Renewal Assessment Report

beta-cyfluthrin

Montur Forte FS 230

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

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Rapporteur Member State: Germany

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Version history

When	What

Table of contents

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

This document summarises the toxicological studies and human exposure for the plant protection product Montur Forte FS 230 (beta-cyfluthrin + imidacloprid FS 230 (80 + 150 g/L)) containing the active substances beta-cyfluthrin (80 g/L) and imidacloprid (150 g/L).
Montur Forte FS 230 was not the representative formulation during the Annex I listing process of the active substance beta-cyfluthrin. Therefore, a complete set of new studies on the toxicity of the product was submitted and evaluated.

B.6.1 Acute toxicity of plant protection product

The toxicological studies on the product were performed with a previous formulation of Montur Forte FS 230 (beta-cyfluthrin + imidacloprid FS 230 (80 + 150 g/L)) named FCR 4545 80 FS & NTN 33893 150. The previous formulation and the current formulation can be considered as toxicologically equivalent. Effectively, the new formulation contains a new preservative which replaces a different preservative of the previous formulation but does not trigger any classification of Montur Forte FS 230 according to the criteria laid down in Council Directive 1999/45/EC or Regulation (EC) No. 1272/2008. The detailed composition of both formulations is presented in Vol. 4. A summary of the toxicological evaluation for Montur Forte FS 230 is given in Table B.6.1-1. The individual studies are described in B.6.1.1 to B.1.6.

Table B.6.1-1: Summary of evaluation of the studies on acute toxicity including irritancy and skin sensitisation for Montur Forte FS 230

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)	>500 mg/kg bw and <2000 mg/kg bw	Yes	R22	H302	[redacted] 2002, ASB2014-7871
LD_{50} dermal, rat (OECD 402)	>4000 mg/kg bw	Yes	None	None	[redacted] 2002, ASB2014-7872
LC_{50} inhalation, rat (OECD 403)	>2.519 mg/L	Yes	None	None	[redacted] 2002, ASB2014-7861
Skin irritation, rabbit (OECD 404)	Non-irritant	Yes	None	None	[redacted], 2002, ASB2014-7859
Eye irritation, rabbit (OECD 405)	Non-irritant	Yes	None	None	[redacted] 2002, ASB2014-7860
Skin sensitisation,	Non-sensitising	Yes	None	None	[redacted]

guinea pig (OECD 406, M&K)					2002, ASB2014-7870
Supplementary studies for combinations of plant protection products	No data – not required				

Montur Forte FS 230 is moderately toxic after acute oral administration and non-toxic after acute dermal and inhalative application. It is not irritating to the skin and eyes of rabbits and shows no sensitising potential in the maximisation test in guinea pigs.

B.6.1.1 Oral toxicity

Reference: KCP 7.1.1
Report [redacted], 2002a, FCR 4545 80 FS & NTN 33893 150 (c.n.: beta-Cyfluthrin; Imidacloprid): Study for acute oral toxicity in rat, AT00174 (M-073996-01-1), ASB2014-7871
Guideline(s): OECD 423, 96/54/EEC B.1, EPA OPPTS 870.1100
Deviations: The test substance is a commercial product known to be stable and homogenous in both undiluted and in ready-to-use dilution with water. Therefore, analytical determinations of stability and homogeneity of the aqueous formulations were not performed. This deviation did not limit the assessment of the results.
GLP: Yes
Acceptability: Yes

Materials and methods

Test material (Lot/Batch No.)	FCR 4545 80 FS & NTN 33893 150 [Batch No. 06200/0146(0106)]
Species	Rat, Wistar, HsdCpb:WU
No. of animals (group size)	2 x 3 males and 3 x 3 females (nulliparous, non-pregnant)
Dose(s)	200, 500 and 2000 mg/kg bw
Exposure	Once by gavage
Vehicle/Dilution	None
Post exposure observation period	14 days
Remarks	None

Results

Table B.6.1-2: Results of acute oral toxicity study in rats of FCR 4545 80 FS & NTN 33893 150

