Renewal Assessment Report

beta-cyfluthrin

Bulldock EC 25

Volume 3 – B.6 Toxicology and metabolism data and assessment of risks for humans

07 March 2017

Rapporteur Member State: Germany

Co-Rapporteur Member State: Hungary

Version history

When	What

Table of contents

B.6 Toxicology and metabolism data and assessment of risks for humans

This document reviews the toxicological studies and human exposure for the plant protection product Bulldock 25 EC (formulation code MCW-5976) containing the active substance beta-cyfluthrin (25 g/L) formulated as an emulsifiable concentrate.

The current formulation MCW-5976 was not the representative formulation during the Annex I listing process of the active substance beta-cyfluthrin. Therefore, new studies on the toxicity of the product were submitted and evaluated. The old studies for the previous formulation (FRC 545 25 EC) evaluated for the first approval were not considered relevant for the renewal (TOX9550283, TOX9550284, TOX9550285, TOX9550287, ASB2014-7857) and were therefore not reported. In addition, the studies TOX2003-430, TOX9850731 and TOX9750939 were not considered relevant for the assessment of the representative formulation within Vol. 3 CP, B.6 and were also not reported.

B.6.1 Acute toxicity of plant protection product

Bulldock 25 EC (MCW-5976), the representative formulation for the renewal, was tested for eye irritation in 2007; tests on acute toxicity, skin irritation and sensitisation of the skin were performed with a previous formulation of Bulldock 25 EC in 2010. The comparison of both formulations reveals that MCW-5976 contains a new emulsifier replacing an emulsifier from the previous formulation; with respect to the toxicological information on this co-formulant provided in the MSDS the study results obtained with the previous formulation are considered to be applicable to the new formulation as well. However, precise information on skin sensitisation should be provided by the notifier for the new co-formulant. The detailed composition of both formulations as well as toxicological information on each co-formulant is presented in Vol. 4. A summary of the toxicological evaluation for Bulldock 25 EC is given in Table B.6.1-1: . The individual studies are presented under B.6.1.1 to B.6.1.6.

Table B.6.1-1: Summary of evaluation of the studies on acute toxicity including irritancy and skin sensitisation for Bulldock 25 EC

Type of test, model system (Guideline)	Result	Acceptability	Classification (acc. to the criteria in Dir. 67/548/EEC)	Classification (acc. to the criteria in Reg. 1272/2008)	Reference
LD_{50} oral, rat (OECD 423)	>300 mg/kg bw and <2000 mg/kg bw	Yes	R22	H302	[redacted] 2010a, ASB2014-6603
LD_{50} dermal, rat (OECD 402)	>2000 mg/kg bw	Yes	None	None	[redacted] 2010b, ASB2014-6604
LC_{50} inhalation, rat (OECD 403)	2.382 mg/L (both sexes)	Yes	R20	H332	[redacted] 2010, ASB2014-6605
Skin irritation, rabbit (OECD 404)	Irritant	Yes	R38	H315	[redacted] 2010, ASB2014-6606

Eye irritation, rabbit (OECD 405)	Irritant	Yes	R41	H318	[redacted] 2007, ASB2014-6607
Skin sensitisation, mouse (OECD 429, LLNA)	Non-sensitising	Yes	None	None	[redacted] 2010, ASB2014-6608

Bulldock 25 EC containing 25 g/L beta-cyfluthrin has a moderate toxicity regarding acute oral and inhalation toxicity and low toxicity by the dermal route. It causes serious eye damage to the rabbit eye and is an irritant to rabbit skin. Bulldock 25 EC is not a skin sensitiser in the Local Lymph Node Assay in mouse.

B.6.1.1 Oral toxicity

Reference: 7.1.1
Report: Acute toxicity in the rat after oral administration, [redacted] 2010a, AT05789, ASB2014-6603
Guideline(s): OECD 423 (2001), EEC 440/2008 Method B.1. tris, EPA OPPTS 870.1100
Deviations: Yes (Stability and homogeneity of the product were not confirmed analytically because the test item is known to be stable and homogeneous in both undiluted and ready-to-use formulation with water.)
GLP: Yes
Acceptability: Yes

Materials and methods

Test material (Lot/Batch No.)	Beta-Cyfluthrin EC 25 g/L (Batch No.04112/0341)
Species	Female Wistar rats (strain: HsdCpb:Wu)
No. of animals (group size)	3 female rats/dose (nullioarous, non-pregnant)
Dose(s)	300-2000 mg/kg bw
Exposure	Once by gavage
Vehicle/Dilution	Tap water
Post exposure observation period	14 days
Remarks	None

Results and discussions

Table B.6.1-2: Results of acute oral toxicity study in rats of beta-cyfluthrin EC 25 g/L

Dose [mg/kg bw]	Toxicological results[1)]	Duration of signs	Time of death	LD_{50} [mg/kg bw] (14 days)
Female rats				
300	0/0/3	-	-	>300
300	0/0/3	-	-	>300
2000	2/3/3	day 1 – day 7	day 3	<2000

[1)] Number of animals which died/number of animals with clinical signs/number of animals used

Table B.6.1-3: Summary of findings of acute oral toxicity study in rats of beta-cyfluthrin EC 25 g/L

Mortality:	Yes.
Clinical signs:	In animals dosed with 2000 mg/kg bw the following clinical signs were observed: decreased motility, increased salivation, narrow palpebral fissure, piloerection, uncoordinated gait, bloody eyes, poor general condition, abdominal position and labored breathing. No clinical signs were observed in animals dosed with 300 mg/kg bw.
Body weight:	Body weight gain was considered to be normal in animals treated with 300 mg/kg bw.
Macroscopic examination:	In animals that died during the observation period the following changes were detected: Brownish-black spotted liver and spleen, hemorrhagic lung and pale kidneys. The necropsy performed at the end of the observation period did not reveal any treatment-related findings in the surviving animals.

Conclusion

Under the experimental conditions, the oral LD_{50} of Bulldock 25 EC (beta-cyfluthrin EC 25 g/L) is >300 mg/kg bw and <2000 mg/kg bw in rats. Thus, classification with R22/H302 is required according to the classification criteria of Council Directive 67/548/EEC and subsequent regulations and according to Regulation (EC) No. 1272/2008.

B.6.1.2 Dermal toxicity

Reference: 7.1.2
Report: Beta-cyfluthrin EC 25 g/L: Acute toxicity in the rat after dermal application, [redacted] 2010b, AT05799, ASB2014-6604
Guideline(s): OECD 402 (1987), EEC 440/2008 Method B.3, EPA OPPTS 870.1200
Deviations: No
GLP: Yes
Acceptability: Yes

Materials and methods

Test material (Lot/Batch No.)	Beta-Cyfluthrin EC 25 g/L (Batch No. 04112/0341)
Species	Wistar rats (strain: HsdCpb:Wu)
No. of animals (group size)	5 males and 5 females (nulliparous, non-pregnant)
Dose(s)	2000 mg/kg bw
Exposure	24 hours (dermal, semi-occlusive)
Vehicle/Dilution	None
Post exposure observation period	14 days
Remarks	None

Results and discussions

Table B.6.1-4: Results of acute dermal toxicity study in rats of beta-cyfluthrin EC 25 g/L

Dose [mg/kg bw]	Toxicological results[1)]	Duration of signs	Time of death	LD_{50} [mg/kg bw] (14 days)
Male rats				
2000	0/5/5	day 3 – day 12	-	>2000
Female rats				
2000	0/5/5	hour 2 – day 15	-	>2000

[1)] Number of animals which died/number of animals with clinical signs/number of animals used

Table B.6.1-5: Summary of findings of acute dermal toxicity study in rats of beta-cyfluthrin EC 25 g/L

Mortality:	No mortality occurred.
Clinical signs:	The clinical signs observed were increased motility and vocalisation of the female animals. Partial reddening, encrustation, formation of scale and indurations of the treatment area were observed in males and females (in two females the partial encrustation and formation of scale of the treatment were not completely healed at final necropsy).
Body weight:	Body weight gain was decreased in four females on day 8 of the study.
Macroscopic examination:	The necropsies performed at the end of the study revealed no apparent findings.

Conclusion

Under the experimental conditions, the dermal LD_{50} of Bulldock 25 EC (beta-cyfluthrin EC 25 g/L) is higher than 2000 mg/kg bw in rats. Thus, no classification is required according to the classification criteria of Council Directive 67/548/EEC and subsequent regulations as well as according to Regulation (EC) No. 1272/2008.

B.6.1.3 Inhalation toxicity

Reference: 7.1.1
Report: Beta-cyfluthrin EC 25 g/L Activity ID TXFRX035: Acute inhalation toxicity in rats, [redacted] 2010, AT05804, ASB2014-6605
Guideline(s): OECD 403 (1981), 92/69/EEC B.2 (1992), EPA OPPTS 870.1300 (1998), Japan MAFF (2000)
Deviations: No
GLP: Yes
Acceptability: Yes

Materials and methods

Test material (Lot/Batch No.)	Beta-cyfluthrin EC 25 g/L (04112/0341)
Species	Rat, Wistar, Hsd Cpb: WU (SPF)
No. of animals (group size)	5 males + 5 females / group (nulliparous, non-pregnant)
Concentration(s)	2.077 and 2.731 mg/L
Exposure	4 hours (nose only)
Vehicle/Dilution	None

Post exposure observation period	14 days
Remarks	None

Results and discussions

Table B.6.1-6: Concentration(s) and exposure conditions

Target conc. [mg/L air]	Nominal conc. [mg/L air]	Actual conc. [mg/L air]	MMAD[1)] [µm]	GSD[2)] [µm]
2.000	8.017	2.077	1.23	1.98
2.800	9.472	2.731	1.26	1.99

1) MMAD = Mass Median Aerodynamic Diameter
2) GSD = Geometric Standard Deviation

Table B.6.1-7: Results of acute inhalation toxicity study in rats of beta-cyfluthrin EC 25 g/L

Concentration [mg/L air]	Toxicological results[1)]	Duration of signs	Time of death	LC_{50} [mg/L air] (14 days)
Male rats				
2.077	1/5/5	day 0 – day 2	d 0	>2.077
2.731	4/1/5	day 0 – day 2	d 0	<2.731
Female rats				
2.077	1/5/5	day 0 – day 3	d 0	>2.077
2.731	4/2/5	day 0 – day 1	d 0	<2.731

1) Number of animals which died/number of animals with clinical signs/number of animals used

Table B.6.1-8: Summary of findings of acute inhalation toxicity study in rats of beta-cyfluthrin EC 25 g/L

Mortality:	Mortality occurred.
Clinical signs:	Bradypnoea, laboured and irregular breathing, reduced motility, limp, piloerection, ungroomed coat, tremor, staggering and high-legged gait, gait straddling, head bent backwards, squatting, uncoordinated movements, choreoathetosis, salivation, mydriasis, cyanosis, and hypothermia were noted.
Body weight:	The day after exposure mean body weights were significantly decreased.
Macroscopic examination:	All rats that died showed findings suggesting lung oedema as cause of death.

