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Fenoxaprop-P-ethyl

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

B.6.1. ACUTE TOXICITY OF PLANT PROTECTION PRODUCT

Acute toxicological testing was performed with CHA 4960 (Fenoxaprop-P-ethyl 69 g/L EW; CHA 4960), an oil in water emulsion that contains 69 g/L fenoxaprop-P-ethyl. The results are summarised in the table below.

Summary of acute toxicological data obtained with CHA 4960

Study [Reference]	Species	Result mg/kg or mg/m^3 or effect	Classification (Regulation (EC) 1272/2008)
Acute oral toxicity [redacted] (2005a), 85 FPE CP 7.1.1/01	Rat	> 2000 mg/kg	None
Acute dermal toxicity [redacted] (2005b), 88 FPE CP 7.1.2/01	Rat	> 2000 mg/kg	None
Acute inhalation toxicity; 4 hours, nose-only [redacted] (2005), 90 FPE CP 7.1.3/01	Rat	4.96 mg/L (highest attainable concentration)	None
Skin irritation [redacted] (2005c), 87 FPE CP 7.1.4/01	Rabbit	Not irritating	None
Eye irritation [redacted] (2005d), 86 FPE CP 7.1.5/01	Rabbit	Not irritating	None
Skin sensitisation (LLNA) [redacted] (2005e), 85 FPE CP 7.1.6/01	Mouse	Sensitising	**Skin Sens 1B** **H317: "May cause an allergic skin reaction".**

CHA 4960 containing 69 g/L fenoxaprop-P-ethyl has a low toxicity in respect to acute oral, dermal and inhalation toxicity and is not irritating to the rabbit skin and eye. It has been found to be skin sensitising in the Local Lymph Node Assay in the mouse.

B.6.1.1. Oral

Reference:	**Fenoxaprop-P-ethyl 69 g/L EW: Acute Oral Toxicity in the Rat – Up and Down Procedure**
Author(s). year:	[redacted] **2005a**
Report/Doc. number:	89 FPE / Study No. 545/347
Guideline(s):	OECD 425 (2001), EPA OPPTS 870.1100 (2002)
Deviations to OECD GD 425 (2008):	None.
GLP:	Yes
Acceptability:	Yes

Materials and Methods:
CHA 4960 was orally administered via gastric intubation to five female nulliparous and non-pregnant young adult rats at a single dose level of 2000 mg/kg bw. Treatment of animals was sequential. The dose volume administered was calculated according to the fasted bodyweight at the time of dosing.

Test material: Fenoxaprop-P-ethyl 69 g/L EW, CHA No. 4960, batch 660-PSH-49
Active ingredient: 7.11% w/w

Test animals: Sprague-Dawley CD rats (Crl: CD® (SD) IGS BR), [redacted]
8-12 weeks, bodyweight 206-333g
Number of animals: 1 + 4

The animals were observed for treatment-related effects at 0.5, 1, 2 and 4 hours after treatment and then once daily for a subsequent 14-day observation period. Clinical observations, body weights and post mortem observations were recorded.

Testing Laboratory and Dates: [redacted]
5 May 2005 – 27 June 2005

Findings:
No mortality was observed.
No signs of systemic toxicity were noted.
All animals showed expected gains in bodyweight over the study period. Two animals showed decreased bodyweight gain in the second week.
No abnormalities were detected at post mortem examination.

Conclusion:
Under the experimental conditions, the oral LD_{50} of CHA 4960 (Fenoxaprop-P-ethyl 69 g/L EW) is higher than 2000 mg/kg bw in rats. **Thus, no classification is required according to Regulation (EC) No. 1272/2008.**

B.6.1.2. Dermal

Reference:	**Fenoxaprop-P-ethyl 69 g/L EW: Acute Dermal Toxicity (Limit test) in the Rat**
Author(s). year:	[redacted] **2005b**
Report/Doc. number:	88 FPE / Study No. 545/348
Guideline(s):	OECD 402 (1987), Method B.3 of 92/69/EEC, EPA OPPTS 870.1200 (1998)
Deviations:	None.
GLP:	Yes
Acceptability:	Yes

Materials and Methods:
CHA 4960 was applied dermally to an area of shaved skin (ca. 10% of body surface area) five male and five female nulliparous and non-pregnant young adult rats at a single dose of 2000 mg/kg bw. A piece of surgical gauze was placed over the treatment area and semi-occluded with a piece of self-adhesive bandage. After a 24 hour contact period, the bandages were removed and residual test material was washed off with water.

Test material: Fenoxaprop-P-ethyl 69 g/L EW, CHA No. 4960, batch 660-PSH-49
Active ingredient: 7.11% w/w

Test animals: Sprague-Dawley CD rats (Crl: CD® (SD) IGS BR), [redacted]
8-12 weeks, bodyweight ♂ 228-239 and ♀ 216-235g
Number of animals: 5 per sex

The animals were evaluated for effects on the day of dosing at 0.5, 1, 2 and 4 hours after dosing and for a subsequent 14-day observation period. Clinical observations, dermal findings, body weights and gross post mortem examinations were recorded.

Testing Laboratory [redacted]
and Dates: 25 May 2005 – 08 June2005

Findings:
No mortality was observed.
There were no clinical signs, no signs of dermal irritation and no abnormal observations at post mortem.
Body weight gains were within acceptable ranges.
No abnormalities were detected at post mortem examination.

Conclusion:
Under the experimental conditions, the dermal LD_{50} of CHA 4960 (Fenoxaprop-P-ethyl 69 g/L EW) is higher than 2000 mg/kg bw in rats. **Thus, no classification is required according to Regulation (EC) No. 1272/2008.**

B.6.1.3. Inhalation

Reference:	**Fenoxaprop-P-ethyl 69 g/L EW: Acute Inhalation Toxicity (Nose only) Study in the Rat**
Author(s). year:	[redacted] **2005**
Report/Doc. number:	90 FPE / Study No. 545/349
Guideline(s):	OECD 403 (1981), EPA OPPTS 870.1300 (1998), Method B.2 of 92/69/EEC
Deviations to OECD 403 (2009):	Pressure in the chamber was not stated.
GLP:	Yes
Acceptability:	Yes

Materials and Methods:
Five male and five female rats were exposed to an aerosol atmosphere of CHA 4960 in water at 4:1 w/w. The single four-hour exposure was "nose only" at a mean concentration of 4.96 mg/L (target concentration was 5.0 mg/L), equivalent to a nominal concentration of 52.8 mg/L.

Test material: Fenoxaprop-P-ethyl 69 g/L EW, CHA No. 4960, batch 660-PSH-49
Active ingredient: 7.11% w/w

Test animals: Sprague-Dawley CD rats (Crl: CD® (SD) IGS BR), [redacted]
8-12 weeks, bodyweight ♂ 321-357 and ♀ 243-265g
Number of animals: 5 per sex

Operational conditions (flow rate, oxygen levels, temperature and humidity in the inhalation systems) were checked throughout the exposure period. Animals were observed for clinical signs at hourly intervals throughout the exposure period, for the first 1-2 h post exposure and thereafter at least once daily during the subsequent 14 days observation period. The body weight of animals was checked before exposure, and on Days 7 and 14 post exposure (or at death). On the last day of the observation period (day 14) the animals were sacrificed by an intravenous overdose of pentobarbitone sodium and subjected to a macroscopic post mortem examination.

The main exposure parameters are indicated in Table 6.1.3-1

Table 6.1.3-1 Exposure parameters for acute inhalation study on CHA 4960

Parameter	Value
Chamber flow rate	45 L/min
Nominal concentration	52.8 mg/L
Mean achieved atmosphere concentration	4.96 ± 0.23 mg/L
Particle size MMAD/GSD	2.79 µm/2.19
Particles < 4 µm (% w/w)	67.9

Testing Laboratory and Dates: [redacted]
16 August 2005 – 22 September 2005

Findings:
Mortality: One death (male) was recorded during the study on Day 1 of the observation period.

Clinical Observations: During exposure increased respiratory rate was noted in all animals and there was an isolated incidence of laboured respiration. On removal from the chamber, animals showed increased respiration, ataxia and pallor of the extremities.
All animals showed increased respiratory rate, hunched posture and pilo-erection one day after exposure. Red staining around the eyes and snout, noisy and gasping respiration and isolated incidences of laboured respiration were observed on Day 1. No abnormalities were detected on from Days 4-6 post exposure.

Bodyweight: Three male animals showed reduced bodyweight gain during Week 1, returning to normal in Week 2. Normal bodyweight gains occurred for all other animals.

Necropsy: Three of the surviving animals exhibited pale or dark patches on the lungs. The animals which died exhibited the following:

Lungs – enlarged, fluid filled, pale patches.
Liver – pale, accentuated lobular pattern.
Stomach – gaseous distension
Small intestine – gaseous distension
Large intestine – gaseous distension

Conclusion:
Under the experimental conditions, the inhalation LC_{50} of CHA 4960 (Fenoxaprop-P-ethyl 69 g/L EW) is higher than 4.96 mg/L air (highest attainable concentration) in rats. **Thus, no classification is required according to Regulation (EC) No. 1272/2008.**

B.6.1.4. Skin irritation

Reference:	**Fenoxaprop-P-ethyl 69 g/L EW: Acute Dermal Irritation in the Rabbit**
Author(s). year:	[redacted] **2005c**
Report/Doc. number:	87 FPE / Study No. 545/350
Guideline(s):	OECD 404 (2002), EPA OPPTS 870.2500 (1998), Method B.4 of 2004/73/EC
Deviations to OECD 404 (2015):	Treatment of animals was not sequential. Individual animal weights at start of study not stated.
GLP:	Yes
Acceptability:	Yes

Materials and Methods:
Three male young adult New Zealand White rabbits were used. Fur was clipped from the dorsal/flank area of the trunk of each rabbit on the day before treatment. Test material, 0.5 mL of CHA 4960, was applied to the intact skin of each rabbit under a 2.5 cm x 2.5 cm patch of gauze. The patch was then covered with surgical adhesive tape and the trunk was wrapped with an elastic corset, which remained in position for 4 h. After this period the corset was removed and residual material swabbed with wet cotton wool, without altering the existing response or the integrity of the epidermis.