Dose [mg/kg bw]	Toxicological results [1)]	Duration of signs	Time of death	LD_{50} [mg/kg bw] (14 days)
Male rats				
200	0/0/3	--	--	>200
500	0/3/3	h 1 – d 2	--	>500
Female rats				
200	0/0/3	--	--	>200
500	0/3/3	h 2 – h 6	--	>500
2000	3/3/3	min 30 – h 5	h 4 – h 5	<2000

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

Summary of findings of acute oral toxicity study in rats of FCR 4545 80 FS & NTN 33893 150:
Mortality: All females treated with 2000 mg/kg bw died.
Clinical signs: At a dose of 500 mg/kg body weight the main clinical signs were decreased motility and uncoordinated gait in both sexes. Additionally, in the male animals of the 500 mg/kg dose group constipation, digging and cleaning gestures, spasmodic state and laboured breathing, increased salivation and narrowed palpebral fissures were observed.
In females of the 2000 mg/kg dose group decreased reactivity, temporary convulsions, temporary rolling over, temporary breathing sounds, and temporary tremor were observed in addition to the signs of the 500 mg/kg dose group.
The signs observed started 30 minutes after administration and lasted up to day 2 of the study.
Body weight: There were no toxicological effects on body weight development in males and females.
Macroscopic examination: In animals that died during the observation period the following changes were detected: dark-red discoloration of the liver.
No gross pathologic changes were observed in animals sacrificed at the end of the study period.

Conclusion

Under the experimental conditions, the oral LD_{50} of Montur Forte FS 230 (FCR 4545 80 FS & NTN 33893 150) is >500 and <2000 mg/kg bw in rats. Thus, classification with Xn; R22 is required according to the classification criteria of Council Directive 67/548/EEC and subsequent regulations and as H302 according to Regulation (EC) No. 1272/2008.

B.6.1.2 Dermal toxicity

Reference: KCP 7.1.2
Report [redacted], 2002,
FCR 4545 80 FS & NTN 33893 150 (c.n.: beta-cyfluthrin + imidacloprid): Study for acute dermal toxicity in rats, AT00173 (M-073993-01-1), ASB2014-7872
Guideline(s): OECD 402, 92/69/EEC B.3., EPA OPPTS 870.1200
Deviations: No
GLP: Yes
Acceptability: Yes

Materials and methods

Test material (Lot/Batch No.)	FCR 4545 80 FS & NTN 33893 150 [Lot/Batch No. 06200/0146(0106)]
Species	Rat, Wistar, Hsd Cpb:WU
No. of animals (group size)	5 males and 5 females (nulliparous, non-pregnant)
Dose(s)	4000 mg/kg bw
Exposure	24 hours (dermal, semi-occlusive)
Vehicle/Dilution	None
Post exposure observation period	14 days
Remarks	None

Results

Table B.6.1-3: Results of acute dermal toxicity study in rats of FCR 4545 80 FS & NTN 33893 150

Dose [mg/kg bw]	Toxicological results[1)]	Duration of signs	Time of death	LD_{50} [mg/kg bw] (14 days)
Male rats				
4000	0/0/5	--	--	>4000
Female rats				
4000	0/0/5	--	--	>4000

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

Summary of findings of acute dermal toxicity study in rats of FCR 4545 80 FS & NTN 33893 150:
Mortality: No mortality occurred.
Clinical signs: No clinical signs of toxicity were observed.
Body weight: Body weight gain was considered to be normal.
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 Montur Forte FS 230 (FCR 4545 80 FS & NTN 33893 150) is higher than 4000 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: KCP 7.1.3
Report [redacted], 2002,
FCR 4545 80 FS & NTN 33893 150 (Common-names: beta-cyfluthrin+ imidacloprid): Study on acute inhalation toxicity in rats according to OECD no. 403, AT00011 (M-051182-01-1), ASB2014-7861
Guideline(s): OECD 403, 92/69/EEC B.2, OPPTS 870.1300
Deviations: No
GLP: Yes
Acceptability: Yes