Conclusion

Under the experimental conditions, the inhalation LC_{50} of Bulldock 25 EC (Beta-Cyfluthrin EC 25 g/L) is approx. 2.382 mg/L air for both sexes in rats. Thus, classification is required as Xn; R20 according to the classification criteria of Council Directive 67/548/EEC and subsequent regulations as 'Warning'; H332 according to Regulation (EC) No. 1272/2008.

B.6.1.4 Skin irritation

Reference: 7.1.4
Report: Beta-Cyfluthrin EC 25 g/L: Acute skin irritation/corrosion on rabbits, [redacted] 2010, AT05773, ASB2014-6606

Guideline(s): OECD 404 (2002), 440/2008/EEC B.4 (2008), EPA OPPTS 870.2500 (1998)
Deviations: No
GLP: Yes
Acceptability: Yes

Materials and methods

Test material (Lot/Batch No.)	Beta-Cyfluthrin EC 25 g/L (Batch No. 04112/0341)
Species	Rabbit, New Zealand White, CRl:KBL(NZW)BR
No. of animals (group size)	3 females
Initial test using one animal	Yes
Exposure	0.5 mL (4 hours, semi-occlusive)
Vehicle/Dilution	None
Post exposure observation period	14 days
Remarks	Desquamation persisted in one animal until the end of the observation time.

Results and discussions

Table B.6.1-9: Skin irritation of beta-cyfluthrin EC 25 g/L

Animal No.		Scores after treatment[1)]				Mean scores (24-72 h)	Reversible [day]
		1 h	24 h	48 h	72 h		
1	Erythema Oedema	2 1	3 2	4 3	4 3	3.7 2.7	14 14
2	Erythema Oedema	1 0	2 2	3 3	4 3	3.0 2.7	14 14
3	Erythema Oedema	2 1	3 2	4 3	4 3	3.7 2.7	14 14

1) scores in the range of 0 to 4

Clinical signs:	None

Conclusion

Under the experimental conditions, Bulldock 25 EC (Beta-Cyfluthrin EC 25 g/L) is a skin irritant. Thus, classification is required as Xi; R38 according to the classification criteria of Council Directive 67/548/EEC and subsequent regulations and as H315 according to Regulation (EC) No. 1272/2008.

B.6.1.5 Eye irritation

Reference: 7.1.5
Report: Acute eye irritation/corrosion test of Bulldock 25 EC in rabbits, [redacted] 2007, 20743/06, R-19699, ASB2014-6607
Guideline(s): OECD 405 (2002), 2004/73/EC B.5
Deviations: No
GLP: Yes
Acceptability: Yes

Materials and methods

Test material (Lot/Batch No.)	Bulldock 25 EC (MCW-5976) (Batch No. 050414)
Species	Rabbit, Himalayan
No. of animals (group size)	3 males
Initial test using one animal	No
Exposure	0.1 mL (single instillation into conjunctival sac)
Irrigation (time point)	Yes (after 24 hours with 0.9 % NaCl)
Vehicle/Dilution	None
Post exposure observation period	21 days
Remarks	Cornea opacity persisted in one animal until the end of the observation period.

Results and discussions

Table B.6.1-10: Eye irritation of Bulldock 25 EC

Animal No.		Scores after treatment[1)]				Mean scores (24-72 h)	Reversible [day]
		1 h	24 h	48 h	72 h		
1	Corneal opacity	0	1	1	1	1.0	>21
	Iritis	0	1	1	1	1.0	5
	Redness conjunctivae	2	2	3	3	2.7	18
	Chemosis conjunctivae	2	2	2	2	2.0	8
2	Corneal opacity	0	1	1	1	1.0	11
	Iritis	0	2	2	2	2.0	8
	Redness conjunctivae	1	2	3	3	2.7	11
	Chemosis conjunctivae	2	2	2	2	2.0	8
3	Corneal opacity	0	1	1	1	1.0	5
	Iritis	0	1	1	1	1.0	4
	Redness conjunctivae	1	2	2	2	2.0	7
	Chemosis conjunctivae	1	2	2	1	1.7	6

[1)] 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

Clinical signs:	None

Conclusion

Under the experimental conditions, Bulldock 25 EC is an eye irritant. Thus, regarding the persistency of the ocular lesion in one animal, classification is required as Xi; R41 according to the classification criteria of Council Directive 67/548/EEC and subsequent regulations and as H318 according to Regulation (EC) No. 1272/2008.

B.6.1.6 Skin sensitisation

Reference: 7.1.6

Report: Beta-cyfluthrin EC 25 g/L - Evaluation of potential skin sensitisation in the local lymph node assay in the mouse, [redacted] 2010, SA 09413, ASB2014-6608

Guideline(s): OECD 429 (2002), EPA OPPTS 870.2600 (2003)

Deviations: Due to technical problems, one animal of the treatment group (2.5 %) did not receive the injection of tritiated thymidine.

GLP: Yes
Acceptability: Yes

Materials and methods

Test material (Lot/Batch No.)	Beta-Cyfluthrin EC 25 g/L (Batch No. 04112/0341)
Species	Mouse, CBA/Ca of CBA/J strain
No. of animals (group size)	Test substance group: 5 female mice / dose Vehicle control goup: 5 female mice Positive control: 5 female mice
Range finding:	Yes
Exposure (concentration(s), no. of applications)	A: 2.5, 5.0 and 10 % B: 1.0 %
Vehicle	1 % Pluronic Acid L92 in water
Reliability check	alpha-Hexylcinnamaldehyde (30 %)
Remarks	Irritation measured by ear weight was observed in all treated groups of study phase A. The mean increase in ear weight was 16 % at a concentration of 2.5 %, 46 % at a concentration of 5 % and 60 % at a concentration of 10 %. The concentration of 1 % was seen non-irritating in a screening test and three complementary groups were added to the study (phase B).

Results and discussions

Table B.6.1-11: Results of skin sensitisation study of beta-cyfluthrin EC 25 g/L (phase A)

	No. of animals	Concentration [%]	DPM/group	Stimulation index (SD)
Beta-Cyfluthrin EC 25 g/L	4	2.5	963.2	2.8 (2.3)
	5	5.0	1937.2	5.7 (2.6)
	5	10	2520.3	7.4 (3.4)
Test Vehicle Control Group	5	0	342.2	1
Positive control	5	30	3453.7	10.1 (3.9)

Table B.6.1-12: Results of skin sensitisation study of beta-cyfluthrin EC 25 g/L (phase B)

	No. of animals	Concentration [%]	DPM/group	Stimulation index (SD)
Beta-Cyfluthrin EC 25 g/L	5	1.0	476	0.5 (0.3)
Test Vehicle Control Group	5	0	926	1
Positive control	5	30	7896	8.5 (3.3)
Clinical signs:	None			

Conclusion

Under the experimental conditions, Bulldock 25 EC (Beta-Cyfluthrin EC 25 g/L) is not a skin sensitiser at a non-irritating concentration of 1 % and an irritating concentration of 2.5 %. Thus, no classification is required according to the classification criteria of Council 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 studies submitted.

B.6.1.8 Supplementary studies for combinations of plant protection products

No studies submitted.

B.6.2 Dermal absorption

Data point: KCP 7.3

Report: [redacted] 2013:
In vitro percutaneous absorption of beta-cyfluthrin, formulated as MCW-5976, through human and rat skin. [redacted] Irvita Plant Protection, Report No: V20330/12 (ASB2014-7885)
Date: 2013-10-31, not published

Guideline(s): OECD 428 (2004); EC B45 (2008); EFSA Guidance on Dermal Absorption (2012)

Deviations: Beta-cyfluthrin technical [redacted] was stored at 2 – 10 ºC, protected from light. The study plan erroneously indicated storage conditions at ambient temperature (15-25ºC).
The expiry date of the blank formulation is July 2014 instead of 1 May 2014 as erroneously indicated in the study plan.
These deviations are considered not to have affected the validity and outcome of study.

GLP: Yes

Acceptability: Acceptable

(Dates of exp. Work: May, 15 2013 – August, 9 2013)

Materials and methods:

Non radio-labelled test substance: beta-cyfluthrin, batch no. RF27163S74, purity: 98.8 %;
Radiolabelled test substance: [cyclopropane-1-^{14}C]beta-cyfluthrin ([^{14}C]beta-cyfluthrin), batch no. KML 9367, radiochemical purity: >98 % (sum of isomers);
Formulation: MCW-5976 (Bulldock 25 EC), concentration of active substance: 25.8 g/L, Lot/Batch: 92110454;
Blank formulation: MCW-5976 (Bulldock 25 EC) blank, concentration of active substance: 0 g/L, Lot/Batch: 120711;
Radiolabelled reference substance: [^{3}H]$H_2$0, Lot/Batch #:628113, purity: not determined;
Human skin, derived from the breast and abdomen, was obtained from four female donors directly after surgery. The skin membranes were prepared from frozen skin samples. Skin was stored in aluminium foil at <-18 °C until use. After thawing, skin was cut to a recorded thickness of approx. 200-400 µm (i.e. split-thickness skin membranes).
Rat skin was obtained from a male rat (Wistar, [redacted]) of 8-10 weeks old. After sacrifice the dorsal and flank skin of the rat was clipped free of fur. Both human and rat skin was cut to a recorded thickness of 200-400 µm (split-thickness skin membranes).
The split-thickness skin membranes were placed in flow-through automated diffusion cells. The mean skin surface temperature was 32 ± 1ºC and exposure was at ambient humidity. The receptor fluid was pumped at a speed of approx. 1.8 mL/h and consisted of saline (0.9 % sodium chloride (w/v) containing 0.01 % sodium azide, w/v), supplemented with 5 % bovine serum albumin (BSA, w/v). Solubility of beta-cyfluthrin was verified in this study.
Beta-cyfluthrin, formulated as MCW-5976, was topically applied to the skin membranes. The exposure time was 8 h and receptor fluid samples were collected from 0 to 24 h.

Table B.6.2-1: Summary of experimental design

Test group	Group size	Total concentration (g/L)	Mean dose as applied (µg/cm^2)[b]
A (Human Conc.)	8[a]	26.5	268 ± 4
B (Human field dilution)	8[a]	0.013	0.13 ± 0.00
C (Rat conc.)	6	26.5	277 ± 2
D (Rat field dilution)	5[c]	0.013	0.13 ± 0.00

[a]: Two skin membranes from four donors in each test group
[b]: A net volume of ca 6.4 µL of the dose preparations was applied on each skin membrane (0.64 cm^2)
[c]: One replicate was excluded from the calculations due to a high recovery value (112.4 %)

The dose preparations were prepared within 24 hours prior to application as follows:

Table B.6.2-2: Summary of test substance applications

Test group	Amount of [^{14}C]beta-cyfluthrin[a]	Amount of concentrate formulation	Amount of blank formulation	Total concentration measured (g/L)	Radioactive concentration measured (MBq/mL)
A/C	56 µL (ca. 2.6 MBq, ca. 0.8 mg)	0.9115 g	-	26.5	2.30
B/D	10 µL (ca. 0.41 MBq, ca. 0.125 mg)	-	ca. 1.24 g[b]	0.013	0.042

[a]: Dissolved in dichloromethane to a radioactive concentration of ca. 46.6 MBq/mL, specific activity 3.27 MBq/mg.
[b]: Blank formulation, diluted 200 times with demineralised water. This dilution was 10 times further diluted with water to the target (radioactive) concentration.

