The representative use scenario includes different spray concentrations for which one worst case dermal absorption value is available (20% for 0.17 g/l dilution).

5 L narrow closure container is considered in the calculations as the worst case for UK-POEM.

Table 6.4.1-2: Predicted operator exposure

Crops	F/G	Application method	PPE	Systemic exposure (mg/kg bw/day)		% of AOEL (2.5 mg/kg bw/day)	
				UK-POEM*	German Model*	UK-POEM*	German Model*
Sugar/fodder beet	F	Field crop sprayer	No ¹	1.465	0.1376	59	6
			With ²	0.125	0.0088	5	< 1

¹ No PPE: German Model: Operator wearing T-shirts and shorts; UK POEM: Operator wearing long sleeved shirt, long trousers ("permeable") but no gloves

² With PPE: German Model: Overall/sturdy footwear during application and gloves during mixing/loading and application; UK POEM: gloves during mixing/loading and application

* Dermal absorption of 3% (concentrate) and 20% (spray), 100% absorption *via* inhalation route

Conclusion

Exposure of unprotected operators is estimated to be 59% of the AOEL in the UK-POEM and 6% of the AOEL in German Model if no PPE is worn. Thus, it is concluded that the use of Ethofol 500 SC does not result in an unacceptable risk for operators.

B.6.4.2. Bystander and resident exposure

A harmonized European guidance for the estimation of bystander and resident exposure is not available. The German guidance (Martin, S. et al., 2008)² is chosen in the following evaluation.

The cGAP for bystanders and residents is presented in the following table. Bystanders and residents will be exposed during and after spray applications in the field by off-target drift.

² Martin, S., Westphal, D., Erdtmann-Vourliotis, M., Dechet, F., Schulze-Rosario, C., Stauber, F., Wicke, H. and Chester, G.: Guidance for Exposure and Risk Evaluation for Bystanders and Residents exposed to Plant Protection Products during and after Application, J. Verbr. Lebensm. 3, 272-28, 2008

Table 6.4.2-1: Summary of critical GAPs for bystanders and residents

Crop (grouping)	Application technique	Max. dose rate (kg a.s./ha)	No. of applications	% Drift (1 appl., 90 th perc., 1 m)
Beet crops	Field crop sprayer	1.0	1	2.77

Justification of the selection of the critical GAP:

The exposure scenario for field crop spray application with off-target drift is in this case to be considered with a maximum dose rate. The worst case for the resident is also the single exposure to 1 kg ethofumesate per hectare. A minimum distance of 1 m in arable crops is considered.

Table 6.4.2-2: Predicted systemic exposures as a proportion of the AOEL

Target group	Scenario	Total systemic exposure (mg/kg bw/d)*	AOEL (mg/kg bw/d)	% of AOEL
Bystander	Adult	0.00923	2.5	0.37
	Child	0.00721		0.29
Resident	Adult	0.0048	2.5	0.19
	Child	0.009		0.36

* Assumes a 60 kg bodyweight for an adult and 16.15 kg for a child

Absorption: 20% (spray) via the dermal route, 100 % via the inhalation route

Conclusion

Exposure is calculated for a distance of 1 m to the application equipment. Estimates of adult and child bystander exposure are 0.37% and 0.29% of the AOEL, respectively. Estimates of adult and child resident exposure are 0.19% and 0.36% of the AOEL, respectively. Thus, it is concluded that the use of Ethofol 500 SC does not result in an unacceptable risk for bystanders and residents.