Materials and methods

Test material (Lot/Batch No.)	FCR 4545 80 FS & NTN 33893 150 [Batch No. 06200/0146(0106)]
Species	Rat, Wistar, Hsd Cpb:WU
No. of animals (group size)	5 males and 5 females (nulliparous, non-pregnant)
Concentration(s)	2.519 mg/L (max. attainable conc.)
Exposure	4 hours (nose only)
Vehicle/Dilution	None
Post exposure observation period	14 days
Remarks	None

Results

Table B.6.1-4: Concentration(s) and exposure conditions

Target conc. [mg/L air]	Nominal conc. [mg/L air]	Actual conc. [mg/mL air]	MMAD [1)] [µm]	GSD [2)] [µm]
5.000	15.587	2.519	2.83	1.83

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

Table B.6.1-5: Results of acute inhalation toxicity study in rats of FCR 4545 80 FS & NTN 33893 150

Concentration [mg/L air]	Toxicological results[1)]	Duration of signs	Time of death	LC_{50} [mg/L air] (14 days)
Male rats				
2.519	0/5/5	d 0 – d 2	--	>2.519
Female rats				
2.519	0/5/5	d 0 – d 1	--	>2.519

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

Summary of findings of acute inhalation toxicity study in rats of FCR 4545 80 FS & NTN 33893 150:
Mortality: No mortality occurred.
Clinical signs: Males: Piloerection, bradypnea, motility reduced, salivation, high-legged gait, limp, choreoathetotic convulsions, mydriasis, nostrils: red encrustations.
Females: Piloerection, hair-coat ungroomed, bradypnea, mortality reduced, salivation, high-legged gait.
Body weight: Comparisons between the control and exposure groups revealed a mild and transient decrease in body weight gains (males only).
Macroscopic examination: The necropsies performed at the end of the study revealed no apparent findings.

Conclusion

Under the experimental conditions, the inhalation LC_{50} of Montur Forte FS 230 (FCR 4545 80 FS & NTN 33893 150) is higher than 2.519 mg/L air 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.6.1.4 Skin irritation

Reference: KCP 7.1.4
Report [redacted], 2002,
Acute skin irritation test (patch test) of FCR 4545 80 FS & NTN 33893 150 in rabbits, R-8259 (M-075070-01-1), ASB2014-7859
Guideline(s): OECD 404, EC B.4
Deviations: No
GLP: Yes
Acceptability: Yes

Materials and methods

Test material (Lot/Batch No.)	FCR 4545 80 FS & NTN 33893 150 [Lot/Batch No. 06200/0146(0106)]
Species	Rabbit, Himalayan
No. of animals (group size)	3 males
Initial test using one animal	No
Exposure	0.5 mL (4 hours, semi-occlusive)
Vehicle/Dilution	None
Post exposure observation period	3 days
Remarks	None

Results

Table B.6.1-6: Skin irritation of FCR 4545 80 FS & NTN 33893 150

Animal No.		Scores after treatment[1)]				Mean scores (24-72 h)	Reversible [day]
		1 h	24 h	48 h	72 h		
1	Erythema Oedema	0 0	0 0	0 0	0 0	0.0 0.0	- -
2	Erythema Oedema	0 0	1 0	1 0	1 0	1.0 0.0	5 -
3	Erythema Oedema	0 0	0 0	0 0	0 0	0.0 0.0	- -

1) scores in the range of 0 to 4

Clinical signs: None

Conclusion

Under the experimental conditions, Montur Forte FS 230 (FCR 4545 80 FS & NTN 33893 150) is not a skin irritant. 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.6.1.5 Eye irritation

Reference: KCP 7.1.5
Report Acute eye irritation study of FCR 4545 80 FS & NTN 33893 150 by instillation into the conjunctival sac of rabbits, [redacted], 2002b, R-