The dose preparations were kept at ambient temperature until application. The concentration and homogeneity of [^{14}C]beta-cyfluthrin in the dose preparations was checked by taking aliquots just before and after dosing. The dose preparations were applied with a pipette and spread evenly on the skin surface within the donor compartment (ca. 10 µL/cm^2) using a disposable glass rod. A slightly higher volume than 6.4 µL (i.e. 6.7 µL) was applied to account for the expected loss of material during the distribution over the skin surface. Thus, a net volume of approx. 6.4 µL was applied. The dose preparations were continuously mixed.
Collection of mass balance samples:
Twenty-four hours after application, the mass balance of the test substance was determined from the following samples: receptor fluid samples, skin wash, receptor compartment wash, donor compartment wash, tape strips, and digested skin.
Receptor fluid samples were collected during the following intervals: 0-1 h, 1-2 h, followed by 2-h intervals until 24 hours after application.
Skin wash: After an exposure period of 8 h, the unabsorbed test substance was removed from the application site using a mild soap solution (i.e. 3 % Teepol in water), water and cotton swabs.
After 24 h of exposure, the diffusion cell was dismantled. Receptor and donor compartments were washed twice with 1.0 mL ethanol.
Each skin membrane was tape stripped 15 times using D-Squame® Skin Sampling Discs (CuDerm Corporation) and a D-Squame pressure device. Tape strips were stored individually for further analysis. Tape stripping was discontinued in case the epidermis was ruptured. Partial removal of the epidermis was recorded.
Skin membranes were digested in a 1.5 M KOH solution with 20 % aqueous ethanol for at least 24 h.
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).

Results:

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 were selected for the study.
Receptor fluid solubility:
The solubility of beta-cyfluthrin in the receptor fluid was determined to be ca. 7.2 µg/mL, which was considered sufficient. Furthermore, in the flow-through cells used, the volume of the receptor fluid in the receptor chamber beneath the skin is ca. 0.2 mL, which at a flow rate of ca. 1.8 mL/h, was replenished continuously (9 times per hour). Thus, it was assured that the rate of diffusion into the receptor fluid did not become a rate-limiting step.
Analyses of dose preparations:
The homogeneity of [^{14}C]beta-cyfluthrin in the dose preparations was checked; the coefficients of variation (CV) of the dose preparations were 0.5 % (Test Group A) and 1.9 % (Test Group B), and therefore considered sufficient. The radiochemical purity of [^{14}C]beta-cyfluthrin was determined to be ca. 95 %. The radiochemical purity of [^{14}C]beta-cyfluthrin in the dose preparations was comparable at ca. 95 %.
Percutaneous absorption of beta-cyfluthrin:
The mean absorption of beta-cyfluthrin from the concentrate formulation into the receptor fluid over the 24 h study duration was 0.71 µg/cm^2, representing 0.27 % of the applied dose. The mean maximal flux for the absorption of beta-cyfluthrin through human skin was 0.049 µg/cm^2/h and the lag time was 1.8 h. It should be noted that replicate A – 7 showed a considerable washing in effect after 8 h. Data for this replicate were included in all calculations, but caused a notable variation in the cumulative absorption values in group A.
The mean absorption of beta-cyfluthrin from the field dilution into the receptor fluid was 0.003 µg/cm^2, representing 2.51 % of the dose applied. The mean maximal flux through human skin was 0.0002 µg/cm^2/h and the lag time was 0.3 h.

Table B.6.2-3: Summary of cumulative absorption data of beta-cyfluthrin formulated as Bulldock 25 EC through human skin – cumulative absorption

Human skin	Concentrate (Group A)		Field dilution (Group B)	
Target concentration [g/L]	25		0.0125	
Concentration measured [g/L]	26.5		0.013	
Dose [µg/cm²]	268 ± 4		0.13 ± 0.00	
Number of cells	8		8	
	Mean cumulative absorption		Mean cumulative absorption	
Sample time [h]	[µg/cm²]	[%]	[µg/cm²]	[%]
0	0.00	0.2	0.000	1.5
1	0.00	0.7	0.000	6.0
2	0.02	2.9	0.000	12.0
4	0.11	15.0	0.001	23.3
6	0.20	27.7	0.001	33.1
8	0.27	37.9	0.001	42.2
10	0.37	52.0	0.002	50.7
12	0.43	60.1 [a]	0.002	58.7[a]
14	0.48	67.3	0.002	66.5
16	0.53	74.2	0.002	73.5
18	0.58	80.6	0.003	80.3
20	0.62	87.1	0.003	86.9
22	0.67	93.5	0.003	93.3
24	0.71	100.0	0.003	100.0
Maximal flux [µg/cm²/h]	0.049	-	0.0002	-
Lag time [h]	1.8	-	0.3	-

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

Human 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 60.1 % and 58.7 % 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 beta-cyfluthrin in human skin was 97.2 % and 99.0 % 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 4.2 % (concentrate formulation) and 21.5 % (field dilution) of the applied dose. 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 8.9 % (concentrate formulation) and 36.5 % (field dilution) of the applied dose.
For the concentrate 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 field dilution group the standard deviation (SD) of the mean absorption estimate was <25 %,

therefore the standard deviation was not added to the mean absorption estimate.
When adjusted dermal absorption estimates were rounded to the number of significant digits according to the guidance, dermal absorption estimates of 13 % and 37 % were determined for the formulation concentrate and 1:2000 field dilution, respectively.

Table B.6.2-4: Overview table of the *in vitro* percutaneous penetration of [14C]beta-cyfluthrin through human skin

Human skin	A (concentrate)		B (field dilution)	
Concentration measured [g/L] Dose [µg/cm] n	26.5 268 ± 4 8		0.013 0.13 ± 0.00 8	
Penetration into the receptor fluid after 24 h	µg/cm²	% of dose	µg/cm2	% of dose
	0.71	0.27	0.003	2.51
Maximal flux [µg/cm²/h]	0.049 ± 0.017		0.0002 ± 0.0002	
Lag time [h]	1.8 ± 0.4		0.3 ± 0.3	
Absorbed dose [% of dose][1]	4.2 ± 2.9		21.5 ± 9.0	
Potentially absorbed dose [% of dose][2]	8.9 ± 3.9		36.5 ± 8.6	

1 The absorbed dose is defined as the amount in the receptor fluid, the receptor compartment wash and skin membrane, excluding tape strips.
2 The potentially absorbed dose is defined as the amount in the receptor fluid, the receptor compartment wash, the skin, and stratum corneum (except for the first 2 tape strips)

Rat skin
The mean absorption of beta-cyfluthrin from the concentrate formulation into the receptor fluid over the 24 h study duration was 7.04 µg/cm², representing 2.54 % of the applied dose. The mean maximal flux for the absorption of beta-cyfluthrin through rat skin was 0.60 µg/cm²/h and the lag time was 0.5 h. The mean absorption of beta-cyfluthrin from the field dilution into the receptor fluid was 0.002 µg/cm², representing 1.74 % of the dose applied. The mean maximal flux through rat skin was 0.0001 µg/cm²/h and the lag time was 0.0 h. One replicate (C - 1), was excluded from the calculations of the mean values because of a high recovery value (i.e. 112.4 %). The mean total absorption through rat skin was 26.5 ± 5.3 % (concentrate formulation) and 49.6 ± 12.8 % (field dilution) of the applied dose. The mean potentially absorbed dose was 36.7 ± 3.2 % (concentrate) and 70.9 ± 4.0 % (field dilution) of the applied dose. The mean recovery of beta-cyfluthrin in rat skin was 98.3 ± 0.3 % and 99.2 ± 0.7 % for the concentrate formulation and field dilution, respectively.

Table B.6.2-5: Overview table of the *in vitro* percutaneous penetration of [14C]beta-cyfluthrin through rat skin

Rat skin	C (concentrate)		D (field dilution)	
Concentration measured [g/L] Dose [µg/cm²] n	26.5 277 ± 2 6		0.013 0.13 ± 0.00 5[3]	
Penetration into the receptor fluid after 24 h	µg/cm²	% of dose	µg/cm²	% of dose
	7.04	2.54	0.002	1.74
Maximal flux [µg/cm²/h]	0.60 ± 0.07		0.0001 ± 0.0000	
Lag time [h]	0.5 ± 0.33		0.0 ± 0.1	
Absorbed dose [% of dose][1]	26.5 ± 5.3		49.6 ± 12.8	
Potentially absorbed dose [% of dose][2]	36.7 ± 3.2		70.9 ± 4.0	

1 The absorbed dose is defined as the amount in the receptor fluid, the receptor compartment wash and skin membrane, excluding tape strips.
2 The potentially absorbed dose is defined as the amount in the receptor fluid, the receptor compartment wash, the skin, and stratum corneum (except for the first 2 tape strips)
3 One replicate was excluded from the calculations due to a high recovery value

Table B.6.2-6: Summarised dermal absorption data formulated as Bulldock 25 EC through human skin – recovery data

Test group	**Concentrate**		**Field dilution**	
Target concentration [mg/mL]	25		0.0125	
Mean actual dose [µg/cm²]	268		0.13	
	Recovery [%]		Recovery [%]	
	Mean	SD	Mean	SD
Unabsorbed dose				
Skin wash	77.4	8.5	42.8	3.3
Donor compartment	6.65	3.34	9.44	4.82
Dose associated to skin				
Tape strips 1 + 2	4.26	2.16	10.35	3.28
Tape strips, rest	4.73	2.38	14.94	2.71
Tape strips, total	8.98	4.31	25.29	4.79
Skin membrane	3.82	2.58	18.73	9.31
Absorbed dose				
Receptor fluid	0.27	0.18	2.51	2.92
Receptor compartment	0.14	0.38	0.26	0.08
Total absorbed dose	0.41	0.55	2.78	3.00
Total recovery	97.23	3.65	99.03	4.28
Assessment accodring 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 analised individually?	Yes		Yes	
Dermal absorption [in %]	8.9	3.9	36.5	8.6
Significant variation between groups or replicates?	Yes		No	
Adjusted dermal absorption&	12.8		36.5	
Dermal absorption used for risk assessment [in %]**	**13**		**37**	

The values presented here might deviate from the values in the study report due to rounding.
* "Guidance on Dermal Absorption", EFSA Journal 2012; 10(4):2665
& Adjustment for significant variation: one SD is added to the DA mean when the SD is ≥25 % of the DA mean.
** Value is rounded according to guidance.