B.6.4.3. Worker exposure

The evaluation of worker exposure provided in the EUROPOEM II report³ is recommended for four different manual harvesting scenarios with bare hands:

Crop group	Transfer Coefficient (cm ² /h)
Fruits (from trees):	4500
Vegetables:	2500
Ornamentals:	5000
Strawberries:	3000

³ EUROPOEM II project FAIR3-CT96-1406; Post Application Exposure of Workers to Pesticides in Agriculture, Report of the Re-entry Working Group; December 2002

Ethofol 500 SC will only be used in beet crops for which a re-entry scenario is not defined. A possible scouting scenario is considered for risk assessment assuming duration of 2 hours/day. Potential re-entry is pre-emergence and early post-emergence when only few leaves are unfolded and leaves cover less than 10% of the ground (up to BBCH 18). Since a transfer coefficient (TC) is not recommended for this scenario a conservative TC of 2500 cm²/h (from hand harvesting of vegetables) is used in the following risk assessment.

A summary of proposed uses and selection of the cGAP used for worker risk assessment is presented in Table 6.4.3-1.

Table 6.4.3-1: Critical GAPS for worker exposure

Crop grouping	Re-entry task	Duration (h)	Max. dose rate		No of applications
			(L/ha product)	(kg a.s./ha)	
Beet crops	Scouting	2	2	1.0	1

Predicted exposures are calculated from a cumulative foliar deposit based on the maximum number of applications, the maximum dose rate and 2 hours/day contact with the foliage. Exposure is compared with the AOEL. Exposure estimates and proportions of the AOEL accounted for by the estimates are summarised in the following table.

Table 6.4.3-2: Predicted worker exposure

Crop grouping	Re-entry task	Systemic exposure* (mg/kg bw/d)	% of AOEL (2.5 mg/kg bw/d)
Beet crops	Scouting	0.05	2

* 20% dermal absorption, 60 kg worker

Conclusions

Exposure of workers re-entering treated beet crops for scouting activities is at maximum 2% of the AOEL. Calculations reflect standard work clothing worn by adult workers (shoes, socks, long-legged pants, and long sleeves) working with bare hands. Thus, an unacceptable risk is therefore not anticipated.

B.6.5. EXPOSURE AND RISK ASSESSMENT**THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM)**

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles		
Product	Ethofol 500 SC	Active substance	Ethofumesate
Formulation type	water-based	a.s. concentration	500 mg/ml
Dermal absorption from product	3 %	Dermal absorption from spray	20,00 %
Container	5 litres narrow closure		
PPE during mix/loading	None	PPE during application	None
Dose	2 l/ha	Work rate/day	50 ha
Application volume	300 l/ha	Duration of spraying	6 h

EXPOSURE DURING MIXING AND LOADING

Container size	5 litres
Hand contamination/operation	0,2 ml
Application dose	2 litres product/ha
Work rate	50 ha/day
Number of operations	20 /day
Hand contamination	4 ml/day
Protective clothing	None
Transmission to skin	100 %
Dermal exposure to formulation	4 ml/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique	Tractor-mounted/trailed boom sprayer: hydraulic nozzles		
Application volume	300 spray/ha		
Volume of surface contamination	10 ml/h		
Distribution	Hands	Trunk	Legs
	65%	10%	25%
Clothing	None	Permeable	Permeable
Penetration	100%	5%	15%
Dermal exposure	6,5	0,05	0,375 ml/h
Duration of exposure	6 h		
Total dermal exposure to spray	41,55 ml/day		

ABSORBED DERMAL DOSE

	Mix/load	Application	
Dermal exposure	4 ml/day	41,55	ml/day
Concen. of a.s. product or spray	500 mg/ml	3,333333333	mg/ml
Dermal exposure to a.s.	2000 mg/day	138,5	mg/day
Percent absorbed	3 %	20	%
Absorbed dose	60 mg/day	27,7	mg/day

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure	0,01 ml/h
Duration of exposure	6 h
Concentration of a.s. in spray	3,333333333 mg/ml
Inhalation exposure to a.s.	0,2 mg/day
Percent absorbed	100 %
Absorbed dose	0,2 mg/day

PREDICTED EXPOSURE

Total absorbed dose	87,9 mg/day
Operator body weight	60 kg
Operator exposure	1,465 mg/kg bw/day
AOEL	2,5 mg/kg bw/day
% AOEL	58,6

THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles		
Product	Ethofol 500 SC	Active substance	Ethofumesate
Formulation type	water-based	a.s. concentration	500 mg/ml
Dermal absorption from product	3 %	Dermal absorption from spray	20,00 %
Container	5 litres narrow closure		
PPE during mix/loading	Gloves	PPE during application	Gloves
Dose	2 l/ha	Work rate/day	50 ha
Application volume	300 l/ha	Duration of spraying	6 h

EXPOSURE DURING MIXING AND LOADING

Container size	5 litres
Hand contamination/operation	0,2 ml
Application dose	2 litres product/ha
Work rate	50 ha/day
Number of operations	20 /day
Hand contamination	4 ml/day
Protective clothing	Gloves
Transmission to skin	5 %
Dermal exposure to formulation	0,2 ml/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique	Tractor-mounted/trailed boom sprayer: hydraulic nozzles		
Application volume	300 spray/ha		
Volume of surface contamination	10 ml/h		
Distribution	Hands 65%	Trunk 10%	Legs 25%
Clothing	Gloves	Permeable	Permeable
Penetration	10%	5%	15%
Dermal exposure	0,65	0,05	0,375 ml/h
Duration of exposure	6 h		
Total dermal exposure to spray	6,45 ml/day		

ABSORBED DERMAL DOSE

	Mix/load	Application
Dermal exposure	0,2 ml/day	6,45 ml/day
Concen. of a.s. product or spray	500 mg/ml	3,333333333 mg/ml
Dermal exposure to a.s.	100 mg/day	21,5 mg/day
Percent absorbed	3 %	20 %
Absorbed dose	3 mg/day	4,3 mg/day

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure	0,01 ml/h
Duration of exposure	6 h
Concentration of a.s. in spray	3,333333333 mg/ml
Inhalation exposure to a.s.	0,2 mg/day
Percent absorbed	100 %
Absorbed dose	0,2 mg/day

PREDICTED EXPOSURE

Total absorbed dose	7,5 mg/day
Operator body weight	60 kg
Operator exposure	0,125 mg/kg bw/day

AOEL	2,5 mg/kg bw/day
% AOEL	5

THE GERMAN MODEL (GEOMETRIC MEAN VALUES)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles		
Product	Ethofol 500 SC	Active substance	Ethofumesate
Formulation type	Liquid	a.s. concentration	500 g/l
Dermal absorption from product	3 %	Dermal absorption from spray	20 %
RPE during mix/loading	None	RPE during application	None
PPE during mix/loading	None		
PPE during application: Head	None	Hands	None
		Body	None
Dose	2 l product/ha	Work rate/day	20 ha

DERMAL EXPOSURE DURING MIXING AND LOADING

Hand contamination/kg a.s.	2,4 mg/kg a.s.
Hand contamination/day	48 mg/day
Protective clothing	none
Transmission to skin	100 %
Dermal exposure to a.s.	48 mg/day

INHALATION EXPOSURE DURING MIXING AND LOADING

Inhalation exposure/kg a.s.	0,0006 mg/kg a.s.
Inhalation exposure/day	0,012 mg/day
RPE	none
Transmission through RPE	100 %
Inhalation exposure to a.s.	0,012 mg/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique	Tractor-mounted/trailed boom sprayer: hydraulic nozzles		
	Head	Hands	Rest of body
Dermal contamination/kg a.s.	0,06	0,38	1,6
Dermal contamination/day	1,2	7,6	32
Protective clothing	none	none	none
Transmission to skin	100	100	100 %
Total dermal exposure to a.s.	40,8 mg/day		

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure/kg a.s.	0,001 mg/kg a.s.
Inhalation exposure/day	0,02 mg/day
RPE	none
Transmission through RPE	100 %
Inhalation exposure to a.s.	0,02 mg/day