8260 (M-075080-01-1), ASB2014-7860
Guideline(s): OECD 405, EC B.5
Deviations: No
GLP: Yes
Acceptability: Yes

Materials and methods

Test material (Lot/Batch No.)	FCR 4545 80 FS & NTN 33893 150 [Lot/Batch No. 06200/0146(0106)]
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)	No
Vehicle/Dilution	None
Post exposure observation period	3 days
Remarks	None

Results

Table B.6.1-7: Eye irritation of FCR 4545 80 FS & NTN 33893 150

Animal No.		Scores after treatment[1)]				Mean scores (24-72 h)	Reversible [day]
		1 h	24 h	48 h	72 h		
1	Corneal opacity	1	0	0	0	0.0	1
	Iritis	0	0	0	0	0.0	-
	Redness conjunctivae	1	1	0	0	0.3	2
	Chemosis conjunctivae	1	0	0	0	0.0	1
2	Corneal opacity	1	0	0	0	0.0	1
	Iritis	1	0	0	0	0.0	1
	Redness conjunctivae	1	1	0	0	0.3	2
	Chemosis conjunctivae	2	1	0	0	0.3	2
3	Corneal opacity	1	1	0	0	0.3	2
	Iritis	1	0	0	0	0.0	1
	Redness conjunctivae	1	1	0	0	0.3	2
	Chemosis conjunctivae	2	1	0	0	0.3	2

[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, Montur Forte FS 230 (FCR 4545 80 FS & NTN 33893 150) is not an eye irritant. 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.6.1.6 Skin sensitisation

Reference: KCP 7.1.6
Report: FCR 4545 80 FS & NTN 33893 150: Study for the skin sensitisation effect in guinea pigs (guinea pig maximisation test according to Magnusson and Kligman), [redacted], 2002, AT00134 (M-072841-01-1), ASB2014-7870
Guideline(s): OECD 406, 96/54/EC B.6., EPA OPPTS 870.2600
Deviations: The test item contains commercial products known to be stable and homogenous both undiluted and in ready-to-use dilution with water. Therefore, analytical determinations of the stability and homogeneity of the formulations in physiological saline solution for administration were not performed. This deviation did not limit the assessment of the results.
GLP: Yes
Acceptability: Yes

Materials and methods

Test material (Lot/Batch No.)	FCR 4545 80 FS & NTN 33893 150 [Batch No. 06200/0146(0106)]
Species	Guinea pig, Hartley albino, Crl: HA
No. of animals (group size)	Test substance group: 20 male guinea pigs Vehicle control group: 10 male guinea pigs
Range finding:	Yes
Exposure (concentration(s), no. of applications)	Intradermal induction: 5 % Topical induction: 100 % Challenge: 100 %
Vehicle	Physiological saline solution
Pretreatment prior to topical application	No
Reliability check	alpha-Hexylcinnamaldehyde (5 % intradermal induction, 25 % topical induction and 12 % challenge; 100 % of the test animals exhibited dermal reactions in the challenge)
Remarks	None

Results

Table B.6.1-8: Results of skin sensitisation study of FCR 4545 80 FS & NTN 33893 150

	48 hours	**72 hours**
	After challenge	
FCR 4545 80 FS & NTN 33893 150	4/20	1/20
Test Vehicle Control Group	0/10	0/10

1) Number of animals with positive dermal response (scores of 1-3) /number of animals in dose group

Clinical signs: None

Conclusion

Under the experimental conditions, Montur Forte FS 230 (FCR 4545 80 FS & NTN 33893 150) is not a skin sensitiser. 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 were submitted.

B.6.1.8 Supplementary studies for combinations of plant protection products

No studies were submitted. This plant protection product is not planned to be combined with other plant protection products.