Test material: Fenoxaprop-P-ethyl 69 g/L EW, CHA No. 4960, batch 660-PSH-49
Active ingredient: 7.11% w/w

Test animals: New Zealand White rabbits, [redacted]
12-20 weeks, bodyweight 2.0-3.5kg
Number of animals: 3

Effects of dermal irritation were recorded. Skin reactions were scored at 1 hour and 24, 48 and 72 hours after removal of the test substance. Observations were also conducted after 7 and 14 days.

Testing Laboratory and Dates: [redacted]
04 May 2005 – 08 September 2005

Findings:
Well-defined erythemas were noticeable at the 1, 24, 48 and 72-hour observations in 3/3 animals. Very slight erythema remained at all skin sites at the 7-day observation juncture.

Very slight to slight oedemas were noted at all treatment sites at the 1, 24, 48 and 72-hour observations.

Light brown discolouration of the epidermis was noted at all treated sites at the 24, 48 and 72-hour observations, with loss of skin elasticity at all treated sites at the 48 and 72-hour observations. Loss of skin flexibility was noted at all treated skin sites at the 72-hour observation. Severe desquamation was noted at all treated skin sites at the 7-day observation juncture with slight desquamation still apparent at all treated sites at the 14-day observation juncture.

Table 6.1.4-1 Individual and total irritation scores

Skin reaction	Observation time	Individual scores* and rabbit numbers		
		1	**2**	**3**
Erythema/Eschar Formation	1 hour	2	2	2
	24 hours	2 Br	2 Br	2 Br
	48 hours	2 BrLe	2 BrLe	2 BrLe
	72 hours	2 BrLeLf	2 BrLeLf	2 BrLeLf
	7 days	1 D	1 D	1 D
	14 days	0 D*	0 D*	0 D*
Mean scores (24-72 h)		**2.0**	**2.0**	**2.0**
Oedema Formation	1 hour	2	1	1
	24 hours	2	2	1
	48 hours	2	2	1
	72 hours	1	2	1
	7 days	0	0	0
	14 days	0	0	0
Mean scores (24-72 h)		**1.67**	**2.0**	**1.0**

* scores in the range of 0 to 4
Br = Light brown discolouration of epidermis
Le = Loss of skin elasticity
Lf = Loss of skin flexibility
D = Severe desquamation
D* = Slight desquamation

Conclusion:
Under the experimental conditions, CHA 4960 (Fenoxaprop-P-ethyl 69 g/L EW) is not a skin irritant. **Thus, no classification is required according to Regulation (EC) No. 1272/2008.**

B.6.1.5. Eye irritation

Reference:	**Fenoxaprop-P-ethyl 69 g/L EW: Acute Eye Irritation in the Rabbit**
Author(s). year:	[redacted] **2005d**
Report/Doc. number:	86 FPE / Study No. 545/351
Guideline(s):	OECD 405 (2002), EPA OPPTS 870.2400 (1998), Method B.5 of 2004/73/EC
Deviations to OECD 405 (2012):	Observation period much shorter (3 days) than recommended in the guideline (21 days). However, as the effects recovered on day 3, this is considered a minor deviation. Individual animal weights at conclusion of test not assessed.
GLP:	Yes
Acceptability:	Yes

Materials and Methods:
Initially a single male Zealand White rabbit was used for the test. On day of dosing, 0.1 mL of CHA 4960 was introduced into the lower conjunctival sac of the right eye and an assessment of the initial pain reaction was made. The remaining 2 rabbits were treated subsequently. The left eye of all animals served as negative control.

Test material: Fenoxaprop-P-ethyl 69 g/L EW, CHA No. 4960, batch 660-PSH-49
Active ingredient: 7.11% w/w

Test animals: New Zealand White rabbits, [redacted]
12-20 weeks, bodyweight 2.0-3.5kg
Number of animals: 3

Assessment of ocular response (in accordance with the method of Draize) was made 1, 24, 48 and 72 hours after dosing. At each interval, the cornea, iris and conjunctivae of the treated eyes were examined and scored.

Testing Laboratory and Dates: [redacted]
25 May 2005 – 09 June 2005

Findings:
Individual and average ocular irritation scores for treated unwashed eyes are presented in Table 6.1.5-1.
No corneal effects were noted during the study. Moderate conjunctival irritation was noted in all treated eyes one hour after treatment with minimal conjunctival irritation in all treated eyes at the 24-hour observation and in one treated eye at the 48-hour observation. Iridial inflammation was noted in all treated eyes one hour after treatment.
Two treated eyes appeared normal at the 48-hour observation and the remaining treated eye appeared normal at the 72-hour observation.

Table 6.1.5-1 Eye irritation scores according to the Draize scheme – unwashed eyes

Rabbit No.	**1**				**2**				**3**				**Mean scores (24-72 h)**
hours post-treatment	1	24	48	72	1	24	48	72	1	24	48	72	
Corneal opacity	0	0	0	0	0	0	0	0	0	0	0	0	**0.0**
Iritis	1	0	0	0	1	0	0	0	1	0	0	0	**0.0**
Redness conjunctivae	2	1	1	0	2	1	0	0	2	1	0	0	**0.44**
Chemosis conjunctivae	2	1	1	0	1	1	0	0	1	1	0	0	**0.44**

* 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

Conclusion:
Under the experimental conditions, CHA 4960 (Fenoxaprop-P-ethyl 69 g/L EW) is not an eye irritant. Thus, no classification is required according to Regulation (EC) No. 1272/2008.

B.6.1.6. Skin sensitization

Reference:	**Fenoxaprop-P-ethyl 69 g/L EW: Local Lymph Node Assay in the Mouse**
Author(s). year:	[redacted] **2005e**
Report/Doc. number:	85 FPE / Study No. 545/352
Guideline(s):	OECD 429 (2002), Method B.42 of 2004/73/EC
Deviations to OECD 429 (2010):	In the preliminary screening test, ear thickness measurements were not conducted. However, as responses were clearly positive in the main test, this is considered a minor deviation.
GLP:	Yes
Acceptability:	Yes

Materials and Methods:
A preliminary screening test was conducted by the application of undiluted test material (25 µL) to the dorsal surface of each ear of the mouse for three consecutive days to determine irritancy potential.
In the main test, groups of female mice were treated with undiluted test material or the test material at concentrations of 25% and 50% v/v in butanone, again for each of three consecutive days. A further group of four mice received vehicle alone in the same manner. Five days following the first topical application of test material, all mice were injected via the tail vein with 250 µL of phosphate buffered saline (PBS) containing 3H-methyl thymidine: each mouse received 20 µCi.

Test material: Fenoxaprop-P-ethyl 69 g/L EW, CHA No. 4960, batch 660-PSH-49
Active ingredient: 7.11% w/w

Control vehicle: Butanone
α-hexylcinnamaldehyde, diluted in 70% ethanol in distilled water

Test animals: ♀ mouse, CBA/Ca (CBA/CaBkl and CBA/Ca CruBR), [redacted]
8-12 weeks, bodyweight 15-23 g
Number of animals: 4 animals per group

Testing Laboratory and Dates: [redacted]
06 May 2005 – 09 June 2005

Five hours later the mice were euthanized, and the lymph nodes removed and pooled from each experimental group. Measurement of radioactivity in the samples was conducted using the Beckmann LS6500 scintillation system. The performing laboratory checked the sensitivity of this particular strain to a known sensitiser, α-hexylcinnamaldehyde, within six months of the main study being conducted.

Findings:
Preliminary study: There were no signs of systemic toxicity.

Main study: No signs of systemic toxicity were noted in the test or control animals during the test. The radioactive disintegrations per minute (dpm) and the SI scores are in table below.
Bodyweight changes were comparable in test and control animals.

Table 6.1.6-1 Dissociations per minute (Dpm), Dpm/Node and Stimulation Index (SI) scores

Test substance (% v/v)	Dpm	Dpm/Node	SI	Result
Vehicle	4764.11	595.51	N/A	N/A
25	20668.41	2583.55	4.34	Positive
50	38596.91	4824.61	8.10	Positive
100	51564.95	6445.62	10.82	Positive
Positive control (% w/v) *				
5	-	-	2.6	Negative
10	-	-	8.4	Positive

25	-	-	12.9	Positive

A = Dpm/node obtained by dividing the Dpm value by 8 (total number of lymph nodes)
N/A = Not applicable
* Not concurrent study. Latest positive control study for LLNA (April 2005).

Conclusion:
Under the experimental conditions, CHA 4960 (Fenoxaprop-P-ethyl 69 g/L EW) is a skin sensitiser. **Thus, classification is required according to Regulation (EC) No. 1272/2008: Skin Sens. 1B: H317: "May cause an allergic skin reaction".**

B.6.1.7. Supplementary studies on the plant protection product
No supplementary studies are required.

B.6.1.8. Supplementary studies for combinations of plant protection products
No supplementary studies are required.

B.6.2. DERMAL ABSORPTION
The *in vitro* (human and rat skin) and *in vivo* (rat) dermal absorption studies were performed with fenoxaprop-P-ethyl formulated as CHA 4960 (Fenoxaprop-P-ethyl 69 g/L EW). The summaries of these studies are presented below.

The dermal absorption of fenoxaprop-P-ethyl is summarised in table below.