ABSORBED DOSE

	Mix/load	Application
Dermal exposure to a.s.	48 mg/day	40,8 mg/day
Percent absorbed	3 %	20 %
Absorbed dose (dermal route)	1,44 mg/day	8,16 mg/day
Inhalation exposure to a.s.	0,012 mg/day	0,02 mg/day
Total systemic exposure	1,452 mg/day	8,18 mg/day

PREDICTED EXPOSURE

Total systemic exposure	9,632 mg/day
Operator body weight	70 kg
Operator exposure	0,1376 mg/kg bw/day

THE GERMAN MODEL (GEOMETRIC MEAN VALUES)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles		
Product	Ethofol 500 SC	Active substance	Ethofumesate
Formulation type	Liquid	a.s. concentration	500 g/l
Dermal absorption from product	3 %	Dermal absorption from spray	20 %
RPE during mix/loading	None	RPE during application	None
PPE during mix/loading	Gloves		
PPE during application: Head	None	Hands	Gloves
		Body	Coverall and sturdy footwear
Dose	2 l product/ha	Work rate/day	20 ha

DERMAL EXPOSURE DURING MIXING AND LOADING

Hand contamination/kg a.s.	2,4 mg/kg a.s.
Hand contamination/day	48 mg/day
Protective clothing	gloves
Transmission to skin	1 %
Dermal exposure to a.s.	0,48 mg/day

INHALATION EXPOSURE DURING MIXING AND LOADING

Inhalation exposure/kg a.s.	0,0006 mg/kg a.s.
Inhalation exposure/day	0,012 mg/day
RPE	none
Transmission through RPE	100 %
Inhalation exposure to a.s.	0,012 mg/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique	Tractor-mounted/trailed boom sprayer: hydraulic nozzles		
	Head	Hands	Rest of body
Dermal contamination/kg a.s.	0,06	0,38	1,6
Dermal contamination/day	1,2	7,6	32
Protective clothing	none	gloves	coverall and sturdy footwear
Transmission to skin	100	1	5 %
Total dermal exposure to a.s.	2,876 mg/day		

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure/kg a.s.	0,001 mg/kg a.s.
Inhalation exposure/day	0,02 mg/day
RPE	none
Transmission through RPE	100 %
Inhalation exposure to a.s.	0,02 mg/day

ABSORBED DOSE

	Mix/load	Application
Dermal exposure to a.s.	0,48 mg/day	2,876 mg/day
Percent absorbed	3 %	20 %
Absorbed dose (dermal route)	0,0144 mg/day	0,5752 mg/day
Inhalation exposure to a.s.	0,012 mg/day	0,02 mg/day
Total systemic exposure	0,0264 mg/day	0,5952 mg/day

PREDICTED EXPOSURE

Total systemic exposure	0,6216 mg/day
Operator body weight	70 kg
Operator exposure	0,00888 mg/kg bw/day

Estimation of bystander and resident exposure (adults and children)			
Active substance (a.s.)	Ethofumesate		
Product	Ethofol 500 SC		
Intended uses	Field Crops, Tractor Mounted (FCTM) ▼		
Treated area per day (A)	20	ha/d	
Application rate (AR)	1	kg a.s./ha	
Number of applications (NA)	1		
¹⁾ Consideration of more than two applications are not necessary if degradation of the active substance on foliage of at least 50 % can be assumed between two applications (otherwise use multiple application factor).			
Dermal absorption (DA)	20	% (worst case, e.g. during application)	
Inhalation absorption (IA)	100	%	
Oral absorption (OA)	100	%	
Systemic AOEL	2,5	mg/kg bw/d	
Body weight (BW)	60	kg/person (adults)	
	16,15	kg/person (children)	
Distance between application and bystander or resident:			
FCTM	1	m	
High crops not selected			
	0	m	
Home & garden not selected			
		m	
Drift deposit (D) for 1 appl. based on appl. technique and distance:		2,77 % (FCTM, 1 m)	
Airborne vapour concentration (AC _v)	0,015	mg/m ^{3,2)}	
²⁾ 1 µg/m ³ for semivolatile substances, i.e. vapour pressure (20 °C): ≥ 1x10 ⁻⁵ - < 5x10 ⁻³ Pa; 15 µg/m ³ for volatile substances, i.e. vapour pressure (20 °C): ≥ 5x10 ⁻³ Pa			