B.6.2 Dermal absorption

Data point:	KCP 7.3
Report:	Odin, M.; 2014: Montur Forte (CYB + IMD FS 80 + 150): 114C]-beta-cyfluthrin in *vitro* dermal absorption study using human skin; (ASB2014-7895) Company: Bayer S.A.S. Bayer CropScience, Cedex France. Report No: SA 13187, Date: 2014-03-07, not published
Guideline(s):	OECD 428 (2004); EC B45 (2008); EFSA Guidance on Dermal Absorption (2012)
Deviations:	None that compromised the validity of the study results.
GLP:	Yes
Acceptability:	Acceptable

(Dates of exp. Work: October 2013 – March 2014)

Materials and methods:

Non-radiolabelled beta-cyfluthrin: Batch: PNBC000792, purity: 99.3 %;
Radiolabelled beta-cyfluthrin: [fluorophenyl-UL-^{14}C]-beta-cyfluthrin, batch: KML 9638, specific activity: 4.36 MBq/mg, radio purity of the formulation: >98 %;
Formulation: Montur Forte FS 230 containing beta-cyfluthrin (80 g/L). It was used at three nominal concentrations of beta-cyfluthrin: 80 g/L, 40 g/L and 11.4 g/L;
Human skin: Source: Xenometrix, Hégenheim France, France, Number and sex: 6 donors, female, from abdominal region; thickness: 377 to 483 µm.
A flow-through diffusion cell system (Franz's cell modified, Gallas, France) was used to study the absorption of the test substance (exposure area of 1 cm^2 skin). A diffusion cell consisted of a donor chamber and a receptor chamber between which the skin was positioned. The receptor fluid was Eagle's medium supplemented with 5 % bovine serum albumin and gentamycin (50 mg/L) at a pH of 7.4. The receptor chamber was warmed by a constant circulation of warm water which maintained the receptor fluid at 32 ± 2 °C (close to the normal skin temperature). The receptor fluid was pumped through the receptor chamber at a rate of 1.5 mL/h and stirred continuously whilst in the receptor chamber by means of a magnetic bar.
Before dose application, the integrity of the skin samples was assessed by measuring the transepidermal water loss (TEWL) from the stratum corneum. An evaporimeter probe (Tewameter TM 300®, Courage & Khazaka), Denmark) was placed securely on the top of the donor chamber and the amount of water diffusing through the skin was measured. Human and rat skin with a TEWL of greater than 15 g/hm² were considered potentially damaged and were not used. These samples were replaced by new skin fragments which were also tested for integrity before use in the study.

The dose preparation was applied to the split-thickness skin sample with a pipette at the rate of approximately 10 µL/cm^2 exposed skin. The dose preparations were assayed for radioactivity content (by LSC).
The receptor fluid passing through the receptor chamber was collected in glass vials held in a fraction collector. The fraction collector was started after dose application. Samples were then collected hourly for the duration of the experiment (24 hours). At 8 hours post-application, the skin was swabbed with freshly prepared 1 % v/v Tween 80 in PBS (phosphate buffer saline) using natural sponge swabs, in order to remove and retain the non-absorbed dose, until no radioactivity was detected with a Geiger-Müller monitor. At the end of the study (24 hours after application), the treated skin and the skin adjacent to the treatment site (surrounding swabs) were swabbed. Each skin sample was tape-stripped to remove the stratum corneum. This involved the application of Monaderm adhesive tape (Monaderm, Monaco) for 5 seconds before the tape was carefully removed against the direction of hair growth. This procedure was continued until a 'shiny' appearance of the epidermis was evident, which indicated that the stratum corneum had been removed. The tape-strips were collected into scintillation vials for analysis. The skin surrounding the application site (surrounding skin) was separated from the treated skin. Both surrounding skin and tape-stripped treated skin were retained for analysis.
The amounts of radioactivity in the various samples were determined by liquid scintillation counting (LSC). Samples were counted for 10 minutes or for 2 sigma % in an appropriate scintillation cocktail using a Packard 1900 TR counter with on-line computing facilities. Quenching effects were determined using an external standard and spectral quench parameter (tSIE) method. Efficiency correlation curves were prepared for each scintillation cocktail and were regularly checked by the use of ^{14}C-n-hexadecane standards. The scintillation counter was recalibrated when a deviation of greater than 2 % was observed when counting quality control standards. The limit of detection was taken to be twice the background values for blank samples in appropriate scintillation cocktails.