Table 6.1.8-1 Summary of dermal absorption studies for Fenoxaprop-P-ethyl 69 g/L EW

Dermal absorption test	% of applied dose		Reference
	Concentrate (69 g/L)	Spray dilution (0.138 g/L)	
In vivo (rat)	7.60#	23.03	[redacted] 2008 Doc No. 252 FPE, filed under KCP 7.3/01
In vitro (human/rat)	0.97 / 2.50	42.81# / 58.33	Maas W.J.M., 2008 Doc No. 256 FPE, filed under KCP 7.3/02
Estimated *in vivo* human dermal absorption	2.95	16.9	Triple pack approach
Dermal absorption estimates used for risk assessment*	3%	17%	

SD value > 25% of the mean value, therefore the absorption estimate was calculated with the addition of standard variation to the mean value
* Dermal absorption estimates rounded to the number of significant digits according to EFSA guidance on Dermal Absorption

Based on these data *in vivo* dermal absorption through human skin is estimated as follows:

$$\textit{In vivo}\ (\text{human}) = \textit{In vivo}\ (\text{rat}) \times \frac{\textit{In vitro}\ (\text{human})}{\textit{In vitro}\ (\text{rat})}$$

The in-use dilution 0.041 kg a.s./ha with 400 L water/ha according to the GAP is not covered by the dermal absorption study conducted with Fenoxaprop-P-ethyl 69 g/L EW. Following the EFSA Guidance on Dermal Absorption, the *pro-rata* correction approach should be applied to derive appropriate dermal absorption values.

For Fenoxaprop-P-ethyl 69 g/L EW field dilutions the following dermal absorption values can be derived:

Fenoxaprop-P-ethyl 69 g/L EW L/ha	Fenoxaprop-P-ethyl (kg/ha)	Water volume L/ha	Concentration g a.s./L	Dermal absorption of in-use dilution
1.2	0.083	100	0.83	17%*
		400	0.2075	17%*
1	0.069	100	0.69	17%*
		400	0.1725	17%*
0.6	0.041	100	0.41	17%*
		400	0.1025	19%

* Covered by spray dilution in the dermal absorption study.

The percentage absorptions used in the operator exposure assessment (resulting in the worst case exposure estimates) are in table below.

Table 6.1.8-2 Dermal absorption endpoints for the risk assessment

Endpoint	Active substance: fenoxaprop-P-ethyl
Dermal penetration	Concentrate (69 g/L): 3% Spray dilutions (0.138 g/L): 17%*

* The application rate of 1.2 L/ha of CHA 4960 (83 g/ha of fenoxaprop-P-ethyl) with the application volume of 100 L water/ha and corresponding dermal absorption value of 17% presents the worst case exposure estimation (comparing to increased water volume/decreased application rate and consequently adjusted dermal absorption value according to *pro-rata* approach as laid out in EFSA Guidance on Dermal Absorption).

Reference:	***In vivo* percutaneous Absorption of an EW Formulation of [^{14}C]Fenoxaprop-P-ethyl in Rats**
Author(s). year:	[redacted] **2008**
Report/Doc. number:	87 FPE / Study No. 545/350
Guideline(s):	OECD 427 (2004), SANCO/222/2000 rev. 7 (19 March 2004), SCP/GUIDE/DERM/002 (30 April 2002)
Deviations:	Dosing was performed via a syringe (0.3 mL) instead of a pipette tip due to leftover test item found by pipetting of the high dose. For determining leftover dose the small plastic rod was extracted with 15 mL of ethanol instead of 20 mL. In the low dose group (Group B) at the last time point (168 h) the rats were observed to have long hairs (over 1 cm long) present at the dose site. Therefore these hairs were shaved and collected in the first skin strip bottle. Due to the large amount of hair it was dissolved in KOH instead of hionic fluor. These deviations are considered not to have affected the validity and outcome of study.
GLP:	Yes
Acceptability:	Yes

Executive Summary

The objective of this study was to evaluate the potential dermal absorption of fenoxaprop-P-ethyl from a Fenoxaprop-P-ethyl 69 g/L EW formulation concentrate, as well as from a representative field dilution (0.138 g/L).

[^{14}C]-Fenoxaprop-P-ethyl was incorporated into the formulation concentrate and dilution prior to application. The doses were applied to the rat skin for an exposure period of 24, 72 and 168 hours. Eight hours after application, the test items were washed off and 24, 72, and 168 hours post-application animals were sacrificed. All samples were analysed by liquid scintillation counting (LSC).

The results of this *in vivo* dermal absorption study indicate that the absorption of fenoxaprop-P-ethyl through rat skin was limited and slow. The vast majority of fenoxaprop-P-ethyl was removed from the skin by the washing procedures.

The total absorbed amounts after 24-hour exposure were 5.04% and 20.14% of the applied dose for the formulation concentrate and dilution, respectively.
The corresponding total potentially absorbable amounts, represented by the mean absorbed dose together with the amounts in the stripped skin were 7.6% and 21.85%, respectively. For the concentrate group the standard deviation of the mean absorption (for stripped skin) estimate exceeded 25% of the mean. Accordingly, the standard deviation value was added to the mean absorption estimate according to the EFSA Guidance on Dermal Absorption (2012).

The dermal penetration estimates were set at 7.6% and 21.85% for the formulation concentrate and dilution, respectively.

Materials and Methods:
The rate of absorption and excretion was investigated in male Wistar rats following single dermal applications of 100 µL of the formulation as either undiluted concentrate (69 g/L) or as a representative field dilution (0.138 g/L). The test items were applied on approximately 10 cm^2 clipped skin in the shoulder and dorsal region under semi-occlusive conditions (protective coverings). Eight hours after application, the test items were washed off using cotton swabs and a mild soap solution.

Test material:

Non-radiolabelled:	Fenoxaprop-P-ethyl analytical standard, batch 703-HF-24, purity 99.3%
Radiolabelled:	[^{14}C]-Fenoxaprop-P-ethyl, batch 2382MFO014-3, purity >99%, specific activity 68.46 mCi/mmol (6.96 MBq/mg)
Formulation:	Fenoxaprop-P-ethyl 69 g/L EW, CHA 4960, batch 660-PSH-76, 6.97% w/w a.s.
Blank formulation:	Fenoxaprop-P-ethyl 69 g/L EW, CHA 4960 – blank formulation, batch 843-djø-104, 0% w/w a.s.

Test animals:	Wistar rat, Wistar (Crl:(WI)WU BR), [redacted] 9-10 weeks, bodyweight 293-329g
Number of animals:	4 per test group, see Table 6.1.8-3

24, 72, and 168 hours post-application, animals were sacrificed and skin was tape-stripped removing the *stratum corneum*. Application site, untreated skin, plasma, whole blood, gastro intestinal tract, and residual carcass were assayed for radioactivity together with faeces, urine and cage-wash. Also the skin wash, skin strips, and protective coverings were assayed for radioactivity. The experimental design is displayed in the table below.

Table 6.1.8-3 Experimental design – overview of test groups

Group	Nominal concentration	Dose*	Number of animals	Exposure/post exposure time			Sacrifice post application
AT1	69 g/L	690 µg/cm^2	4	8 h	+	16 h**	24 h
AT2	69 g/L	690 µg/cm^2	4	8 h	+	64 h**	72 h
AT3	69 g/L	690 µg/cm^2	4	8 h	+	160 h**	168 h
BT1	0.138 g/L	1.38 µg/cm^2	4	8 h	+	16 h**	24 h
BT2	0.138 g/L	1.38 µg/cm^2	4	8 h	+	64 h**	72 h
BT3	0.138 g/L	1.38 µg/cm^2	4	8 h	+	160 h**	168 h

* 100 µL of the dose preparation was applied to 10 cm^2 of clipped skin.
** Post-exposure monitoring after washing skin with a neutral aqueous detergent to remove non-absorbed material.

Testing Laboratory and Dates:	[redacted] 24 September 2007-09 September 2008

Findings:
Analysis of dose preparations: Stability and radiochemical purity in the high and low dose solution was demonstrated. The low dose groups received a somewhat higher concentration than the intended 0.138 mg/g, while the deviation between actual and intended concentrations in the high dose groups was approx. 3%. Animals of group A received a dose between 670 and 713 µg fenoxaprop-P-ethyl/cm^2 and animals of group B between 1.36 and 1.49 µg/cm^2.

Percutaneous absorption: Mean radioactivity found in the carcass, skin, urine, faeces, skin wash and coverings are shown in Table 6.1.8-4. Mean recovery rates for all time points were higher than 95%, except in the high dose group at 24 hours it was slightly lower (94.5%). Therefore a correction was made according to EFSA GD on Dermal Absorption (EFSA Journal 2012;10(4):2665)

Table 6.1.8-4 Summary table of absorption and excretion, Average values (n=4) expressed as % of the applied dose