Conclusion:

The results of this *in vitro* dermal absorption study indicate that the absorption of beta-cyfluthrin through human skin was limited and very slow. The vast majority of beta-cyfluthrin was removed from the skin by the washing procedures. The total absorbed amounts after 24 hour exposure were 0.41 % and 2.78 % of the applied dose for the formulation concentrate and 1:2000 field dilution, respectively.
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 8.9 % and 36.5 %, respectively. For the concentrate group the standard deviation of the mean absorption estimate was >25 %. Accordingly, the standard deviation value was added to the mean absorption estimate.
Based on the potentially absorbed dose, for the concentrate formulation human skin was 4.1 times less permeable for beta-cyfluthrin compared to rat skin (36.7/8.9), while for the field dilution, human skin was 1.9 times less permeable for beta-cyfluthrin compared to rat skin (70.9/36.5).
The dermal penetration estimates in human skin to be used for risk assessment were set at 13 % and 37 % for the formulation concentrate and 1:2000 field dilution, respectively.
The dermal penetration estimates in rat skin were set at 37 % and 71 % for the formulation concentrate and 1:2000 field dilution, respectively.
Only the values obtained with human skin is essential for risk assessment.
The study is considered acceptable under the conditions of the study and based on the information given in the report.

B.6.3 Available toxicological data relating to co-formulants

Toxicological information on the co-formulants is presented in Vol. 4. Additional labelling of the product with R65 according to Council Directive 67/548/EEC and subsequent regulations and with H304 and H336 according to Regulation (EC) No. 1272/2008 is required due to the classification of the solvent. Classification with R66, R67 and EUH066 can be omitted with respect to the classification of the product as harmful via inhalation and as skin irritant.

B.6.4 Exposure data

The plant protection product Bulldock 25 EC containing 25 g/L of beta-cyfluthrin is intended to be used as an insecticide on potato and wheat in the field and on tomato in greenhouse. A summary of the critical uses and the overall conclusion regarding exposure for operators, workers, bystanders and residents is presented in B.6.5.
The calculations for beta-cyfluthrin are based on the parameters and endpoints given in Table B.6.4-1.

Table B.6.4-1: Product information and toxicological reference values used for exposure assessment

Product name and code	Bulldock 25 EC (MCW-5976)
Formulation type	Emulsifiable concentate (EC)
Category	Insecticide
Container size(s), short description	1 L bottle and 5 L container
Active substance(s) (incl. content)	**beta-cyfluthrin** 25 g/L
AOEL systemic	0.01 mg/kg bw/d
AOEL inhalative	0.000243 mg/kg bw/d
Inhalative absorption	100 %

Oral absorption	100 %
Dermal absorption	Concentrate: 13 % Dilution: 37 % (Dilution: 0.013 g/L) based on Bulldock 25 EC

B.6.4.1 Operator exposure

B.6.4.1.1 Estimation of operator exposure

A summary of the exposure models used for estimation of operator exposure to beta-cyfluthrin during application of Bulldock 25 EC according to the critical uses is presented in Table B.6.4-2. Outcome of the estimation is presented in Table B.6.4-3. Detailed calculations are given in Appendix 1.
Calculation of operator exposure in greenhouses was performed by the notifier using the Southern European Greenhouse model. As this model is not accepted in all EU MS, the RMS chose a different approach. The exposure estimates for spraying in greenhouses presented in Table B.6.4-3 are based on the results of an operator exposure study by Mich (1996). The study is described in detail in Appendix 2.

Table B.6.4-2: Exposure models for intended uses

Critical use(s)	Potato, wheat (max. 0.5 L product/ha)
Model(s)	German model [Uniform Principles for Safeguarding the Health of Applicators of Plant Protection Products (Uniform Principles for Operator Protection), Mitteilungen aus der Biologischen Bundesanstalt für Land-und Forstwirtschaft, Berlin-Dahlem, Heft 277, 1992]
	UK POEM (revised) [Estimation of Exposure and Absorption of Pesticides by Spray Operators, Scientific subcommittee on Pesticides and British Agrochemical association Joint Medical Panel Report (UK MAFF), 1986 and the Predictive Operator Exposure Model (POEM) V 1.0, (UK MAFF), 1992. ("UK model")]
Critical use(s)	Tomato (max. 0.7 L product/ha)
Model(s)	German model [Uniform Principles for Safeguarding the Health of Applicators of Plant Protection Products (Uniform Principles for Operator Protection), Mitteilungen aus der Biologischen Bundesanstalt für Land-und Forstwirtschaft, Berlin-Dahlem, Heft 277, 1992] and Exposure study according to Mich (1996) (see Appendix 2)

Table B.6.4-3: Estimated operator exposure

		Beta-cyfluthrin			
Model data	**Level of PPE**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**	**Total inhaled dose (mg/kg bw/day**	**% of inhalative AOEL**
Tractor mounted boom spray application outdoors to low crops Application rate: 0.0125 kg as/ha					
German Model Body weight: 70 kg	no PPE[1)]	0.0038	38.2	0.0000057	2.4
UK POEM Application volume: 150 L/ha Container: 5 L, 45 or	no PPE[2)]	0.0241	241.4	0.0000833	34.3
	+ gloves during mixing/loading and	0.0037	36.7		

63 mm closure[3)] Body weight: 60 kg	appl.				
Spray applications in greenhouses to high crops Application rate: 0.0175 kg as/ha					
German Model and Exposure study Body weight: 70 kg	no PPE[1)]	0.0157	157.0	0.0000396	16.3
	+ gloves during mixing/loading	0.0249	91.0		

1) no PPE: Operator wearing T-shirt and shorts

2) no PPE: Operator wearing long sleeved shirt, long trousers ("permeable") but no gloves

3) realistic worst-case for the treatment of 50 ha

B.6.4.1.2 Measurement of operator exposure

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

B.6.4.2 Bystander and resident exposure

B.6.4.2.1 Estimation of bystander and resident exposure

Table B.6.4-4 shows the exposure model used for estimation of bystander and resident exposure to beta-cyfluthrin. Outcome of the estimation is presented in Table B.6.4-5. Detailed calculations are shown in Appendix 1.

Table B.6.4-4: Exposure models for intended uses

Critical use(s)	Potato, wheat (max. 2 x 0.5 L product/ha)
Model	Martin, S. et al. (2008) [Guidance for Exposure and Risk Evaluation for Bystanders and Residents Exposed to Plant Protection Products During and After Application; J. Verbr. Lebensm. 3 (2008): 272-281 Birkhäuser Verlag Basel] and Bundesanzeiger (BAnz), 06 January 2012, Issue No. 4, pp. 75-76

Table B.6.4-5: Estimated bystander and resident exposure

	Beta-cyfluthrin			
Model data	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**	**Total inhaled dose (mg/kg bw/day**	**% of inhalative AOEL**
Tractor mounted boom spray application outdoors to low crops Application rate: 2 x 0.0125 kg as/ha				
Bystanders (adult) Drift rate: 2.77 % (1 m) Body weight: 60 kg	0.000214	2.14	0.00000006	0.02
Bystanders (children) Drift rate: 2.77 % (1 m) Body weight: 16.15 kg	0.000167	1.67	0.00000012	0.05
Residents (adult) Drift rate: 2.38 % (1 m) Body weight: 60 kg	0.000027	0.27	not relevant (vapour pressure: 8.5×10^{-8} Pa)	not relevant (vapour pressure: 8.5×10^{-8} Pa)

Residents (children) Drift rate: 2.38 % (1 m) Body weight: 16.15 kg	0.000045	0.45	not relevant (vapour pressure: $8.5x10^{-8}$ Pa)	not relevant (vapour pressure: $8.5x10^{-8}$ Pa)

B.6.4.2.2 Measurement of bystander and/or resident exposure

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

B.6.4.3 Worker exposure

B.6.4.3.1 Estimation of worker exposure

Table B.6.4-6 shows the exposure model used for estimation of worker exposure after entry into a previously treated area or handling a crop treated with Bulldock 25 EC according to the critical use(s). Outcome of the estimation is presented in Table B.6.4-7. Detailed calculations are in Appendix 1.

Table B.6.4-6: Exposure models for intended uses

Critical use(s)	Tomato (max. 2 x 0.7 L product/ha)
Model	German re-entry model, Krebs et al. (2000) [Uniform Principles for Safeguarding the Health of Workers Re-entering Crop Growing Areas after Application of Plant Protection Products, Nachrichtenbl. Deut. Pflanzenschutzdienst., 52(1), p. 5-9]

Table B.6.4-7: Estimated worker exposure

		Beta-cyfluthrin			
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**	**Total inhaled dose (mg/kg bw/day**	**% of inhalative AOEL**
Number of applications and application rate: 2 x 0.0175 kg as/ha					
8 h/day [1], TC: 2500 cm^2/person/h [2] Body weight: 60 kg	no PPE [3]	0.0043	43.2	covered by operator exposure	covered by operator exposure

[1] 8 h/day for professional applications for harvesting, pruning, tying, thinning or weeding activities

[2] EUROPOEM II, 2002, Post-Application Exposure of Workers to Pesticides in Agriculture or

[3] no PPE: Worker wearing long sleeved shirt, long trousers (“permeable”) but no gloves

B.6.4.3.2 Measurement of worker exposure

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

B.6.5 Exposure and risk assessment

The risk assessment for field applications on potatoes and wheat has shown that the estimated exposure towards beta-cyfluthrin in Bulldock 25 EC will not exceed the systemic AOEL as well as the inhalative AOEL for operators, workers, bystanders and residents. According to the German model no specific PPE is necessary for operators and for workers whereas gloves during mixing/loading and during application are necessary for the operator according to the UK-POEM. No unacceptable risk was identified for greenhouse application on tomatoes when the product is used as intended and provided that the operator wears gloves during mixing/loading.
A summary of the critical uses and the overall conclusion regarding exposure for operators, workers and bystanders/residents is presented in Table B.6.5-1.