Estimation of bystander exposure during/after application in Field Crops, Tractor Mounted

Input parameters considered for the estimation of bystander exposure:

Intended use(s):		Drift (D):	2,77 % (FCTM, 1 m)
Application rate (AR):	1 kg a.s./ha	Exposed Body Surface Area (BSA):	1 m ² (adults)
			0,21 m ² (children)
Body weight (BW):	60 kg/person (adults)	Specific Inhalation Exposure (I ^a _A):	0,001 mg/kg a.s. (6 hours, adults)
	16,15 kg/person (children)		0,00057 mg/kg a.s. (6 hours, children)
Dermal absorption (DA):	20,00 % ('worst case')	Area Treated (A):	20 ha/d (based on Field Crops, Tractor Mounted (FCTM))
Inhalation absorption (IA):	100 %	Exposure duration (I):	5 min
AOEL:	2,5 mg/kg bw/d		

Bystander exposure towards Ethofumesate			
Adults		Children	
Bystander: Dermal exposure after application in (via spray drift)			
SDE _B = (AR x D x BSA x DA) / BW		SDE _B = (AR x D x BSA x DA) / BW	
(100 x 2,77% x 1 x 20%) / 60		(100 x 2,77% x 0,21 x 20%) / 16,15	
External exposure	2,77 mg/person	External exposure	0,5817 mg/person
External exposure	0,0461667 mg/kg bw/d	External exposure	0,0360186 mg/kg bw/d
Absorbed dose:	0,0092333 mg/kg bw/d	Absorbed dose:	0,0072037 mg/kg bw/d
Bystander: Inhalation exposure after application in			
SIE _B = (I ^a _A x AR x A x T x IA) / BW		SIE _B = (I ^a _A x AR x A x T x IA) / BW	
(0,001 / 360 x 1 x 20 x 5 x 100%) / 60		(0,001 / 360 x 1 x 20 x 5 x 100%) / 16,15	
External exposure	0,0002778 mg/person	External exposure	0,0001596 mg/person
External exposure	4,63E-06 mg/kg bw/d	External exposure	9,885E-06 mg/kg bw/d
Absorbed dose:	0,0000046 mg/kg bw/d	Absorbed dose:	0,0000099 mg/kg bw/d
Total systemic exposure: SE _B = SDE _B + SIE _B		Total systemic exposure: SE _B = SDE _B + SIE _B	
Total systemic exposure (absorbed dose)	0,5542778 mg/person	Total systemic exposure (absorbed dose)	0,1164996 mg/person
Total systemic exposure (absorbed dose)	0,0092380 mg/kg bw/d	Total systemic exposure (absorbed dose)	0,0072136 mg/kg bw/d
% of AOEL:	0,37 %	% of AOEL:	0,29 %

Estimation of resident exposure after application in Field Crops, Tractor Mounted (FCTM)

Input parameters considered for the estimation of resident exposure:

Intended use(s):		Drift (D):	2,77	% (FCTM, 1 m)
Application rate (AR):	1 kg a.s./ha	Transfer coefficient (TC):	7300	cm ² /h (adults)
			2600	cm ² /h (children)
Number of applications (NA):	1	Turf Transferable Residues (TTR):	5	%
Body weight (BW):	60 kg/person (adults)	Exposure Duration (H):	2	h
	16,15 kg/person (children)	Airborne Concentration of Vapour (ACV):	0,015	mg/m ³
Dermal absorption (DA):	20,00 % ('worst case')	Inhalation Rate (IR):	16,57	m ³ /d (adults),
Inhalation absorption (IA):	100 %		8,31	m ³ /d (children)
Oral absorption (OA)	100 %	Saliva Extraction Factor (SE):	50	%
AOEL	2,5 mg/kg bw/d	Surface Area of Hands (SA):	20	cm ²
		Frequency of Hand to Mouth (Freq):	20	events/h
		Dislodgeable foliar residues (DFR):	20	%
		Ingestion Rate for Mouthing of Grass/Day (IgR):	25	cm ² /d