Dose	**A: 690 µg/cm^3**			**B: 1.38 µg/cm^3**		
Time group	**T1**	**T2**	**T3**	**T1**	**T2**	**T3**
Sacrificed after	**24 h**	**72 h**	**168 h**	**24 h**	**72 h**	**168 h**
Urine (total)	1.12 ± 0.22	2.38 ± 0.53	2.63 ± 0.88	5.04 ± 0.90	11.59 ± 1.53	9.42 ± 2.04
Faeces (total)	0.98 ± 0.24	2.15 ± 0.48	2.41 ± 0.49	4.12 ± 2.90	11.10 ± 0.59	8.72 ± 1.49
Cage wash	0.08 ± 0.01	0.06 ± 0.02	0.03 ± 0.01	0.28 ± 0.12	0.31 ± 0.07	0.05 ± 0.01
Tissues*	0.24 ± 0.07	0.08 ± 0.01	0.05 ± 0.01	0.96 ± 0.21	0.34 ± 0.07	0.12 ± 0.02
GI-tract	0.83 ± 0.12	0.19 ± 0.04	0.08 ± 0.02	3.88 ± 0.22	0.93 ± 0.31	0.12 ± 0.02
Carcass	1.79 ± 0.82	0.94 ± 0.18	0.48 ± 0.20	5.86 ± 1.28	2.77 ± 0.43	0.84 ± 0.13
Absorbed	**5.04 ± 1.04**	**5.80 ±0.99**	**5.68 ±1.54**	**20.14 ± 3.90**	**27.03 ± 2.68**	**19.16 ± 3.53**
Skin strips total	2.44 ± 1.62	1.29 ± 0.60	1.90 ± 0.47	4.98 ± 1.62	5.79 ± 1.00	4.94 ± 1.61
Stripped skin	1.34 ± 1.22	1.40 ± 0.94	0.16 ± 0.14	1.71 ± 0.19	0.66 ± 0.41	0.05 ± 0.00
Total skin	**3.78 ± 2.83**	**2.69 ± 1.46**	**2.06 ± 0.58**	**6.68 ± 1.68**	**6.45 ± 1.01**	**4.99 ± 1.61**
Total skin wash	82.64 ± 7.99	84.47 ± 0.50	86.19 ± 1.84	66.35 ± 3.95	61.70 ± 4.92	72.59 ± 5.96
O-ring and cover	4.83 ± 2.22	3.68 ± 0.56	2.74 ± 0.46	1.29 ± 0.23	1.62 ± 1.08	1.42 ± 0.41
Not absorbed	87.47 ± 5.77	88.15 ± 0.94	88.93 ± 1.45	67.64 ± 4.18	63.33 ± 4.20	74.00 ± 5.75
Total recovery	**96.29 ± 2.36**	**96.64 ± 0.15**	**96.67 ± 0.20**	**94.47 ± 0.95**	**96.81 ± 0.98**	**98.15 ± 3.12**

* Terminal blood obtained by exsanguination + control skin

High dose group (corresponding to formulation concentrate)
After a single topical application of [^{14}C]-Fenoxaprop-P-ethyl at 69 g/L, the mean total recoveries of radioactivity were in the range of 96.29 to 96.67% of the dose.

A high proportion of the applied dose was removed from the skin by the swabbing ranging from 82.64 to 86.19% of the dose applied. The mean total radioactivity considered non-absorbed was in the range of 87.47 to 88.93% of the applied dose.

The material remaining in the treated skin following the removal of the residual dose ranged between 0.16% and 1.40% of dose applied. The amount of radioactivity dislodged by the tape-stripping procedure ranged between 1.29% and 2.44% of dose applied. Most of the radioactivity in the skin was removed by skin stripping with the majority of the dose being observed in the first strip indicating that fenoxaprop-P-ethyl remained on the surface of the *stratum corneum* and would not therefore be available for absorption.

The mean percentage of [^{14}C]-Fenoxaprop-P-ethyl in the Fenoxaprop-P-ethyl 69 g/L EW formulation directly absorbed, corresponding to amounts found in urine, faeces, tissues, GI-tract, carcass and cage-wash was 5.04, 5.80, and 5.68% after 24, 72, and 168 hours.
The mean percentage of [^{14}C]-Fenoxaprop-P-ethyl considered potentially absorbable (directly absorbed plus stripped skin) was 6.38, 7.20, and 5.84% after 24, 72, and 168 hours

The absorption was essentially complete at the end of study (> 75% absorption within half the study duration); accordingly all tape strips were excluded from the calculation of dermal absorption.

Since there was a significant variation of replicates in this dose group (5.84% ± 1.50; standard deviation of the absorption estimate was > 25% of the mean value), the absorption estimate was calculated with the addition of standard variation to the mean value.

Dilution group
After a single topical application of [^{14}C]-Fenoxaprop-P-ethyl at 0.138 g/L, the mean total recoveries of radioactivity were in the range of 94.47 to 98.15% of the dose.

A high proportion of the applied dose was removed from the skin by the swabbing ranging from 61.70 to 72.59% of the dose applied. The mean total radioactivity considered non-absorbed was in the range of 63.33 to 74.00% of the applied dose.

The material remaining in the treated skin following the removal of the residual dose ranged between 0.05% and 1.71% of dose applied. The amount of radioactivity dislodged by the tape-stripping procedure ranged between 4.94% and 5.79% of dose applied. Most of the radioactivity in the skin was removed by skin stripping with the majority of the dose being observed in the first strip indicating that fenoxaprop-P-ethyl remained on the surface of the *stratum corneum* and would not therefore be available for absorption.

The mean percentage of [^{14}C]-Fenoxaprop-P-ethyl directly absorbed, corresponding to amounts found in urine, faeces, tissues, GI-tract, carcass and cage-wash was 20.14, 27.03, and 19.16% after 24, 72, and 168 hours. As mean recovery rate was lower than 95% for the 24h sample, the value was corrected to 21.32%.

The mean percentage of [^{14}C]-Fenoxaprop-P-ethyl considered potentially absorbable (directly absorbed plus stripped skin) was 23.03, 27.69, and 19.21% after 24, 72, and 168 hours.

The absorption was essentially complete at the end of study (> 75% absorption within half the study duration); accordingly all tape strips were excluded from the calculation of dermal absorption.

Since there was no significant variation of replicates in this dose group (19.21% ± 3.53; standard deviation of the absorption estimate was < 25% of the mean value), the absorption estimate was calculated without the addition of standard variation to the mean value.

Conclusion:
Based on the findings in this study, the determined dermal absorption rate in rats within 168 hours can be considered as a worst case scenario for the occupational exposure of typically 6 to 8 h. Thus, worst case assumptions are taken into account determining the penetration of fenoxaprop-P-ethyl through rat skin at a typical concentration used in the field (0.138 g/L and for the formulated concentration (69 g/L).

Following 24-hour exposure to the concentrated product, the direct absorption after 24 h was 5.04%. The mean percentage of [^{14}C]-Fenoxaprop-P-ethyl that was considered potentially absorbable (directly absorbed plus stripped skin) was 6.38% after 24 hours. By taking into account the standard deviation value (for stripped skin), dermal absorption rate of 7.60% was determined for the concentrate.

Following 24-hour exposure to the low dose, the direct absorption after 24 h was 21.32% (corrected for low recovery). The mean percentage of [^{14}C]-Fenoxaprop-P-ethyl that was considered potentially absorbable (directly absorbed plus stripped skin) was 23.03% after 24 hours. Dermal absorption rate of 23.03% was determined for the low dose.

Reference:	***In vitro* percutaneous Absorption of an EW Formulation of [^{14}C]Fenoxaprop-P-ethyl through human and rat skin membranes using flow-through diffusion cells**
Author(s). year:	**Maas W.J.M., 2008**
Report/Doc. number:	256 FPE / Study No. V7623/02.02
Guideline(s):	OECD 428 (2004), SANCO/222/2000 rev. 7 (19 March 2004), SCP/GUIDE/DERM/002 (30 April 2002)
Deviations:	Rat skin was isolated from two rats instead of one. The batch number of the placebo formulation was 843-djø-104 instead of 840-djø-104 as erroneously stated in the study plan. These deviations are considered not to have affected the validity and outcome of the study.
GLP:	Yes
Acceptability:	Yes

Executive Summary
The objective of this study was to evaluate the potential dermal absorption of fenoxaprop-P-ethyl from a Fenoxaprop-P-ethyl 69 g/L EW formulation concentrate, as well as from representative field dilution (0.138 g/L).

[^{14}C]-Fenoxaprop-P-ethyl was incorporated into the formulation concentrate and dilution prior to application. The doses were applied to human and rat skin membranes for an exposure period of 24 hours. The absorption process was followed by taking samples of the receptor fluid at recorded intervals throughout the exposure period. The distribution of fenoxaprop-P-ethyl within the test system and a 24-hour absorption profile were determined. All samples were analysed by liquid scintillation counting (LSC).

The results of this *in vitro* dermal absorption study indicate that the absorption of fenoxaprop-P-ethyl through human skin was limited and slow. The vast majority of fenoxaprop-P-ethyl was removed from the skin by the washing procedures.

The total absorbed amounts after 24 hour exposure were 0.47% (concentrate formulation) and 17.74% (field dilution) of the applied dose for human skin and 2.39% (concentrate formulation) and 48.38% (field dilution) of the applied dose for rat skin.

The corresponding total potentially absorbable amounts, represented by the mean absorbed dose together with the amounts in the skin membrane and the *stratum corneum*, except for the first 2 tape strips, were 0.97% (concentrate formulation) and 33.55% (field dilution) of the applied dose for human skin and 2.50% (concentrate formulation) and 58.33% (field dilution) of the applied dose for rat skin.
For the human skin field dilution group the standard deviation of the mean absorption estimate exceeded 25% of the mean. Although not considered scientifically appropriate, but in line with current regulatory practice in Europe, the standard deviation value was added to the mean absorption estimate.

For human skin, the dermal penetration estimates of 0.97% and 42.81% were determined for the formulation concentrate and field dilution, respectively.
For rat skin, the dermal penetration estimates of 2.50% and 58.33% were determined for the formulation concentrate and field dilution, respectively.

Materials and Methods:
Preparation of skin membranes**:**
Human skin membranes were prepared from skin samples obtained directly after abdominal surgery. Human skin was obtained from three female donors directly after surgery. Skin was stored in aluminium foil at <-18°C until use. After thawing, skin was cut to a recorded thickness of approximately 400 µm.
Upon thawing of the rat skin, discs with a diameter of 16 mm were punched out and subcutaneous tissue was removed. Skin thickness for rat skin samples were between 0.441-0.617mm.

Flow-through diffusion cells and receptor fluid**:** The skin membranes were placed in flow-through automated diffusion cells. The mean skin surface temperature was 32.1-32.3 ºC, at ambient humidity.
The receptor fluid was pumped at a speed of *ca* 1.6 mL/h and consisted of saline (0.9 % sodium chloride (w/v) containing 6% polyoxy-ethylene 20-olelyl ethyl glycol (w/v). Solubility of fenoxaprop-P-ethyl was verified in this study.