Results:

Beta-cyfluthrin was demonstrated to be soluble in the receptor fluid up to a concentration of 0.3 mg/mL. During the study the maximal concentration per hour of [^{14}C]-beta-cyfluthrin in the receptor fluid was 0.170 µg/mL, therefore there was no risk of back diffusion.
Measurements of the homogeneity of the three concentrations of formulation applied indicated that it was acceptable.
The study results are presented in the following Table.

Table B.6.2-1: Mean distribution of radioactivity at 24 hours after dose application of [^{14}C]-beta-cyfluthrin in an FS 230 formulation at the rates of 80 g/L, 40 g/L and 11.4 g/L to human skin samples.

	Distribution of radioactivity (% dose)					
Dose Levels	**Neat formulation: High dose (80 g/L)**		**Dilution: Intermediate dose (40 g/L)**		**Dilution: Low dose (11.4 g/L)**	
Species	Human (n=4)		Human (n=6)		Human (n=6)	
	Mean	SD	Mean	SD	Mean	SD
SURFACE COMPARTMENT						
Skin swabs (8h)	96.25	18.33	97.47	1.34	97.83	2.04
Skin swabs (24 h)[a]	8.57	16.97	0.15	0.14	1.58	1.37
Surface Dose (1st two tape-strips)	0.05	0.04	0.25	0.21	0.32	0.30
Donor chamber	n.d.	n.a.	0.03	0.02	0.06	0.06
Total % non-absorbed	104.9	2.43	97.90	1.21	99.79	1.11
SKIN COMPARTMENT						
Skin[b]	0.01	0.01	0.02	0.02	0.17	0.22

Stratum corneum[c]	0.04	0.03	0.11	0.13	0.17	0.11
Total % at dose site	0.04	0.03	0.13	0.13	0.34	0.30
RECEPTOR COMPARTMENT						
Receptor fluid (0-24 h)	0.0006	0.0012	0.02	0.03	0.03	0.02
Receptor fluid terminal	n.d.	n.a.	n.d.	n.a.	n.d.	n.a.
Receptor chamber	n.d.	n.a.	n.d.	n.a.	n.d.	n.a.
Total % directly absorbed [d]	0.0006	0.0012	0.02	0.03	0.03	0.02
STUDY: Total % Potentially Absorbable[e]	0.04	0.03	0.15	0.12	0.37	0.30
TOTAL % RECOVERY	104.9	2.43	98.06	1.13	100.16	0.98
Evaluation according to EFSA Guidance						
absorption >75 % within half of study duration	No		Yes		No	
standard deviation >25 %	Yes		Yes		Yes	
recovery <95 %	No		No		No	
Adjusted: Total % Potentially Absorbable[f]	**0.1**	**-**	**0.3**	**-**	**0.7**	**-**

Results expressed in terms of percentage of applied radioactivity.
[a]: sum of radioactivity found in swabs at termination and in surrounding swabs.
[b]: sum of radioactivity found in skin after tape-stripping procedure and in surrounding skin.
[c]: tape-strips excluding numbers 1 & 2 which are considered to be non-absorbed dose.
[d]: sum of radioactivity found in receptor fluid (0-24 h), receptor fluid terminal and receptor chamber.
[e]: total % directly absorbed + total % at dose site
[f]: values considered for the adjusted Total % PotentiallyAbsorbable according to EFSA are in ***boldItalics***

SD: standard deviation
n.d.: not detected (below the limit of detection)
n.a. : not applicable
n: number of skin cells used for calculation
In the above table, the presented means do not always calculate exactly from the presented individual data. This is due to rounding-up differences resulting from the use of the spreadsheet program.