Table B.6.5-1: Critical uses and overall conclusion of exposure assessment

Crops[1] and situation (e.g. growth stage of crop)	F/G or I[2]	Application		Application rate		Remarks: (e.g. surfactant (L/ha)) critical gap for operator, worker, bystander or resident exposure based on [*Exposure model*]	Acceptability of exposure assessment			
		Method / Kind (incl. application technique[3])	Max. number (min. interval between applications) a) per use b) per crop/ season	kg as/ha a) max. rate per appl. b) max. total rate per crop/season	Water L/ha min/max		Operator	Worker	Bystander	Residents
Potato, wheat	F	Foliar spray	a) 2 (14) b) 2 (14)	a) 0.0125 b) 0.025	150-1000	German model				
						UK-POEM				
Tomato	G	Foliar spray	a) 2 (14) b) 2 (14)	a) 0.0175 b) 0.035	500-1000	German model + exposure study (Mich, 1996)				

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

[1] Pooled critical GAPS with the same max. application rate per application and using the same application technique
[2] F: field or outdoor application, G: greenhouse application, I: indoor application

B.6.6 References relied on

Reference list of vertebrate studies sorted by Annex point

Annex point/ reference number	**Author(s)**	**Year**	**Title** **Report No.** **Source** (where different from company) **GLP status** (where relevant) **published or not**	**Vertebrate study**	**Data protection claimed**	**Justification**	**Owner**
KCP 7.1.1/02	[redacted]	2010a	Beta-cyfluthrin EC 25 g/L - Acute toxicity in the rat after oral administration. Report No.: AT05798 Edition No: M-364489-01-1; R-27986 [redacted] GLP not published BVL-2633421, BVL-2633421, ASB2014-6603	Y	Y	replacement [redacted]	BCS/IRV
KCP 7.1.2/02	[redacted]	2010b	Beta-cyfluthrin EC 25 g/L - Acute toxicity in the rat after dermal application. Report No.: AT05799 A Edition No: M-366055-02-1; R-27965 a+b [redacted] GLP not published BVL-2633423, BVL-2633423, ASB2014-6604	Y	Y	replacement [redacted]	BCS/IRV

Annex point/ reference number	**Author(s)**	**Year**	**Title** **Report No.** **Source** (where different from company) **GLP status** (where relevant) **published or not**	**Vertebrate study**	**Data protection claimed**	**Justification**	**Owner**
KCP 7.1.3/02	[redacted]	2010	Beta-cyfluthrin EC 25g/L - Activity ID TXFRX035 - Acute inhalation toxicity in rats. Report No.: AT05804 Edition No: M-364503-01-1; R-27964 [redacted] GLP not published BVL-2633425, BVL-2633425, ASB2014-6605	Y	Y	replacement [redacted]	BCS/IRV
KCP 7.1.4/02	[redacted]	1989	FCR 4545 25 EC - Assessment of local irritant potential (skin and eye) of the 0.05 % application concentration Edition No.: M-060514-01-1 Not GLP not published TOX9550287	Y	N	-	BCS
KCP 7.1.4/03	[redacted]	2010	Beta-cyfluthrin EC 25 g/L - Acute skin irritation/ corrosion on rabbits. Report No.: AT05773 Edition No: M-362708-01-1; R-30615 [redacted] GLP not published BVL-2633428, BVL-2633428, ASB2014-6606	Y	Y	replacement [redacted]	BCS/IRV

Annex point/ reference number	**Author(s)**	**Year**	**Title** **Report No.** **Source** (where different from company) **GLP status** (where relevant) **published or not**	**Vertebrate study**	**Data protection claimed**	**Justification**	**Owner**
KCP 7.1.5/03	[redacted]	2007	Acute eye irritation/corrosion test of Bulldock 25 EC in rabbits. Report No.: 20743/06 Edition No: R-19699 [redacted] GLP not published BVL-2633431, BVL-2633431, ASB2014-6607	Y	Y	replacement [redacted]	IRV
KCP 7.1.6/01	[redacted]	2010	Beta-cyfluthrin EC 25 g/L - Evaluation of potential skin sensitisation in the local lymph node assay in the mouse. Report No.: SA 09413 Edition No: M-366999-01-1: R-30614 [redacted] GLP not published BVL-2633432, BVL-2633432, ASB2014-6608	Y	Y	replacement [redacted]	BCS/IRV

Annex point/ reference number	**Author(s)**	**Year**	**Title** **Report No.** **Source** (where different from company) **GLP status** (where relevant) **published or not**	**Vertebrate study**	**Data protection claimed**	**Justification**	**Owner**
KCP 7.2.1	Mich, G.	1996	Operator exposure in greenhouses during practical use of plant protection products EF 94-02-03 ! MO-00-002686 ! M-024096-01-1 ECON Forschung GmbH, Germany GLP: Yes Published: No BVL-1752398, BVL-1760625, BVL-1771380, BVL-1771381, BVL-1937458, BVL-2616003, TOX2000-2081	N	N	Add	

IRV = Irvita Plant Protection, Curacao – a member of Makhteshim Agan Holding B.V., The Netherlands
BCS = Bayer CropScience AG, Monheim, Germany

Studies submitted for the Annex I inclusion of beta-cyfluthrin and already evaluated at EU level are listed in grey (owner Bayer CropScience, license Irvita Plant Protection B.V.).

Studies submitted for the first time in support of the renewal approval of beta-cyfluthrin are listed in black.

Reference list of non-vertebrate studies sorted by Annex point

Annex point/ reference number	**Author(s)**	**Year**	**Title** **Report No.** **Source** (where different from company) **GLP status** (where relevant) **published or not**	**Vertebrate study**	**Data protection claimed**	**Justification**	**Owner**
KCP 7.3/01	Maas, W.J.M.	2013	[^{14}C]-beta-Cyfluthrin - *In vitro* percutaneous absorption of beta-cyfluthrin, formulated as MCW-5976, through human and rat skin. Report No.: 20330/12 Edition No.: R-30604 TNO triskelion, The Netherlands GLP not published BVL-2633437, BVL-2633437, ASB2014-7885	N	Y	due to new EFSA guidance	IRV

IRV = Irvita Plant Protection, Curacao – a member of Makhteshim Agan Holding B.V., The Netherlands
BCS = Bayer CropScience AG, Monheim, Germany

Studies submitted for the Annex I inclusion of beta-cyfluthrin and already evaluated at EU level are listed in grey.

Studies submitted for the first time in support of the renewal approval of beta-cyfluthrin are listed in black.

Exposure calculations

A 1.1 Operator exposure (total systemic exposure)

Table A 1: Input parameters considered for the estimation of operator exposure with the German model

Formulation type:	EC		**Application technique:**	Field Crop Tractor Mounted (FCTM)	
Application rate (AR):	0.0125	kg as/ha			
Area treated per day (A):	20	ha	**Dermal hands m/l ($D_{M(H)}$):**	2.4	mg/person/kg as
Dermal absorption (DA):	13	% (concentr.)	**Dermal hands appl. ($D_{A(H)}$):**	0.38	mg/person/kg as
	37	% (dilution)	**Dermal body appl. ($D_{A(B)}$):**	1.6	mg/person/kg as
Inhalation absorption (IA):	100	%	**Dermal head appl. ($D_{A(C)}$):**	0.06	mg/person/kg as
Body weight (BW):	70	kg/person	**Inhalation m/l (I_M):**	0.0006	mg/person/kg as
AOEL	0.01	mg/kg bw/d	**Inhalation appl. (I_A):**	0.001	mg/person/kg as

Table A 2: Estimation of operator exposure towards beta-cyfluthrin using the German model

Without PPE			**With PPE**		
Operators: Systemic dermal exposure after application in potato, wheat					
Dermal exposure during mixing/loading					
Hands			Hands		
$SDE_{OM(H)} = (D_{M(H)} \times AR \times A \times DA) / BW$			$SDE_{OM(H)} = (D_{M(H)} \times AR \times A \times PPE$ [1)] $\times DA) / BW$		
(2.4 x 0.0125 x 20 x 13 %) / 70			(2.4 x 0.0125 x 20 x 0.01 x 13 %) / 70		
External dermal exposure	0.6	mg/person	External dermal exposure	0.006	mg/person
External dermal exposure	0.008571	mg/kg bw/d	External dermal exposure	0.000086	mg/kg bw/d
Systemic dermal exposure	**0.001114**	**mg/kg bw/d**	**Systemic dermal exposure**	**0.000011**	**mg/kg bw/d**
Dermal exposure during application					
Hands			Hands		
$SDE_{OA(H)} = (D_{A(H)} \times AR \times A \times DA) / BW$			$SDE_{OA(H)} = (D_{A(H)} \times AR \times A \times PPE \times DA) / BW$		
(0.38 x 0.0125 x 20 x 37 %) / 70			(0.38 x 0.0125 x 20 x 1 x 37 %) / 70		
External dermal exposure	0.095	mg/person	External dermal exposure	0.095	mg/person
External dermal exposure	0.001357	mg/kg bw/d	External dermal exposure	0.001357	mg/kg bw/d
Systemic dermal exposure	**0.000502**	**mg/kg bw/d**	**Systemic dermal exposure**	**0.000502**	**mg/kg bw/d**
Body			Body		
$SDE_{OA(B)} = (D_{A(B)} \times AR \times A \times DA) / BW$			$SDE_{OA(B)} = (D_{A(B)} \times AR \times A \times PPE \times DA) / BW$		
(1.6 x 0.0125 x 20 x 37 %) / 70			(1.6 x 0.0125 x 20 x 1 x 37 %) / 70		
External dermal exposure	0.4	mg/person	External dermal exposure	0.4	mg/person
External dermal exposure	0.005714	mg/kg bw/d	External dermal exposure	0.005714	mg/kg bw/d
Systemic dermal exposure	**0.002114**	**mg/kg bw/d**	**Systemic dermal exposure**	**0.002114**	**mg/kg bw/d**
Head			Head		
$SDE_{OA(C)} = (D_{A(C)} \times AR \times A \times DA) / BW$			$SDE_{OA(C)} = (D_{A(C)} \times AR \times A \times PPE \times DA) / BW$		
(0.06 x 0.0125 x 20 x 37 %) / 70			(0.06 x 0.0125 x 20 x 1 x 37 %) / 70		
External dermal exposure	0.015	mg/person	External dermal exposure	0.015	mg/person
External dermal exposure	0.000214	mg/kg bw/d	External dermal exposure	0.000214	mg/kg bw/d
Systemic dermal exposure	**0.000079**	**mg/kg bw/d**	**Systemic dermal exposure**	**0.000079**	**mg/kg bw/d**
Total systemic dermal exposure: $SDE_O = SDE_{OM(H)} + SDE_{OA(H)} + SDE_{OA(B)} + SDE_{OA(C)}$			Total systemic dermal exposure: $SDE_O = SDE_{OM(H)} + SDE_{OA(H)} + SDE_{OA(B)} + SDE_{OA(C)}$		
Total external dermal exposure	1.11	mg/person	Total external dermal exposure	0.516	mg/person
Total external dermal exposure	0.015857	mg/kg bw/d	Total external dermal exposure	0.007371	mg/kg bw/d
Total systemic dermal exposure	**0.00381**	**mg/kg bw/d**	**Total systemic dermal exposure**	**0.002707**	**mg/kg bw/d**
Operators: Systemic inhalation exposure after application in potato, wheat					
Inhalation exposure during mixing/loading					
$SIE_{OM} = (I_M \times AR \times A \times IA) / BW$			$SIE_{OM} = (I_M \times AR \times A \times PPE \times IA) / BW$		
(0.0006 x 0.0125 x 20 x 100 %) / 70			(0.0006 x 0.0125 x 20 x 1 x 100 %) / 70		
External inhalation exposure	0.00015	mg/person	External inhalation exposure	0.00015	mg/person
External inhalation exposure	0.000002	mg/kg bw/d	External inhalation exposure	0.000002	mg/kg bw/d

Systemic inhalation exposure	**0.000002**	**mg/kg bw/d**	**Systemic inhalation exposure**	**0.000002**	**mg/kg bw/d**
Inhalation exposure during application					
$SIE_{OA} = (I_A$ x AR x A x IA) / BW			$SIE_{OA} = (I_A$ x AR x A x PPE x IA) / BW		
(0.001 x 0.0125 x 20 x 100 %) / 70			(0.001 x 0.0125 x 20 x 1 x 100 %) / 70		
External inhalation exposure	0.00025	mg/person	External inhalation exposure	0.00025	mg/person
External inhalation exposure	0.000004	mg/kg bw/d	External inhalation exposure	0.000004	mg/kg bw/d
Systemic inhalation exposure	**0.000004**	**mg/kg bw/d**	**Systemic inhalation exposure**	**0.000004**	**mg/kg bw/d**
Total systemic inhalation exposure: $SIE_O = SIE_{OM} + SIE_{OA}$			Total systemic inhalation exposure: $SIE_O = SIE_{OM} + SIE_{OA}$		
Total external inhalation exposure	0.0004	mg/person	Total external inhalation exposure	0.0004	mg/person
Total external inhalation exposure	0.000006	mg/kg bw/d	Total external inhalation exposure	0.000006	mg/kg bw/d
Total systemic inhalation exposure	**0.000006**	**mg/kg bw/d**	**Total systemic inhalation exposure**	**0.000006**	**mg/kg bw/d**
Total systemic exposure: $SE_O = SDE_O + SIE_O$			Total systemic exposure: $SE_O = SDE_O + SIE_O$		
Total systemic exposure	0.2671	mg/person	Total systemic exposure	0.18988	mg/person
Total systemic exposure	**0.003816**	**mg/kg bw/d**	**Total systemic exposure**	**0.002713**	**mg/kg bw/d**
% of AOEL	**38.2**	**%**	**% of AOEL**	**27.1**	**%**

[1)] reduction factor for gloves is 0.01 (professional appl.)