Resident exposure towards Ethofumesate					
Adults			Children		
Residents: Dermal exposure after application in (via deposits caused by spray drift)					
$SDE_R = (AR \times NA \times D \times TTR \times TC \times H \times DA) / BW$			$SDE_R = (AR \times NA \times D \times TTR \times TC \times H \times DA) / BW$		
$(0,01 \times 1 \times 2,77\% \times 5\% \times 7300 \times 2 \times 20\%) / 60$			$(0,01 \times 1 \times 2,77\% \times 5\% \times 2600 \times 2 \times 20\%) / 16,15$		
External exposure	0,20221	mg/person	External exposure	0,07202	mg/person
External exposure	0,0033702	mg/kg bw/d	External exposure	0,0044594	mg/kg bw/d
Absorbed dose:	0,0006740	mg/kg bw/d	Absorbed dose:	0,0008919	mg/kg bw/d
Residents: Inhalation exposure to vapour					
$SIE_R = (AC_V \times IR \times IA) / BW$			$SIE_R = (AC_V \times IR \times IA) / BW$		
$(0,015 \times 16,57 \times 100\%) / 60$			$(0,015 \times 8,31 \times 100\%) / 16,15$		
External exposure	0,24855	mg/person	External exposure	0,12465	mg/person
External exposure	0,0041425	mg/kg bw/d	External exposure	0,0077183	mg/kg bw/d
Absorbed dose:	0,0041425	mg/kg bw/d	Absorbed dose:	0,0077183	mg/kg bw/d
			Residents: Oral exposure (hand-to-mouth transfer)		
			$SOE_H = (AR \times NA \times D \times TTR \times SE \times SA \times Freq \times H \times OA) /$		
			$(0,01 \times 1 \times 2,77\% \times 5\% \times 50\% \times 20 \times 20 \times 2 \times 100\%) /$		
			External exposure	0,00554	mg/person
			External exposure	0,000343	mg/kg bw/d
			Absorbed dose	0,0003430	mg/kg bw/d
			Residents: Oral exposure (object-to-mouth transfer)		
			$SOE_O = (AR \times NA \times D \times DFR \times IgR \times OA) / BW$		
			$(0,01 \times 1 \times 2,77\% \times 20\% \times 25 \times 100\%) / 16,15$		
			External exposure	0,001385	mg/person
			External exposure	8,576E-05	mg/kg bw/d
			Absorbed dose	0,0000858	mg/kg bw/d
Total systemic exposure: $SE_R = SDE_R + SIE_R$			Total systemic exposure: $SE_R = SDE_R + SIE_R + SOE_H + SOE_O$		
Total systemic exposure (absorbed dose)	0,288992	mg/person	Total systemic exposure (absorbed dose)	0,145979	mg/person
Total systemic exposure (absorbed dose)	0,0048165	mg/kg bw/d	Total systemic exposure (absorbed dose)	0,0090389	mg/kg bw/d
% of AOEL:	0.19	%	% of AOEL:	0.36	%