Conclusion:

According to the new EFSA guidance[1] there is the provision that when the sampling period is 24 hours (which is the case for this study) and over 75 % of the total absorption (material in the receptor fluid at the end of the study) within half of the duration (12 hours). These criteria were met for the intermediate dose group in this study. There is also the provision that a standard deviation equal to or larger than 25 % of the mean of the absorption requires the use of an alternative value or rejection of the study. The guidance prefers the approach of adding the standard deviation to the mean to cover the upper 84th percentile value of the results. Additionally where an overall recovery of less than 95 % occurs, a normalisation procedure is to be used by preference. Albeit that the notifier considers that both the value of 25 % for the standard deviation limit and the 95 % recovery limit to be too conservative, the application of the guidance results in the following values for [^{14}C]-beta-cyfluthrin in the Montur Forte FS 230 formulation:
Dermal absorption of [^{14}C]-beta-cyfluthrin in the Montur Forte FS 230 formulation is as follows:
0.1 % for the neat formulation (80 g/L)
0.3 % for the intermediate dose (40 g/L)
0.7 % for the low dose (11.4 g/L).
The study is considered acceptable under the conditions of the study and based on the information given in the report.

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

B.6.3 Available toxicological data relating to co-formulants

Toxicological information on the co-formulants is presented in Vol. 4. Additional labelling with 'Contains 1,2-benzisothiazole-3(2H)-one. May produce allergic reactions.' [EUH208] and with 'Contains 5-chloro-2-methyl-2H-isothiazole-3-on and 2-methyl-2H-isothiazole-3-one. May produce allergic reactions.' [EUH208] is required due to the content of these skin sensitisers in the product exceeding 1/10 of their specific concentration limits.

B.6.4 Exposure data

The plant protection product Montur Forte FS 230 containing 80 g/L beta-cyfluthrin and 150 g/L imidacloprid is intended to be used as insecticide for the treatment of sugar beet seeds. A summary of the critical use and the overall conclusion regarding exposure for operators, workers, bystanders and residents is presented in Table B.6.4-1.
The calculations for beta-cyfluthrin are based on the parameters and endpoints given in Table B.6.4-1.
No exposure assessment for the active substance imidacloprid is considered necessary for the review of beta-cyfluthrin. Hence, the notifier did not submit a risk assessment and did not propose dermal absorption values for imidacloprid.
However, the coRMS argued that an exposure assessment for imidacloprid is required to address cumulative and synergistic effects as mentioned in Commission Regulation (EU) No 284/2013. The RMS proposes that exposure to imidacloprid as well as combined exposure to both active substances should be evaluated during product authorisation. No refined risk assessment would be possible for imidacloprid at the moment since no specific absorption data on imidacloprid were submitted by the notifier.

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

Product name and code	Montur Forte FS 230 (FCR 4545 80 FS & NTN 33893 150)
Formulation type	Flowable concentrate for seed treatment (FS)
Category	Insecticide
Container size(s), short description	200 L drum
Active substance(s) (incl. content)	beta-cyfluthrin 80 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: 0.1 % Dilution: 0.7 % (Dilution: 11.4 g/L; for cleaning and seed loading/sowing) based on Montur Forte FS 230

B.6.4.1 Operator exposure

B.6.4.1.1 Estimation of operator exposure

Operator exposure to beta-cyfluthrin during application of Montur Forte FS 230 according to the critical use was estimated using the Seed TROPEX model. The input parameters for the model are

presented in Table B.6.4-2: . Outcome of the estimation is presented in *) Thousend grain weight: 10 g/1000 seeds
Table B.6.4-3 and Table B.6.4-4. Detailed calculations are shown in Appendix 1.