Test material:

Non-radiolabelled: Fenoxaprop-P-ethyl analytical standard, batch 703-HF-24, purity 99.3%

Radiolabelled: [^{14}C]-Fenoxaprop-P-ethyl, batch 2382MFO014-3, purity >99%, specific activity 68.46 mCi/mmol (6.96 MBq/mg)

Formulation: Fenoxaprop-P-ethyl 69 g/L EW, CHA 4960, batch 660-PSH-76, 6.97% w/w a.s.

Blank formulation: Fenoxaprop-P-ethyl 69 g/L EW, CHA 4960 – blank formulation, batch 843-djø-104, 0% w/w a.s.

Radiolabelled reference substance: [^{3}H]$H_2$0, batch 3559732, specific activity 37 MBq/g, purity not determined

Test systems: Human abdominal skin, 35-37 years (directly after surgery)
Rat skin (dorsal and flank skin) from ca 7 weeks old rat, Wistar (Crl:(WI)WU BR), [redacted]

Number of donors: Three human donors
Two male rat (see deviations)

Experimental design**:** Fenoxaprop-P-ethyl was applied at two dose levels of nominal 69 g/L (representing the formulation concentrate) and of nominal 0.138 g/L (representing the field dilution). Eight hours after application, the unabsorbed test item was removed from the application site using cotton swabs and a mild soap solution (3% Teepol in water). Receptor fluid was sampled until 24 hour post-application. *Stratum corneum* was removed by tape-stripping 10 times 24 hours after application. At termination, radioactivity in the skin, in tape-strips, in the donor compartment, and in the receptor compartment was determined. The experimental design is displayed in table below.

Table 6.1.8-5 Experimental design – overview of test groups

Test group	Group size	Species	Measured conc.	Mean dose a.s. applied**	Exposure time	Sampling of receptor fluid
A	9*	Human	70.1 g/L	676.7 µg/cm^2	8 h	0-24 h
B	9*	Human	0.154 g/L	1.48 µg/cm^2	8 h	0-24 h
C	9	Rat	70.1 g/L	680.9 µg/cm^2	8 h	0-24 h
D	9	Rat	0.154 g/L	1.46 µg/cm^2	8 h	0-24 h

* Three skin membranes from three donors in each test group
** The dose remaining in the pipette tip after application was subtracted from the gross dose. Thus, a new volume of approx. 6.4 µL of the dose preparation was applied on each skin membrane.

Determination of radioactivity: The radioactivity content in the samples was determined using liquid scintillation counter (LSC) analyses. The radiochemical purity of the radiolabelled test substance was determined by high performance liquid chromatography (HPLC).

Testing Laboratory and Dates: TNO Quality of Life, Zeist, the Netherlands;
29 August 2007 – 11 September 2008

Findings:

Integrity of skin membranes: Prior to the determination of the percutaneous absorption of beta-cyfluthrin, the permeation coefficient (K_p) for tritiated water was determined in human and rat skin membranes.
Skin membranes with a K_p value below the cut-off value of 2.5×10^{-3} cm/h (human) or 3.5×10^{-3} cm/h (rat) were selected for the study.

Receptor fluid solubility: The solubility of fenoxaprop-P-ethyl in the receptor fluid is considered to be adequate. The maximum applied dose was approx. 690 µg/cm^2. Assuming that 10% of this dose will reach the receptor fluid in 24 h, the required solubility would be 44.2 µg in 38.4 mL (i.e. approx. 1.2 µg/mL). The solubility of fenoxaprop-P-ethyl in the receptor fluid was determined to be approx. 21 µg/mL, thus exceeding the required solubility with a factor of 17.5.

Percutaneous absorption: Summary of cumulative absorption data are presented in Table 6.1.8-6.

Table 6.1.8-6 Cumulative absorption, Summary of the in vitro percutaneous penetration of fenoxaprop-P-ethyl formulated as Fenoxaprop-P-ethyl 69g/L EW through human and rat skin

	Human skin				**Rat skin**			
	Concentrate (Group A)		**Field dilution (Group B)**		**Concentrate (Group C)**		**Field dilution (Group D)**	
Target concentration [g/L]	69		0.138		69		0.138	
Mean dose applied [µg/cm^2] ± standard deviation	676.7 ± 4.5		1.48 ± 0.02		680.9 ± 11.4		1.46 ± 0.02	
Number of cells	9		9		9		9	
Sample time [h]	[µg/cm²]	[%]	[µg/cm²]	[%]	[µg/cm²]	[%]	[µg/cm²]	[%]
1	0.00		0.000		0.002		0.000	
2	0.00		0.001		0.024		0.005	
4	0.02		0.013		0.297		0.026	
6	0.04		0.020		0.745		0.050	
8	0.07		0.028		1.307		0.076	
10	0.12		0.036		2.119		0.104	
12	**0.18**	**23.7[a]**	**0.044**	**46.8[a]**	**2.841**	**44.3[a]**	**0.125**	**64.4[a]**
14	0.25		0.052		3.576		0.143	
16	0.34		0.060		4.263		0.158	
18	0.44		0.069		4.897		0.171	
20	0.54		0.077		5.461		0.183	
22	0.65		0.086		5.963		0.194	
24	0.76	100%	0.094	100%	6.406	100%	0.204	100%
Maximal flux [µg/cm^2/h]	0.051		0.004		0.384		0.013	
Lag time [h]	8.8		2.2		4.3		2.1	

[a]: Mean cumulative absorption rate in receptor fluid at first half of the study

Using maximal flux values, human skin was 7.5 time less permeable for fenoxaprop-P-ethyl formulated as the concentrate as compared to rat skin. When the field dilution was applied, human skin was 3.25 times less permeable for fenoxaprop-P-ethyl than rat skin.

In both dose groups absorption was below 75% after 12 hours. For the concentrate group and field dilution group cumulative absorption in receptor fluid at the first half of the study was 23.7% and 46.8% for human skin and 44.3% and 64.4 for rat skin of the total absorbed radioactivity, respectively. Accordingly, all tape strips, except for the first 2 tape strips, were added to the absorption estimate.

The mean recovery of fenoxaprop-P-ethyl in human skin was 107.9% and 97.8% for the concentrate formulation and field dilution, respectively.

The mean recovery of fenoxaprop-P-ethyl in rat skin was was 106.4% and 100.5% for the concentrate formulation and field dilution, respectively.

Accordingly, as the mean total recoveries for both concentrate and field dilution groups were >95%, no adjustment of the dermal penetration values was necessary.

The mean total absorption, defined as the compound-related radioactivity present in the receptor fluid, the receptor compartment wash and the skin membranes (excluding tape strips) was 0.47% (concentrate formulation) and 17.74% (field dilution) of the applied dose for human skin and 2.39% (concentrate formulation) and 48.38% (field dilution) of the applied dose for rat skin.

The mean potentially absorbed dose, which is defined as the compound-related radioactivity present in the receptor fluid, the receptor compartment wash, the skin membranes and the *stratum corneum* (except for the first 2 tape strips) was 0.97% (concentrate formulation) and 33.55% (field dilution) of the applied dose for human skin and 2.50% (concentrate formulation) and 58.33% (field dilution) of the applied dose for rat skin.

For the human skin field dilution group the standard deviation (SD) of the mean absorption estimate was > 25%. Accordingly, one standard deviation was added to the mean absorption estimate.

For the human skin concentrate group and rat skin concentrate and field dilution group the standard deviation (SD) of the mean absorption estimate was below 25% of the mean, therefore the standard deviation was not added to the mean absorption estimate.

For human skin, the adjusted dermal absorption estimates of 0.97% and 42.81% were determined for the formulation concentrate and field dilution, respectively.

For rat skin, the adjusted dermal absorption estimates of 2.50% and 58.33% were determined for the formulation concentrate and field dilution, respectively.

The dermal absorption data are summarized in tables below.

Table 6.1.8-7 Recovery data – human skin, Summary of the in vitro percutaneous penetration of fenoxaprop-P-ethyl formulated as Fenoxaprop-P-ethyl 69g/L EW through human skin and rat skin

Test substance name	**Concentrate**		**Dilution**	
Target concentration [mg/mL]	**69**		**0.138**	
Target dose [µg/cm^2]	**690**		**1.38**	
Mean actual dose [µg/cm^2]	**676.1**		**1.48**	
	Recovery [%]		**Recovery [%]**	
	Mean	SD	Mean	SD
Unabsorbed dose				
Skin washing	106.00	4.10	49.60	9.10
Donor chamber	0.16	0.09	2.70	4.02
Dose associated to skin				
Tape strips 1 + 2	0.73	0.46	12.03	3.34
Tape strips, rest	0.50	0.24	15.80	4.91
Tape strips, total	1.23	0.67	27.76	5.04
Skin sample	0.35	0.09	11.12	4.54
Absorbed dose				
Receptor fluid	0.11	0.09	6.37	3.13
Receptor chamber	0.01	0.00	0.25	0.11
Total absorbed dose	0.12	0.09	6.62	3.23
Total recovery	107.89	4.26	97.78	2.06
Assessment according to EFSA guideline*				
Is the overall recovery >= 95%?[§]	YES		YES	
Is the study duration up to 24 hours?	YES		YES	
Did >=75% of the absorption occur in the first half of the study?	NO		NO	
Were tape strips analyzed individually?	YES		YES	
Dermal absorption [in %]	0.97	0.2	33.55	9.26
Significant variation between groups or replicates?	NO		YES	
Adjusted dermal absorption[&]	0.97		42.81	

The values presented here might deviate from the values presented in the study report due to rounding.
* "Guidance on Dermal Absorption", EFSA Journal 2012; 10(4):2665
[§] When the recovery is below 95% dermal absorption is presented as a percentage of the total amount recovered, i.e. "normalised".
[&] Adjustment for significant variation: one SD is added to the DA mean when the SD is >= 25% of the DA mean.