Table A 3: Estimation of operator exposure towards beta-cyfluthrin using the UK-POEM (without PPE)

Active substance	**beta-cyfluthrin**			
Product	Bulldock			
Formulation type	organic solvent-based			
Concentration of as	25	mg/mL		
Dose	0.5	L preparation/ha	(0.0125 kg as/ha)	
Application volume	150	L/ha		
Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles			
Container	5 litres 45 or 63 mm closure			
Work rate/day	50	ha		
Duration of spraying	6	h		
PPE during mix./loading	None			
PPE during application	None			
Dermal absorption from product	13	%		
Dermal absorption from spray	37	%		
EXPOSURE DURING MIXING AND LOADING				
Container size	5	Litres		
Hand contamination/operation	0,01	mL		
Application dose	0.5	Litres product/ha		
Work rate	50	ha/day		
Number of operations	5	/day		
Hand contamination	0.05	mL/day		
Protective clothing	None			
Transmission to skin	100	%		
Dermal exposure to formulation	0.05	mL/day		
DERMAL EXPOSURE DURING SPRAY APPLICATION				
Application technique	Tractor-mounted/trailed boom sprayer: hydraulic nozzles			
Application volume	150	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	0.05	mL/day	41.55	mL/day
Concen. of as product or spray	25	mg/mL	0.083	mg/mL
Dermal exposure to as	1.25	mg/day	3.463	mg/day
Percent absorbed	13	%	37	%
Absorbed dose	0.163	mg/day	1.281	mg/day
INHALATION EXPOSURE DURING SPRAYING				
Inhalation exposure	0.01	mL/h		
Duration of exposure	6	h		
Concentration of as in spray	0.083	mg/mL		
Inhalation exposure to as	0.005	mg/day		
Percent absorbed	100	%		
Absorbed dose	0.005	mg/day		
PREDICTED EXPOSURE				
Total absorbed dose	1.449	mg/day		
Operator body weight	60	kg		
Operator exposure	0.024	mg/kg bw/day		
Amount of AOEL	**241.4**	**%**		

Table A 4: Estimation of operator exposure towards beta-cyfluthrin using the UK-POEM (with gloves during mixing/loading and application)

Active substance	**beta-cyfluthrin**			
Product	Bulldock			
Formulation type	organic solvent-based			
Concentration of as	25	mg/mL		
Dose	0.5	L preparation/ha	(0.0125 kg as/ha)	
Application volume	150	L/ha		
Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles			
Container	5 litres 45 or 63 mm closure			
Work rate/day	50	ha		
Duration of spraying	6	h		
PPE during mix./loading	Gloves			
PPE during application	Gloves			
Dermal absorption from product	13	%		
Dermal absorption from spray	37	%		
EXPOSURE DURING MIXING AND LOADING				
Container size	5	Litres		
Hand contamination/operation	0,01	mL		
Application dose	0.5	Litres product/ha		
Work rate	50	ha/day		
Number of operations	5	/day		
Hand contamination	0.05	mL/day		
Protective clothing	Gloves			
Transmission to skin	10	%		
Dermal exposure to formulation	0.005	mL/day		
DERMAL EXPOSURE DURING SPRAY APPLICATION				
Application technique	Tractor-mounted/trailed boom sprayer: hydraulic nozzles			
Application volume	150	spray/ha		
Volume of surface contamination	10	mL/h		
Distribution	Hands	Trunk	Legs	
	65 %	10 %	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	0.005	mL/day	6.45	mL/day
Concen. of as product or spray	25	mg/mL	0.083	mg/mL
Dermal exposure to as	0.125	mg/day	0.538	mg/day
Percent absorbed	13	%	37	%
Absorbed dose	0.016	mg/day	0.199	mg/day
INHALATION EXPOSURE DURING SPRAYING				
Inhalation exposure	0.01	mL/h		
Duration of exposure	6	h		
Concentration of as in spray	0.083	mg/mL		
Inhalation exposure to as	0.005	mg/day		
Percent absorbed	100	%		
Absorbed dose	0.005	mg/day		
PREDICTED EXPOSURE				
Total absorbed dose	0.22	mg/day		
Operator body weight	60	kg		
Operator exposure	0.004	mg/kg bw/day		
Amount of AOEL	**36.7**	**%**		

Table A 5: Input parameters considered for the estimation of operator exposure towards beta-cyfluthrin in the greenhouse (German model and Mich, 1996)

Formulation type:	EC		**Application technique:**	High crops hand held	
Application rate (AR):	0.0175	kg as/ha			
Area treated per day (A):	1	ha	**Dermal hands m/l ($D_{M(H)}$):**		
Dermal absorption (DA):			**Dermal hands appl. ($D_{A(H)}$):**		
			Dermal body appl. ($D_{A(B)}$):		
Inhalation absorption (IA):	100	%	**Dermal head appl. ($D_{A(C)}$):**		
Body weight (BW):	70	kg/person	**Inhalation m/l (I_M):**	0.05	mg/person/kg as
AOEL	0.01	mg/kg bw/d	**Inhalation appl. (I_A):**	0.10841	mg/person/kg as

Table A 6: Estimation of operator exposure towards beta-cyfluthrin in the greenhouse (German model and Mich, 1996)

Without PPE			**With PPE**		
Operators: Systemic dermal exposure after application in tomato					
Dermal exposure during mixing/loading			-		
Hands			Hands		
$SDE_{OM(H)} = (D_{M(H)} \times AR \times A \times DA) / BW$			$SDE_{OM(H)} = (D_{M(H)} \times AR \times A \times PPE$ [1)] $\times DA) / BW$		
(205 x 0.0175 x 1 x 13 %) / 70			(205 x 0.0175 x 1 x 0.01 x 13 %) / 70		
External dermal exposure	3.5875	mg/person	External dermal exposure	0.035875	mg/person
External dermal exposure	0.05125	mg/kg bw/d	External dermal exposure	0.000513	mg/kg bw/d
Systemic dermal exposure	**0.006663**	**mg/kg bw/d**	**Systemic dermal exposure**	**0.000067**	**mg/kg bw/d**
Dermal exposure during application			-		
Hands			Hands		
$SDE_{OA(H)} = (D_{A(H)} \times AR \times A \times DA) / BW$			$SDE_{OA(H)} = (D_{A(H)} \times AR \times A \times PPE \times DA) / BW$		
(13.1884 x 0.0175 x 1 x 37 %) / 70			(13.1884 x 0.0175 x 1 x 1 x 37 %) / 70		
External dermal exposure	0.230797	mg/person	External dermal exposure	0.230797	mg/person
External dermal exposure	0.003297	mg/kg bw/d	External dermal exposure	0.003297	mg/kg bw/d
Systemic dermal exposure	**0.00122**	**mg/kg bw/d**	**Systemic dermal exposure**	**0.00122**	**mg/kg bw/d**
Body			Body		
$SDE_{OA(B)} = (D_{A(B)} \times AR \times A \times DA) / BW$			$SDE_{OA(B)} = (D_{A(B)} \times AR \times A \times PPE \times DA) / BW$		
(82.47509 x 0.0175 x 1 x 37 %) / 70			(82.47509 x 0.0175 x 1 x 1 x 37 %) / 70		
External dermal exposure	1.443314	mg/person	External dermal exposure	1.443314	mg/person
External dermal exposure	0.020619	mg/kg bw/d	External dermal exposure	0.020619	mg/kg bw/d
Systemic dermal exposure	**0.007629**	**mg/kg bw/d**	**Systemic dermal exposure**	**0.007629**	**mg/kg bw/d**
Head			Head		

$SDE_{OA(C)} = (D_{A(C)} \times AR \times A \times DA) / BW$			$SDE_{OA(C)} = (D_{A(C)} \times AR \times A \times PPE \times DA) / BW$		
(1.56194 x 0.0175 x 1 x 37 %) / 70			(1.56194 x 0.0175 x 1 x 1 x 37 %) / 70		
External dermal exposure	0.027334	mg/person	External dermal exposure	0.027334	mg/person
External dermal exposure	0.00039	mg/kg bw/d	External dermal exposure	0.00039	mg/kg bw/d
Systemic dermal exposure	**0.000144**	**mg/kg bw/d**	**Systemic dermal exposure**	**0.000144**	**mg/kg bw/d**
Total systemic dermal exposure: $SDE_O = SDE_{OM(H)} + SDE_{OA(H)} + SDE_{OA(B)} + SDE_{OA(C)}$			Total systemic dermal exposure: $SDE_O = SDE_{OM(H)} + SDE_{OA(H)} + SDE_{OA(B)} + SDE_{OA(C)}$		
Total external dermal exposure	5.288945	mg/person	Total external dermal exposure	1.73732	mg/person
Total external dermal exposure	0.075556	mg/kg bw/d	Total external dermal exposure	0.024819	mg/kg bw/d
Total systemic dermal exposure	**0.015656**	**mg/kg bw/d**	**Total systemic dermal exposure**	**0.00906**	**mg/kg bw/d**
Operators: Systemic inhalation exposure after application in tomato					
Inhalation exposure during mixing/loading					
$SIE_{OM} = (I_M \times AR \times A \times IA) / BW$			$SIE_{OM} = (I_M \times AR \times A \times PPE \times IA) / BW$		
(0.05 x 0.0175 x 1 x 100 %) / 70			(0.05 x 0.0175 x 1 x 1 x 100 %) / 70		
External inhalation exposure	0.000875	mg/person	External inhalation exposure	0.000875	mg/person
External inhalation exposure	0.000013	mg/kg bw/d	External inhalation exposure	0.000013	mg/kg bw/d
Systemic inhalation exposure	**0.000013**	**mg/kg bw/d**	**Systemic inhalation exposure**	**0.000013**	**mg/kg bw/d**
Inhalation exposure during application					
$SIE_{OA} = (I_A \times AR \times A \times IA) / BW$			$SIE_{OA} = (I_A \times AR \times A \times PPE \times IA) / BW$		
(0.10841 x 0.0175 x 1 x 100 %) / 70			(0.10841 x 0.0175 x 1 x 1 x 100 %) / 70		
External inhalation exposure	0.001897	mg/person	External inhalation exposure	0.001897	mg/person
External inhalation exposure	0.000027	mg/kg bw/d	External inhalation exposure	0.000027	mg/kg bw/d
Systemic inhalation exposure	**0.000027**	**mg/kg bw/d**	**Systemic inhalation exposure**	**0.000027**	**mg/kg bw/d**
Total systemic inhalation exposure: $SIE_O = SIE_{OM} + SIE_{OA}$			Total systemic inhalation exposure: $SIE_O = SIE_{OM} + SIE_{OA}$		
Total external inhalation exposure	0.002772	mg/person	Total external inhalation exposure	0.002772	mg/person
Total external inhalation exposure	0.00004	mg/kg bw/d	Total external inhalation exposure	0.00004	mg/kg bw/d
Total systemic inhalation exposure	**0.00004**	**mg/kg bw/d**	**Total systemic inhalation exposure**	**0.00004**	**mg/kg bw/d**
Total systemic exposure: $SE_O = SDE_O + SIE_O$			Total systemic exposure: $SE_O = SDE_O + SIE_O$		
Total systemic exposure	1.098682	mg/person	Total systemic exposure	0.636971	mg/person
Total systemic exposure	0.015695	**mg/kg bw/d**	**Total systemic exposure**	0.0091	**mg/kg bw/d**
% of AOEL	**157.0**	**%**	**% of AOEL**	**91.0**	**%**