WORKER EXPOSURE		EUROPOEM II MODEL	
form		Re-entry in the field	
a.s.			
Parameter	Value	Unit	References, comments
Re-entry activities in the field			
AR Application rate	1	kg a.s./ha	summary of intended uses
Worker			
Duration			
T	2	hours / day	default: 6 h (Europoem II)
Inhalation Exposure			
no model available	-		without PPE
Dermal Exposure			
DFR Dislodgeable foliar residue	30	mg a.s./m ² /kg a.s./ha	default (Europoem II)
TC Transfer coefficient	0,25	m ² / hour	vegetable (field): 0.25; ornamentals: 0.5; small fruit: 0.3; large fruit: 0.45 (Europoem II)
Dermal Exposure	15	mg a.s./ day	DE = DFR x AR x TC x T
Internal exposure			
DA Dermal Absorption	20	%	
PPE-factor dermal	5		gloves*
AOEL	150	mg a.s./ day	based on 60 kg bw
	Without PPE	With PPE	
Internal exposure	[mg a.s./ day]	[mg a.s./ day]	
Inhalation	-	-	no model available
Dermal	3,000	0,600	DE(int) = DE x (DA/100)
Total	3,000	0,600	sum
% AOEL			
Inhalation	-	-	no model available
Dermal	2	0	%AOEL = 100 x DE(int) / AOEL
Total	2	0	sum

* It is assumed in the used TC values, that body exposure is already reduced by (protective) clothing. The use of gloves will result in an extra reduction factor of 5.

B.6.6. REFERENCES RELIED ON

Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
KCP 7.1.1	[REDACTED]	1996a	AD 496: ACUTE ORAL TOXICITY (LIMIT TEST) IN THE RAT United Phosphorus Ltd., 665/058 [REDACTED] GLP: yes Published: no	Y	Y	New data for existing formulation, not previously submitted nor evaluated	UPL	Submitted for the purpose of renewal (2014)
KCP 7.1.2	[REDACTED]	1996b	AD 496: ACUTE DERMAL TOXICITY (LIMIT TEST) IN THE RAT United Phosphorus Ltd., 665/059 [REDACTED] GLP: yes Published: no	Y	Y	New data for existing formulation, not previously submitted nor evaluated	UPL	Submitted for the purpose of renewal (2014)
KCP 7.1.4	[REDACTED]	1996c	AD 496: ACUTE DERMAL IRRITATION TEST IN THE RABBIT United Phosphorus Ltd., 665/060 [REDACTED] GLP: yes Published: no	Y	Y	New data for existing formulation, not previously submitted nor evaluated	UPL	Submitted for the purpose of renewal (2014)
KCP 7.1.5	[REDACTED]	1996d	AD 496: ACUTE EYE IRRITATION TEST IN THE RABBIT United Phosphorus Ltd., 665/061 [REDACTED]	Y	Y	New data for existing formulation, not previously submitted nor evaluated	UPL	Submitted for the purpose of renewal (2014)

			GLP: yes Published: no					
KCP 7.1.6		2010	ETHOFUMESATE 500 G/L ASSESSMENT OF THE SKIN SENSITISATION POTENTIAL IN THE MOUSE USING THE LOCAL LYMPH NODE ASSAY(LLNA) AgriChem B.V., LLNA-PH-10/0154 [REDACTED] GLP: yes Published: no	Y	Y	New data for existing formulation, not previously submitted nor evaluated	UPL	Submitted for the purpose of renewal (2014)
KCP 7.1.6		2003	ETHOFOL 500 SC: SKIN SENSITISATION IN THE GUINEA PIG - MAGNUSSON AND KLIGMAN MAXIMISATION METHOD United Phosphorus Ltd., 237/207 [REDACTED] GLP: yes Published: no	Y	Y	New data for existing formulation, not previously submitted nor evaluated	UPL	Submitted for the purpose of renewal (2014)
KCP 7.3	Dodd, E.	2012	ETHOFUMESATE - IN VITRO DERMAL ABSORPTION STUDY USING HUMAN SKIN United Phosphorus Ltd., YRK0017 Huntingdon Life Sciences Limited, Suffolk, UK GLP: yes Published: no	Y	Y	New data for existing formulation, not previously submitted nor evaluated	UPL	Submitted for the purpose of renewal (2014)