Table 6.1.8-8 Recovery data – rat skin, Summary of the in vitro percutaneous penetration of fenoxaprop-P-ethyl formulated as Fenoxaprop-P-ethyl 69g/L EW through human skin and rat skin

Test substance name	**Concentrate**		**Dilution**	
Target concentration [mg/mL]	**69**		**0.138**	
Target dose [µg/cm^2]	**690**		**1.38**	
Mean actual dose [µg/cm^2]	**680.9**		**1.46**	
	Recovery [%]		**Recovery [%]**	
	Mean	SD	Mean	SD
Unabsorbed dose				
Skin washing	103.60	3.90	35.70	7.40
Donor chamber	0.11	0.04	0.79	0.76
Dose associated to skin				
Tape strips 1 + 2	0.13	0.10	5.69	2.40
Tape strips, rest	0.11	0.11	9.95	6.01
Tape strips, total	0.24	0.17	15.64	7.34
Skin sample	1.40	0.31	33.61	3.93
Absorbed dose				
Receptor fluid	0.94	0.22	13.99	2.78
Receptor chamber	0.05	0.03	0.78	0.33
Total absorbed dose	0.99	0.24	14.76	2.88
Total recovery	106.37	3.95	100.5	1.35
Assessment according to EFSA guideline*				
Is the overall recovery >= 95%?[§]	YES		YES	
Is the study duration up to 24 hours?	YES		YES	
Did >=75% of the absorption occur in the first half of the study?	NO		NO	
Were tape strips analyzed individually?	YES		YES	
Dermal absorption [in %]	2.50	0.45	58.33	5.03
Significant variation between groups or replicates?	NO		NO	
Adjusted dermal absorption[&]	2.50		58.33	

The values presented here might deviate from the values presented in the study report due to rounding.
* "Guidance on Dermal Absorption", EFSA Journal 2012; 10(4):2665
[§] When the recovery is below 95% dermal absorption is presented as a percentage of the total amount recovered, i.e. "normalised".
[&] Adjustment for significant variation: one SD is added to the DA mean when the SD is >= 25% of the DA mean.

Conclusion:
The results of this *in vitro* dermal absorption study indicate that the absorption of fenoxaprop-P-ethyl through human skin was limited and slow. The vast majority of fenoxaprop-P-ethyl was removed from the skin by the washing procedures.

The total absorbed amounts after 24 hour exposure were 0.47% (concentrate formulation) and 17.74% (field dilution) of the applied dose for human skin and 2.39% (concentrate formulation) and 48.38% (field dilution) of the applied dose for rat skin.

The corresponding total potentially absorbable amounts, represented by the mean absorbed dose together with the amounts in the skin membrane and the *stratum corneum*, except for the first 2 tape strips, were 0.97% (concentrate formulation) and 33.55% (field dilution) of the applied dose for human skin and 2.50% (concentrate formulation) and 58.33% (field dilution) of the applied dose for rat skin.

For the human skin field dilution group the standard deviation of the mean absorption estimate exceeded 25% of the mean. Although not considered scientifically appropriate, but in line with current regulatory practice in Europe, the standard deviation value was added to the mean absorption estimate.

For human skin, the dermal penetration estimates of 0.97% and 42.81% were determined for the formulation concentrate and field dilution, respectively.

For rat skin, the dermal penetration estimates of 2.50% and 58.33% were determined for the formulation concentrate and field dilution, respectively.

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

CONFIDENTIAL information - data provided separately (Document J)

B.6.4. EXPOSURE DATA

B.6.4.1. Operator exposure

The plant protection product CHA 4960 containing 69 g/L of fenoxaprop-P-ethyl is intended to be used on cereals as an herbicide. Usage information pertinent to operator exposure is summarised in the table below.

Table 6.4.1-1 Summary of representative uses of CHA 4960

Crop	F*	Application rate		Water volume L/ha	Method of application	Max. no of appl.
		kg a.s./ha	L product/ha			
Cereals	F	0.083	1.2	100	Tractor-mounted boom	1

* F – field

Estimations of potential operator exposure have been undertaken for fenoxaprop-P-ethyl using the list of representative uses and the following predictive model:

- Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. EFSA Journal 2014;12(10):3874.

The estimations were compared to following data:

Endpoint	Active substance: fenoxaprop-P-ethyl
Dermal penetration*	Concentrate (69 g/L): 3% Spray dilutions (0.138 g/L): 17%**
AOEL	0.014 mg/kg bw/day
Oral absorption	100%

* Dermal penetration data – please refer to Section CP 7.3 for further details.
** The application rate of 1.2 L/ha of CHA 4960 (83 g/ha of fenoxaprop-P-ethyl) with the application volume of 100 L water/ha and corresponding dermal absorption value of 14% presents the worst case exposure estimation (as compared to increased water volume/decreased application rate and consequently adjusted dermal absorption value according to pro-rata approach as laid out in EFSA Guidance on Dermal Absorption); please refer to B.6.2 and Table 6.1.8-2

Corresponding results of the exposure calculations are presented in the following tables.

Table 6.4.1-2 Estimated operator exposure to fenoxaprop-P-ethyl

Model data	Level of PPE	Total absorbed dose (mg/kg/day)	% of AOEL*
Vehicle-mounted downward spraying outdoors on cereals Application rate: 1.2 L product/ha (0.083 kg/ha fenoxaprop-P-ethyl)			
EFSA Guidance: 50 ha/day, 8 h/day 100 L/ha 60 kg operator	no PPE	0.0094	66.85

* Reference Value Non Acutely Toxic Active Substance (RVNAS) for EFSA Guidance
No PPE: Operator wearing work wear – arms body and legs covered, but no gloves

CONCLUSION
According to the EFSA Guidance calculations, it can be concluded that the risk for the operator using CHA 4960 for the intended uses is acceptable without the use of personal protective equipment.

B.6.4.1.1. Estimation of operator exposure

Vehicle-mounted downward spraying outdoors on cereals
Exposure estimation according to EFSA Guidance

Assumptions to assess operator exposure according to the EFSA Guidance are summarised below:

Application equipment:	Vehicle-mounted downward spraying outdoors on cereals
Application rate:	1.2 L product/ha (0.083 kg/ha fenoxaprop-P-ethyl)
Treated area	50 ha per day
Spray volume	100 L/ha
Work duration	8 hours
Dermal absorption	Fenoxaprop-P-ethyl: 3% for concentrate; 17% for in-use dilution
Body weight	60 kg
PPE	Operator wearing work wear – arms body and legs covered, but no gloves

The results are summarised in Table 6.4.1-2 above. Detailed calculations are given in Appendix 1.1.

B.6.4.1.2. Measurement of operator exposure

Since the exposure estimates carried out indicated that the AOEL will not be exceeded under practical conditions of use, a study to provide a measure of operator exposure is not deemed necessary.

B.6.4.2. Bystander and resident exposure

Bystander and resident exposure estimations were performed for the application of CHA 4960 for the representative uses according to the EFSA Guidance[1] and German guidance (Martin *et al.* 2008[2]), taking into account the highest application rate as a worst-case.

It has to be noted that according to the Commission Guidance Document[3], for the approval of active substances under Regulation (EC) No 1107/2009, the risk assessment on residents and bystanders cannot be fully considered until a procedure for the derivation of the Acute AOEL (AAOEL) and higher risk assessment schemes, identified as missing by the Standing Committee, are available.

Since there is no accepted relevant endpoint (e.g. Acute AOEL), calculation of bystander exposure according to EFSA Guidance assessment is not addressed. The risk assessment for residents and bystanders is therefore also presented according to Martin *et al.* (2008).

Corresponding results of the exposure calculations are presented in the following tables.

Table 6.4.2-1 Estimated resident exposure to fenoxaprop-P-ethyl and % of the AOEL* according to EFSA Guidance

	Fenoxaprop-P-ethyl

[1] EFSA, 2014. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. EFSA Journal 2014;12(10):3874
[2] Martin S. *et al.* Guidance for exposure and risk evaluation for bystanders and residents exposed to plant protection products during and after application, J. Verbr. Lebensm., Vol 3, No. 3, p. 272-281, August 2008
[3] Commission Guidance Document. SANTE-10832-2015, 29 May 2015. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products.

	Absorbed dose (mg/kg bw/day)	% of AOEL*
Resident – Child		
Spray drift (75th percentile)	0.0038	27.16
Vapour (75 the percentile)	0.0011	7.64
Surface deposits (75th percentile)	0.0003	1.95
Entry into treated crops (75th percentile)	0.0024	17.01
All pathways (mean)	0.0053	**37.61**
Resident – Adult		
Spray drift (75th percentile)	0.0009	6.48
Vapour (75 the percentile)	0.0002	1.64
Surface deposits (75th percentile)	0.0001	0.69
Entry into treated crops (75th percentile)	0.0018	9.45
All pathways (mean)	0.0018	**12.76**

* Reference Value Non Acutely Toxic Active Substance (RVNAS) for EFSA Guidance

Table 6.4.2-2 Estimated bystander and resident exposure to fenoxaprop-P-ethyl and % of the AOEL according to Martin *et al.*

	Fenoxaprop-P-ethyl	
	Adult	**Child**
Bystander		
Dermal exposure (mg/kg bw/day)	6.51×10^{-4}	5.08×10^{-4}
Inhalation exposure (mg/kg bw/day)	3.84×10^{-7}	8.20×10^{-7}
Total systemic exposure (mg/kg bw/day)	6.52×10^{-4}	5.09×10^{-4}
% of AOEL	4.66	3.64
Resident		
Dermal exposure (mg/kg bw/day)	4.76×10^{-5}	6.29×10^{-5}
Inhalation exposure (mg/kg bw/day) (mg/kg bw/day)	-	-
Oral exposure (hand-to-mouth transfer) (mg/kg bw/day)	-	2.85×10^{-5}
Oral exposure (object-to-mouth transfer) (mg/kg bw/day)	-	7.12×10^{-6}
Total systemic exposure (mg/kg bw/day)	4.76×10^{-5}	9.85×10^{-5}
% of AOEL	0.28	0.62

CONCLUSION
It is concluded that there is no undue risk to any bystander and resident after accidental short-term exposure to CHA 4960.