[1)] reduction factor for gloves is 0.01 (professional appl.)

A 1.2 Operator exposure (inhalative route only)

Table A 7: Input parameters considered for the estimation of operator exposure with the German model

Formulation type:	EC		**Application technique:**	Field Crop Tractor Mounted (FCTM)	
Application rate (AR):	0.0125	kg as/ha			
Area treated per day (A):	20	ha	**Dermal hands m/l ($D_{M(H)}$):**	2.4	mg/person/kg as
Dermal absorption (DA):		% (concentr.)	**Dermal hands appl. ($D_{A(H)}$):**	0.38	mg/person/kg as
		% (dilution)	**Dermal body appl. ($D_{A(B)}$):**	1.6	mg/person/kg as
Inhalation absorption (IA):	100	%	**Dermal head appl. ($D_{A(C)}$):**	0.06	mg/person/kg as
Body weight (BW):	70	kg/person	**Inhalation m/l (I_M):**	0.0006	mg/person/kg as
AOEL	0.0002431	mg/kg bw/d	**Inhalation appl. (I_A):**	0.001	mg/person/kg as

Table A 8: Estimation of operator exposure towards beta-cyfluthrin using the German model

Without PPE			**With PPE**		
Operators: Systemic inhalation exposure after application in potato, wheat					
Inhalation exposure during mixing/loading					
$SIE_{OM} = (I_M \times AR \times A \times IA) / BW$			$SIE_{OM} = (I_M \times AR \times A \times PPE$ [1)] $\times IA) / BW$		
(0.0006 x 0.0125 x 20 x 100%) / 70			(0.0006 x 0.0125 x 20 x 0.08 x 100 %) / 70		
External inhalation exposure	0.00015	mg/person	External inhalation exposure	0.000012	mg/person
External inhalation exposure	0.000002	mg/kg bw/d	External inhalation exposure	0	mg/kg bw/d

Systemic inhalation exposure	**0.000002**	**mg/kg bw/d**	**Systemic inhalation exposure**	**0**	**mg/kg bw/d**
Inhalation exposure during application					
$SIE_{OA} = (I_A$ x AR x A x IA) / BW			$SIE_{OA} = (I_A$ x AR x A x PPE x IA) / BW		
(0.001 x 0.0125 x 20 x 100 %) / 70			(0.001 x 0.0125 x 20 x 1 x 100 %) / 70		
External inhalation exposure	0.00025	mg/person	External inhalation exposure	0.00025	mg/person
External inhalation exposure	0.000004	mg/kg bw/d	External inhalation exposure	0.000004	mg/kg bw/d
Systemic inhalation exposure	**0.000004**	**mg/kg bw/d**	**Systemic inhalation exposure**	**0.000004**	**mg/kg bw/d**
Total systemic inhalation exposure: $SIE_O = SIE_{OM} + SIE_{OA}$			Total systemic inhalation exposure: $SIE_O = SIE_{OM} + SIE_{OA}$		
Total external inhalation exposure	0.0004	mg/person	Total external inhalation exposure	0.000262	mg/person
Total external inhalation exposure	0.000006	mg/kg bw/d	Total external inhalation exposure	0.000004	mg/kg bw/d
Total systemic inhalation exposure	**0.000006**	**mg/kg bw/d**	**Total systemic inhalation exposure**	**0.000004**	**mg/kg bw/d**
% of AOEL	**2.4**	**%**	**% of AOEL**	**1.5**	**%**

[1)] reduction factor for RPE is 0.08 (particle filter)

Table A 9: Estimation of operator exposure towards beta-cyfluthrin using the UK-POEM (without PPE)

Active substance	**beta-cyfluthrin**	
Product	Bulldock	
Formulation type	organic solvent-based	
Concentration of as	25	mg/mL
Dose	0.5	L preparation/ha (0.013 kg as/ha)
Application volume	150	L/ha
Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles	
Container	5 litres 45 or 63 mm closure	
Work rate/day	50	ha
Duration of spraying	6	h
PPE during mix./loading	None	
PPE during application	None	
INHALATION EXPOSURE DURING SPRAYING		
Inhalation exposure	0.01	mL/h
Duration of exposure	6	h
Concentration of as in spray	0.083	mg/mL
Inhalation exposure to as	0.005	mg/day
Percent absorbed	100	%
Absorbed dose	0.005	mg/day
PREDICTED EXPOSURE		
Total absorbed dose	0.005	mg/day
Operator body weight	60	kg
Operator exposure	0.0000833	mg/kg bw/day
Amount of AOEL	**34.3**	**%**

Table A 10: Input parameters considered for the estimation of operator exposure towards beta-cyfluthrin in the greenhouse (German model and Mich, 1996)

Formulation type:	EC		**Application technique:**	High crops hand held	
Application rate (AR):	0.0175	kg as/ha			
Area treated per day (A):	1	ha	**Dermal hands m/l ($D_{M(H)}$):**		
Dermal absorption (DA):			**Dermal hands appl. ($D_{A(H)}$):**		
			Dermal body appl. ($D_{A(B)}$):		
Inhalation absorption (IA):	100	%	**Dermal head appl. ($D_{A(C)}$):**		
Body weight (BW):	70	kg/person	**Inhalation m/l (I_M):**	0.05	mg/person/kg as
AOEL	0.000243	mg/kg bw/d	**Inhalation appl. (I_A):**	0.10841	mg/person/kg as

Table A 11: Estimation of operator exposure towards beta-cyfluthrin in the greenhouse (German model and Mich, 1996)

Without PPE			**With PPE**		
Operators: Systemic inhalation exposure after application in tomato					
Inhalation exposure during mixing/loading					
$SIE_{OM} = (I_M \times AR \times A \times IA) / BW$			$SIE_{OM} = (I_M \times AR \times A \times PPE$ [1)] $\times IA) / BW$		
(0.05 x 0.0175 x 1 x 100 %) / 70			(0.05 x 0.0175 x 1 x 0.08 x 100 %) / 70		
External inhalation exposure	0.000875	mg/person	External inhalation exposure	0.00007	mg/person
External inhalation exposure	0.000013	mg/kg bw/d	External inhalation exposure	0.000001	mg/kg bw/d
Systemic inhalation exposure	**0.000013**	**mg/kg bw/d**	**Systemic inhalation exposure**	**0.000001**	**mg/kg bw/d**
Inhalation exposure during application					
$SIE_{OA} = (I_A \times AR \times A \times IA) / BW$			$SIE_{OA} = (I_A \times AR \times A \times PPE \times IA) / BW$		
(0.10841 x 0.0175 x 1 x 100 %) / 70			(0.10841 x 0.0175 x 1 x 1 x 100 %) / 70		
External inhalation exposure	0.001897	mg/person	External inhalation exposure	0.001897	mg/person
External inhalation exposure	0.000027	mg/kg bw/d	External inhalation exposure	0.000027	mg/kg bw/d
Systemic inhalation exposure	**0.000027**	**mg/kg bw/d**	**Systemic inhalation exposure**	**0.000027**	**mg/kg bw/d**
Total systemic inhalation exposure: $SIE_O = SIE_{OM} + SIE_{OA}$			Total systemic inhalation exposure: $SIE_O = SIE_{OM} + SIE_{OA}$		
Total external inhalation exposure	0.002772	mg/person	Total external inhalation exposure	0.001967	mg/person
Total external inhalation exposure	0.00004	mg/kg bw/d	Total external inhalation exposure	0.000028	mg/kg bw/d
Total systemic inhalation exposure	**0.00004**	**mg/kg bw/d**	**Total systemic inhalation exposure**	**0.000028**	**mg/kg bw/d**
% of AOEL	**16.3**	**%**	**% of AOEL**	**11.6**	**%**

[1)] reduction factor for RPE is 0.08 (particle filter) and 0.02 (combined vapour and particle filter), resp. (professional appl.)