B.6.4.2.1. Estimation of bystander and resident exposure

EFSA Guidance

Bystander exposure
Since there is no accepted relevant endpoint (e.g. Acute AOEL) bystander exposure risk according to EFSA Guidance assessment is not addressed.

Resident Exposure
Further assumptions are presented in the following:

Application equipment:	Vehicle-mounted downward spraying outdoors on cereals
Application rate:	1.2 L product/ha (0.083 kg/ha fenoxaprop-P-ethyl)
Buffer strip:	2-3 m
Drift on surface:	5.60% (75th perc.); 4.10% (mean)
Exposure duration (dermal):	2 hours
Exposure duration (inhalation):	24 hours

Exposure duration (entry into treated crops):	0.25 hours
Maximum air concentration of active substance:	1 µg/m^3/24h
Breathing rate:	0.23 m^3/day/kg for adults 1.07 m^3/day/kg for children
Turf transferable residues:	5%
Transfer coefficient:	7300 m^2/h for adults 2600 m^2/h for children
Turf transferable residues – mouthing:	20% for children
Hand surface area:	20 cm^2/event for children
Frequency of hand-to-mouth:	9.5 events/h for children
Salivation extraction factor:	50% for children
Ingestion rate for mouthing of grass:	25 cm^2/day for children
Transfer coefficient for entry into treated crops (75th percentile):	7500 m^2/h for adults 2250 m^2/h for children
Transfer coefficient for entry into treated crops (mean):	5980 m2/h for adults 1794 m2/h for children
Dermal absorption:	Fenoxaprop-P-ethyl: 17%
Body weight:	60 kg for adults 10 kg for children

The results are summarised in

Table 6.4.2-1 above. Detailed calculations are given in Appendix 1.2.

<u>German guidance</u>

Bystander exposure

Further assumptions are presented in the following:

Application equipment:	Vehicle-mounted downward spraying outdoors on cereals
Application rate:	1.2 L product/ha (0.083 kg/ha fenoxaprop-P-ethyl)
Drift:	2.77% at 1 m
Exposure duration:	5 minutes
Exposed body surface:	1 m^2 for adults 0.21 m^2 for children
Dermal absorption:	Fenoxaprop-P-ethyl: 17%
Body weight:	60 kg for adults 16.15 kg for children

The results are summarised in

Table 6.4.2-2 above. Detailed calculations are given in Appendix 1.3.

Resident exposure

Further assumptions are presented in the following:

Application rate:	1.2 L product/ha (0.083 kg/ha fenoxaprop-P-ethyl)
Drift:	2.77% at 1 m
Exposure duration:	2 hours for dermal exposure 24 hours for inhalation exposure
Maximum air concentration of active substance:	1 µg/m^3/24h
Turf transferable residues:	5%
Transfer coefficients:	7300 cm^2/hour for adults 2600 cm^2/hour for children
Saliva extraction factor:	50% for hand-to-mouth transfer for children
Frequency of hand-to-mouth:	20 events/hour for children
Dislodgeable foliar residues:	20% for children
Surface area of hands:	20 cm^2 for children
Ingestion rate for mouthing of grass:	25 cm^2/day for children
Dermal absorption:	Fenoxaprop-P-ethyl: 17%
Body weight:	60 kg for adults 16.15 kg for children

The results are summarised in

Table 6.4.2-2 above. Detailed calculations are given in Appendix 1.4.

B.6.4.2.2. Measurement of bystander and resident exposure

Since the exposure estimate carried out indicated that the AOEL will not be exceeded under practical conditions of use, a study to provide a measure of bystander and resident exposure is not deemed necessary.

B.6.4.3. Worker exposure

The plant protection product CHA 4960 will be used on cereals in the field and will be applied once per season.

Crops treated with CHA 4960 potentially have to be re-entered by workers after the application. Regarding the intended crops, the work activities include re-entry activity as inspection/scouting of the crop.

Exposure assessment of a worker during inspection/scouting in cereals wheat treated with the highest recommended application rate 1.2 L product/ha (i.e. 0.083 kg/ha fenoxaprop-P-ethyl) is presented.
The worker exposure evaluation for the application of CHA 4960 is performed according to EFSA Guidance.

Corresponding results of the exposure calculations are presented in the following tables.

Table 6.4.3-1 Estimated worker exposure to fenoxaprop-P-ethyl / EFSA Guidance

		Exposure parameter	
Exposure scenario	**AOEL* (mg/kg bw/day)**	**Absorbed dose (mg/kg bw/day)**	**% of AOEL***
		unprotected worker[1]	
Inspection	0.014	0.0020	14.11

* Reference Value Non Acutely Toxic Active Substance (RVNAS) for EFSA Guidance
[1] Worker wearing work wear - arms, body and legs covered, but no gloves

CONCLUSION

It is concluded that there is no unacceptable risk anticipated for the worker wearing adequate work clothing (but no PPE), when re-entering crops treated with CHA 4960.

B.6.4.3.1. Estimation of worker exposure

Exposure of workers when performing re-entry activities is calculated considering the approach proposed by the EFSA Guidance.

Further assumptions are presented in the following:

Application rate:	1.2 L product/ha (0.083 kg/ha fenoxaprop-P-ethyl)
Dislodgeable Foliar Residues (DFR):	3 µg/cm^2 per kg a.s./ha (default)
Transfer Coefficient (TC):	1400 cm^2/h
Work duration:	2 hours/day
Dermal absorption:	Fenoxaprop-P-ethyl: 17%
Body weight:	60 kg
No PPE:	Worker wearing work wear - arms, body and legs covered, but no gloves

The results are summarised in Table 6.4.3-1 above. Detailed calculations are given in Appendix 1.5.

B.6.4.3.2. Measurement of worker exposure

Since the exposure estimate carried out indicated that the AOEL will not be exceeded under practical conditions of use if no PPE is worn, a study to provide a measure of worker exposure is not deemed necessary.

B.6.5. EXPOSURE AND RISK ASSESSMENT

Detailed exposure assessments with result tables are provided in Appendix 1.

B.6.6. REFERENCES RELIED ON

A literature search was performed according to the EFSA guidance document "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). No specific search was included for any product names. For further details please refer to Volume 3 CA_B-6.

Annex point / reference number	Author(s)	Year	Title **Source** *(where different from company)* **Company name, Report No., Date, GLP status** *(where relevant)*, **published or not**	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
KCP 7.1.1/01	[redacted]	2005a	Fenoxaprop-p-ethyl 69 g/l EW: Acute Oral Toxicity in the Rat, - Up and Down Procedure [redacted] Study No.: 545/347 Cheminova A/S Report No.: 89 FPE GLP, Unpublished	Y	Y	New representative formulation	CHE	
KCP 7.1.2/01	[redacted]	2005b	Fenoxaprop-p-ethyl 69 g/l EW: Acute Dermal Toxicity (Limit Test) in the Rat [redacted] Study No.: 545/348 Cheminova A/S Report No.: 88 FPE GLP, Unpublished	Y	Y	New representative formulation	CHE	
KCP 7.1.3/01	[redacted]	2005	Fenoxaprop-p-ethyl 69 g/l EW: Acute Inhalation Toxicity (Nose only) Study in the Rat [redacted] Study No.: 545/349 Cheminova A/S Report No.: 90 FPE GLP, Unpublished	Y	Y	New representative formulation	CHE	
KCP 7.1.4/01	[redacted]	2005c	Fenoxaprop-p-ethyl 69 g/l EW: Acute Dermal Irritation in the Rabbit [redacted] Study No.: 545/350 Cheminova A/S Report No.: 87 FPE GLP, Unpublished	Y	Y	New representative formulation	CHE	
KCP 7.1.5/01	[redacted]	2005d	Fenoxaprop-p-ethyl 69 g/l EW: Acute Eye Irritation in the Rabbit [redacted] Study No.: 545/351 Cheminova A/S Report No.: 86 FPE GLP, Unpublished	Y	Y	New representative formulation	CHE	
KCP 7.1.6/01	[redacted]	2005e	Fenoxaprop-p-ethyl 69 g/l EW: Local Lymph Node Assay in the Mouse [redacted] Study No.: 545/352 Cheminova A/S Report No.: 85 FPE GLP, Unpublished	Y	Y	New representative formulation	CHE	
KCP 7.3/01	[redacted]	2008	In vivo percutaneous Absorption of an EW Formulation of [14C]Fenoxaprop-P-ethyl in Rats [redacted] Study No.: V7623/01.02 Cheminova A/S Report No.: 252 FPE GLP, Unpublished	Y	Y	New representative formulation	CHE	

Annex point / reference number	**Author(s)**	**Year**	**Title** **Source** *(where different from company)* **Company name, Report No., Date, GLP status** *(where relevant)*, **published or not**	**Vertebrate study Y/N**	**Data protection claimed Y/N**	**Justification if data protection is claimed**	**Owner**	**Previous evaluation**
KCP 7.3/02	Maas, W.J.M.	2008	In vitro percutaneous Absorption of [14C]Fenoxaprop-P-ethyl through Human and Rat Skin Membranes using flow-through Diffusion Cells TNO Quality of Life, Study No.: V7623/02.02 Cheminova A/S Report No.: 256 FPE GLP, Unpublished	N	Y	New representative formulation	CHE	

Appendix 1 Detailed exposure calculations

Appendix 1.1 Estimation of operator exposure to fenoxaprop-P-ethyl during vehicle-mounted downward spraying application assuming no personal protective equipment is worn (according to the EFSA Guidance)

Substance	fenoxaprop	Formulation = Soluble concentrates, emulsifiable concentrate, etc.	Application rate-0,083 kg a.s. /ha	Spray dilution = 0,83 g a.s./l	Vapour pressure = low volatile substances having a vapour pressure of
Scenario	Cereals / Outdoor / Downward spraying / Vehicle-mounted			Buffer = 2-3	Number applications = 1, Application interval = 365 days
Percentage Absoprtion	Dermal for product = 3	Dermal for in use diluation = 17	Oral = 100	Inhalation = 100	
RVNAS	0,014 mg/kg bw/day		RVAAS	mg/kg bw/day	
DFR	3 µg a.s./cm2 per kg a.s./ha		DT50	30 days	

Operator Model		Mixing, loading and application AOEM			
Potential exposure	Longer term systemic exposure mg/kg bw/day		0,0151	% of RVNAS	107,97%
	Acute systemic exposure mg/kg bw/day		0,1062	% of RVAAS	
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		0,0094	% of RVNAS	66,85%
	Acute systemic exposure mg/kg bw/day		0,0471	% of RVAAS	

Appendix 1.2 Estimation of resident exposure to fenoxaprop-P-ethyl after application of CHA 4960 in field crops, vehicle-mounted downward spraying application (according to the EFSA Guidance)

Substance	fenoxaprop	Formulation = Soluble concentrates, emulsifiable concentrate, etc.	Application rate-0,083 kg a.s. /ha	Spray dilution = 0,83 g a.s./l	Vapour pressure = low volatile substances having a vapour pressure of
Scenario	Cereals / Outdoor / Downward spraying / Vehicle-mounted			Buffer = 2-3	Number applications = 1, Application interval = 365 days
Percentage Absoprtion	Dermal for product = 3	Dermal for in use diluation = 17	Oral = 100	Inhalation = 100	
RVNAS	0,014 mg/kg bw/day		RVAAS	mg/kg bw/day	
DFR	3 µg a.s./cm2 per kg a.s./ha		DT50	30 days	
Resident - child	Spray drift (75th percentile) mg/kg bw/day		0,0038	% of RVNAS	27,16%
	Vapour (75th percentile) mg/kg bw/day		0,0011	% of RVNAS	7,64%
	Surface deposits (75th percentile) mg/kg bw/day		0,0003	% of RVNAS	1,95%
	Entry into treated crops (75th percentile) mg/kg bw/day		0,0024	% of RVNAS	17,01%
	All pathways (mean) mg/kg bw/day		0,0053	% of RVNAS	37,61%
Resident - adult	Spray drift (75th percentile) mg/kg bw/day		0,0009	% of RVNAS	6,48%
	Vapour (75th percentile) mg/kg bw/day		0,0002	% of RVNAS	1,64%
	Surface deposits (75th percentile) mg/kg bw/day		0,0001	% of RVNAS	0,69%
	Entry into treated crops (75th percentile) mg/kg bw/day		0,0013	% of RVNAS	9,45%
	All pathways (mean) mg/kg bw/day		0,0018	% of RVNAS	12,76%

Appendix 1.3 Estimation of bystander exposure to fenoxaprop-P-ethyl during/after application of CHA 4960 in field crops, tractor-mounted boom sprayer application (according to Martin *et al.*)

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

Input parameters considered for the estimation of bystander exposure:

Intended use(s):	cereals		**Drift (D):**	2,77	% (FCTM, 1 m)
Application rate (AR):	0,083	kg a.s./ha	**Exposed Body Surface Area (BSA):**	1	m² (adults)
				0,21	m² (children)
Body weight (BW):	60	kg/person (adults)	**Specific Inhalation Exposure (I^*_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):	17,00	% ('worst case')	**Area Treated (A):**	20	ha/d (based on Field Crops, Tractor Mounted (FCTM))
Inhalation absorption (IA):	100	%	**Exposure duration (T):**	5	min
AOEL:	0,014	mg/kg bw/d			

Bystander exposure towards Fenoxaprop-P-ethyl					
Adults			**Children**		
Bystander: Dermal exposure after application in cereals (via spray drift)					
SDE_B = (AR x D x BSA x DA) / BW			SDE_B = (AR x D x BSA x DA) / BW		
(8,3 x 2,77% x 1 x 17%) / 60			(8,3 x 2,77% x 0,21 x 17%) / 16,15		
External exposure	0,22991	mg/person	External exposure	0,0482811	mg/person
External exposure	0,00383183	mg/kg bw/d	External exposure	0,00298954	mg/kg bw/d
Absorbed dose:	**0,0006514**	**mg/kg bw/d**	**Absorbed dose:**	**0,0005082**	**mg/kg bw/d**
Bystander: Inhalation exposure after application in cereals					
SIE_B = (I^*_A x AR x A x T x IA) / BW			SIE_B = (I^*_A x AR x A x T x IA) / BW		
(0,001 / 360 x 0,083 x 20 x 5 x 100%) / 60			(0,001 / 360 x 0,083 x 20 x 5 x 100%) / 16,15		
External exposure	2,3056E-05	mg/person	External exposure	1,325E-05	mg/person
External exposure	3,8426E-07	mg/kg bw/d	External exposure	8,2045E-07	mg/kg bw/d
Absorbed dose:	**0,0000004**	**mg/kg bw/d**	**Absorbed dose:**	**0,0000008**	**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)	0,03910776	mg/person	Total systemic exposure (absorbed dose)	0,00822104	mg/person
Total systemic exposure (absorbed dose)	**0,0006518**	**mg/kg bw/d**	**Total systemic exposure** (absorbed dose)	**0,0005090**	**mg/kg bw/d**
% of AOEL:	**4,66**	**%**	**% of AOEL:**	**3,64**	**%**

Appendix 1.4 Estimation of resident exposure to fenoxaprop-P-ethyl after application of CHA 4960 in field crops, tractor-mounted boom sprayer application (according to Martin *et al.*)

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

Input parameters considered for the estimation of resident exposure:

Intended use(s):	cereals		**Drift (D):**	2,77	% (FCTM, 1 m)
Application rate (AR):	0,083	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):**	none	
Dermal absorption (DA):	17,00	% ('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	0,014	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 Fenoxaprop-P-ethyl					
Adults			**Children**		
Residents: Dermal exposure after application in cereals (via deposits caused by spray drift)					
SDE_R = (AR x NA x D x TTR x TC x H x DA) / BW			SDE_R = (AR x NA x D x TTR x TC x H x DA) / BW		
(0,00083 x 1 x 2,77% x 5% x 7300 x 2 x 17%) / 60			(0,00083 x 1 x 2,77% x 5% x 2600 x 2 x 17%) / 16,15		
External exposure	0,01678343	mg/person	External exposure	0,00597766	mg/person
External exposure	0,00027972	mg/kg bw/d	External exposure	0,00037013	mg/kg bw/d
Absorbed dose:	**0,0000476**	**mg/kg bw/d**	**Absorbed dose:**	**0,0000629**	**mg/kg bw/d**
Residents: Inhalation exposure to vapour					
SIE_R = (AC_V x IR x IA) / BW			SIE_R = (AC_V x IR x IA) / BW		
(0 x 16,57 x 100%) / 60			(0 x 8,31 x 100%) / 16,15		
External exposure		mg/person	External exposure		mg/person
External exposure		mg/kg bw/d	External exposure		mg/kg bw/d
Absorbed dose:		**none**	**Absorbed dose:**		**none**
			Residents: Oral exposure (hand-to-mouth transfer)		
			SOE_H = (AR x NA x D x TTR x SE x SA x Freq x H x OA) /		
			(0,00083 x 1 x 2,77% x 5% x 50% x 20 x 20 x 2 x 100%) / 16,15		
			External exposure	0,00045982	mg/person
			External exposure	2,8472E-05	mg/kg bw/d
			Absorbed dose	**0,0000285**	**mg/kg bw/d**
			Residents: Oral exposure (object-to-mouth transfer)		
			SOE_O = (AR x NA x D x DFR x IgR x OA) / BW		
			(0,00083 x 1 x 2,77% x 20% x 25 x 100%) / 16,15		
			External exposure	0,00011496	mg/person
			External exposure	7,118E-06	mg/kg bw/d
			Absorbed dose	**0,0000071**	**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)	0,00285318	mg/person	Total systemic exposure (absorbed dose)	0,00159098	mg/person
Total systemic exposure (absorbed dose)	**0,0000476**	**mg/kg bw/d**	**Total systemic exposure** (absorbed dose)	**0,0000985**	**mg/kg bw/d**
% of AOEL:	**0,34**	**%**	**% of AOEL:**	**0,70**	**%**

Appendix 1.5 Estimation of worker exposure to fenoxaprop-P-ethyl during the crop inspection (according to the EFSA Guidance)

Substance	fenoxaprop	Formulation = Soluble concentrates, emulsifiable concentrate, etc.	Application rate-0,083 kg a.s. /ha	Spray dilution = 0,83 g a.s./l	Vapour pressure = low volatile substances having a vapour pressure of
Scenario	Cereals / Outdoor / Downward spraying / Vehicle-mounted			Buffer = 2-3	Number applications = 1, Application interval = 365 days
Percentage Absoprtion	Dermal for product = 3	Dermal for in use diluation = 17	Oral = 100	Inhalation = 100	
RVNAS	0,014 mg/kg bw/day		RVAAS	mg/kg bw/day	
DFR	3 µg a.s./cm2 per kg a.s./ha		DT50	30 days	
Worker - Inspection, irrigation	Potential exposure mg/kg bw/day		0,0176	% of RVNAS	125,98%
	Working clothing mg/kg bw/day		0,0020	% of RVNAS	14,11%
	Working clothing and gloves mg/kg bw/day			% of RVNAS	