A 1.3 Bystander and resident exposure

Table A 12: Input parameters considered for the estimation of bystander exposure

Intended use(s):	potato, wheat		**Drift (D):**	2.77	% (FC, 1 m)
Application rate (AR):	0.0125	kg as/ha	**Exposed body surface area (BSA):**	1	m² (adults)
	1.25	mg/m²		0.21	m² (children)
Body weight (BW):	60	kg/person (adults)	**Specific Inhalation Exposure (I^*_A):**	0.001	mg/kg as (6 hours, adults)
	16.15	kg/person (children)		0.000575	mg/kg as (6 hours, children)
Dermal absorption (DA):	37	% ('worst case')	**Area Treated (A):**	20	ha/d (based on FCTM)
Inhalation absorption (IA):	100	%			
AOEL:	0.01	mg/kg bw/d	**Exposure duration (T):**	5	min

Table A 13: Estimation of bystander exposure towards beta-cyfluthrin

Adults			**Children**		
Bystander: Systemic dermal exposure during/after application (via spray drift)					
$SDE_B = (AR \times D \times BSA \times DA) / BW$			$SDE_B = (AR \times D \times BSA \times DA) / BW$		
(1.25 x 2.77 % x 1 x 37 %) / 60			(1.25 x 2.77 % x 0.21 x 37 %) / 16.15		
External dermal exposure	0.034625	mg/person	External dermal exposure	0.007271	mg/person
External dermal exposure	0.000577	mg/kg bw/d	External dermal exposure	0.00045	mg/kg bw/d
Systemic dermal exposure	**0.000214**	**mg/kg bw/d**	**Systemic dermal exposure**	**0.000167**	**mg/kg bw/d**
Bystander: Systemic inhalation exposure during/after application (via spray drift)					
$SIE_B = (I^*_A \times AR \times A \times T \times IA) / BW$			$SIE_B = (I^*_A \times AR \times A \times T \times IA) / BW$		
(0.001 / 360 x 0.0125 x 20 x 5 x 100 %) / 60			(0.000575 / 360 x 0.0125 x 20 x 5 x 100 %) / 16.15		
External inhalation exposure	0.000003	mg/person	External inhalation exposure	0.000002	mg/person
External inhalation exposure	0	mg/kg bw/d	External inhalation exposure	0	mg/kg bw/d
Systemic inhalation exposure	**0**	**mg/kg bw/d**	**Systemic inhalation exposure**	**0**	**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	0.012815	mg/person	Total systemic exposure	0.002692	mg/person
Total systemic exposure	**0.000214**	**mg/kg bw/d**	**Total systemic exposure**	**0.000167**	**mg/kg bw/d**
% of AOEL	**2.14**	**%**	**% of AOEL**	**1.67**	**%**

Table A 14: Input parameters considered for the estimation of resident exposure

Intended use(s):	potato, wheat		**Drift (D):**	2.38	% (FC, 1 m, 2 appl.)
Application rate (AR):	0.0125	kg as/ha	**Transfer coefficient (TC):**	7300	cm^2/h (adults)
	0.000125	mg/cm^2		2600	cm^2/h (children)
Number of applications (NA):	2		**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	mg/m^3
Dermal absorption (DA):	37	% ('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:	0.01	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

Table A 15: Estimation of resident exposure towards beta-cyfluthrin

Adults			**Children**		
Residents: Systemic dermal exposure after application (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		
(0.000125 x 2 x 2.38 % x 5 % x 7300 x 2 x 37 %) / 60			(0.000125 x 2 x 2.38 % x 5 % x 2600 x 2 x 37 %) / 16.15		
External dermal exposure	0.004344	mg/person	External dermal exposure	0.001547	mg/person
External dermal exposure	0.000072	mg/kg bw/d	External dermal exposure	0.000096	mg/kg bw/d
Systemic dermal exposure	**0.000027**	**mg/kg bw/d**	**Systemic dermal exposure**	**0.000035**	**mg/kg bw/d**
Residents: Systemic inhalation exposure after application (via 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 inhalation exposure		none	External inhalation exposure		none
Systemic inhalation exposure		**none**	**Systemic inhalation exposure**		**none**
			Residents: Systemic oral exposure (hand-to-mouth transfer)		
			$SOE_{R(H)}$ = (AR x NA x D x TTR x SE x SA x Freq x H x OA) / BW		
			(0.000125 x 2 x % x 5 % x 50 % x 20 x 20 x 2 x 100 %) / 16.15		
			External oral exposure	0.000119	mg/person
			External oral exposure	0.000007	mg/kg bw/d
			Systemic oral exposure	**0.000007**	**mg/kg bw/d**
			Residents: Systemic oral exposure (object-to-mouth transfer)		
			$SOE_{R(O)}$ = (AR x NA x D x DFR x IgR x OA) / BW		
			(0.000125 x 2 x % x 20 % x 25 x 100 %) / 16.15		
			External oral exposure	0.00003	mg/person
			External oral exposure	0.000002	mg/kg bw/d
			Systemic oral exposure	**0.000002**	**mg/kg bw/d**
Total systemic exposure: SE_R = SDE_R + SIE_R			Total systemic exposure: SE_R = SDE_R + SIE_R + $SOE_{R(H)}$ + $SOE_{R(O)}$		
Total systemic exposure	0.001607	mg/person	Total systemic exposure	0.000721	mg/person
Total systemic exposure	**0.000027**	**mg/kg bw/d**	**Total systemic exposure**	**0.000045**	**mg/kg bw/d**
% of AOEL	**0.27**	**%**	**% of AOEL**	**0.45**	**%**

A 1.4 Bystander exposure (inhalative route only)

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

Intended use(s):	potato, wheat tomato		**Drift (D):**		
Application rate (AR):	0.0125	kg as/ha	**Exposed body surface area (BSA):**		
	1.25	mg/m²			
Body weight (BW):	60	kg/person (adults)	**Specific Inhalation Exposure (I^*_A):**	0.001	mg/kg as (6 hours, adults)
	16.15	kg/person (children)		0.000575	mg/kg as (6 hours, children)
Dermal absorption (DA):			**Area Treated (A):**	20	ha/d (based on FCTM)
Inhalation absorption (IA):	100	%			
AOEL:	0.000243	mg/kg bw/d	**Exposure duration (T):**	5	min

Table A 17: Estimation of bystander exposure towards beta-cyfluthrin

Adults			**Children**		
Bystander: Systemic inhalation exposure during/after application (via spray drift)					
$SIE_B = (I^*_A \times AR \times A \times T \times IA) / BW$			$SIE_B = (I^*_A \times AR \times A \times T \times IA) / BW$		
(0.001 / 360 x 0.0125 x 20 x 5 x 100 %) / 60			(0.00057471 / 360 x 0.0125 x 20 x 5 x 100 %) / 16.15		
External inhalation exposure	0.00000347	mg/person	External inhalation exposure	0.000002	mg/person
External inhalation exposure	0.00000006	mg/kg bw/d	External inhalation exposure	0.00000012	mg/kg bw/d
Systemic inhalation exposure	**0.00000006**	**mg/kg bw/d**	**Systemic inhalation exposure**	**0.00000012**	**mg/kg bw/d**
% of AOEL	**0.02**	**%**	**% of AOEL**	**0.05**	**%**

A 1.5 Worker exposure

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

Intended use(s):	Tomato (greenhouse)		**Dislodgeable foliar residues (DFR):**	1	µg/cm²/kg as
Application rate (AR):	0.0175	kg as/ha	**Transfer coefficient (TC):**	2500	cm²/person/h
Number of applications (NA):	2		**Work rate per day (WR):**	8	h/d
Body weight (BW):	60	kg/person	**PPE**	5	%
Dermal absorption (DA):	37	% ('worst case')			
AOEL	0.01	mg/kg bw/d			

Table A 19: Estimation of worker exposure towards beta-cyfluthrin using the German re-entry model

Without PPE			**With PPE (gloves and coverall)**		
Worker (re-entry): Systemic dermal exposure after application in tomato					
$SDE_W = (DFR \times TC \times WR \times AR \times NA \times DA) / BW$			$SDE_W = (DFR \times TC \times WR \times AR \times NA \times PPE \times DA) / BW$		
(1 x 2500 x 8 x 0.0175 x 2 x 37 %) / 60			(1 x 2500 x 8 x 0.0175 x 2 x 5 % x 37 %) / 60		
External dermal exposure	0.7	mg/person	External dermal exposure	0.035	mg/person
External dermal exposure	0.011667	mg/kg bw/d	External dermal exposure	0.000583	mg/kg bw/d
Total systemic exposure	0.259	mg/person	Total systemic exposure	0.01295	mg/person
Total systemic exposure	**0.004317**	**mg/kg bw/d**	**Total systemic exposure**	**0.000216**	**mg/kg bw/d**
% of AOEL	**43.2**	**%**	**% of AOEL**	**2.2**	**%**

Detailed evaluation of exposure studies relied upon

Reference:	7.2.1
Report	Mich, G.; 1996; Operator exposure in greenhouses during practical use of plant protection products. Report No. EF 94-02-03, Doc. No. M-024096-01, June 6, 1996; ECON GmbH Ingelheim, conducted in Germany, Dates of work July, 1994 – June, 1996, TOX2000-2081
Guideline(s):	Following the OECD guidance document for the conduct of studies of occupational exposure to pesticides during agricultural application, Series on Testing and Assessment No. 9, 1997
GLP:	Yes (certified laboratory)
Acceptability:	The study is considered to be acceptable.

Materials and methods

To elucidate the potential of operator's exposure by application of plant protection products in greenhouses an exposure study was performed. Dermal and inhalation exposure were measured using the patch technique (passive dosimetry technique), by analysis of whole body underwear, glove and hand rinsing and absorbent air filters during mixing/loading. The following plant protection products were applied on ornamentals at 2 sites in Germany: the wettable powder fungicide Euparen® WP 50 (as dichlofluanid), the insecticide Rody® (as fenpropathrin) and the fungicide Saprol® Neu (as triforine) (both emulsifiable concentrates). Twelve experienced operators were monitored. The products were applied with conventionally used knapsack sprayers at recommended rates. All analytical methods were validated for the various matrixes in a wide range of concentrations.
Samples were extracted for analysis followed by gas chromatographic determination. The results of the measurements are reported as determined (i.e. µg active substance per sample) and as specific exposure values, i.e. as mg of exposure per kg of active substance handled. The latter facilitates the use of the data for generic purposes. Samples were analysed for each of the 3 active substances.
The following scenarios were investigated:
a) mixing and loading Euparen WP 50 for hydraulic knapsack sprayers,
b) application using knapsack sprayers to low cultures on tables,
c) application using knapsack sprayers to high cultures,
d) airborne concentrations after application.
The test substances Euparen® WP 50, Rody® and Saprol® Neu were applied in 4 greenhouses in the low crop scenario. 4 trials were performed in each house. The treated plants (hibiscus, cyclamen, anturium and scutelarium) had a height of 10-25 cm (+ 1.15 m table height). In the high crop scenario the test substances Euparen® WP 50, Rody® and Saprol® Neu were applied in 3 greenhouses. Again 4 trials were performed in each house. In this scenario roses were treated. They covered a height from 1.2-1.75 metres.

Results and discussion

All data were evaluated according to Lundehn et al., 1992 (German Model). For the calculation of exposure recorded values below limit of quantification were calculated as half the limit of quantification. Results of geometric mean exposure during application for the three scenarios are given below.

Table IIIA 6.6-1: Specific exposure during knapsack application in greenhouse low crops

Route of exposure during application in low crops	Exposure [mg/kg as handled]	
	Actual	Potential
Dermal (head)	0.43926	0.43926
Dermal (hands)	0.00894	0.7357

Dermal (body)	0.22265	6.31994
Inhalation	0.39849	0.39849

Table IIIA 6.6-2: Specific exposure during knapsack application in greenhouse high crops

Route of exposure during application in high crops	Exposure (mg/kg as handled)	
	Actual	Potential
Dermal (head)	1.56194	1.56194
Dermal (hands)	0.00746	13.1884
Dermal (body)	0.22789	82.47509
Inhalation	0.10841	0.10841

Conclusions

The study provides appropriate data for hand held scenarios in greenhouses. Application data may be used for generic purposes. Mixing/loading data are available for one wettable powder preparation (WP) only. However, it should be considered that the process of mixing/loading for both indoor and outdoor applications is comparable. Therefore, generic exposure estimates for mixing/loading can be taken from other models.