Table B.6.4-2: Input parameters for Seed TROPEX model for beta-cyfluthrin

Concentration of as	80 g/L beta-cyfluthrin
Application rate:	8 kg as/1000 kg seed*
Treatment capacity:	5 t seed/day (estimate for a seed treatment plant with a low level of automation)
Packaging:	200 L
Amount as handled per day:	40 kg as/day (requires 3 mixing/loading tasks)
Dilution factor	1
Mixing/Loading-System:	Fast-couple
Standard operator body weight:	70 kg and 60 kg
Personal protective equipment (PPE):	In the Seed TROPEX studies operators wore coveralls and gloves for all tasks except for bagging where only coveralls were worn; therefore, the estimated actual dermal exposure values reflect this level of PPE.
Dermal absorption:	0.1 % for calibration, mixing/loading, bagging
	0.7 % for cleaning

*) Thousend grain weight: 10 g/1000 seeds

Table B.6.4-3: Estimated operator exposure towards beta-cyfluthrin (70 kg body weight)

Calibration, mixing/loading, bagging (8 hrs/d) and cleaning			**% syst. AOEL**	**% inhal. AOEL**
Absorbed dose (mg/kg bw/day, dermal/inhalation):	0.0008	0.02628		10797
Absorbed dose (mg/kg bw/day, total):	0.0270		270.2	
Absorbed dose with RPE for cleaning (mg/kg bw/day, dermal/inhalation):	0.0008	0.0096		3930
Absorbed dose with RPE for cleaning (mg/kg bw/day, total):	0.0103		103.3	
Absorbed dose with RPE for all tasks (mg/kg bw/day, dermal/inhalation):	0.0008	0.0021		864
Absorbed dose with RPE for all tasks (mg/kg bw/day, total):	0.0029		28.8	

Table B.6.4-4: Estimated operator exposure towards beta-cyfluthrin (60 kg body weight)

Calibration, mixing/loading, bagging (8 hrs/d) and cleaning			**% syst. AOEL**	**% inhal. AOEL**
Absorbed dose (mg/kg bw/day, dermal/inhalation):	0.0009	0.0306		12596
Absorbed dose (mg/kg bw/day, total):	0.0315		315.2	
Absorbed dose with RPE for cleaning (mg/kg bw/day, dermal/inhalation):	0.0009	0.0111		4585
Absorbed dose with RPE for cleaning (mg/kg	0.0121		120.5	

bw/day, total):				
Absorbed dose with RPE for all tasks (mg/kg bw/day, dermal/inhalation):	0.0009	0.0024		1007
Absorbed dose with RPE for all tasks (mg/kg bw/day, total):	0.0034		33.6	

B.6.4.1.2 Measurement of operator exposure

The operator exposure estimations carried out indicated that the inhalative acceptable operator exposure level (AOEL) will be exceeded under conditions of intended uses. Therefore, the applicant submitted two exposure studies on seed treatment in sugar beets to demonstrate a safe use (Marcenac, 2006, ASB2012-1715; Brennecke, 2007, ASB2011-5997). The treatment of sugar beet seeds differs significantly from the treatment of cereals on which the Seed TROPEX model is based on. Hence, the studies are accepted for a refinement of the Seed TROPEX model.
A summary document (Anft, 2015, ASB2016-1480) containing short study reports of the two exposure studies by Marcenac (2006, ASB2012-1715) and Brennecke (2007, ASB2011-5997) was also submitted by the applicant but was not separately described.

Data point: KCP 7.2.1

Report: Determination of operator exposure to imdiacloprid during treatment of sugar beet seeds with Imprimo in France: Amended final report; Marcenac, F., 2006, study 04B033 HI, ASB2012-1715

Guideline(s): OECD guidance document for the conduct of studies of occupational exposure to pesticides during agricultural application, Series on Testing and Assessment No. 9, 1997

Deviations: No

GLP: Yes

Acceptability: Yes

The study was already reported and evaluated during the EU peer review of imidacloprid.

Materials and methods

Exposure was monitored in two of the three sugar beet seed treatment plants existing in France using Imprimo, a water-based FS formulation containing the active substances imidacloprid (400 g/L) and tefluthrin (17.8 g/L).
Dermal exposure was determined via whole body dosimetry (protective coveralls, work clothing, long sleeved T-shirt, long johns), face-neck wipes and hand/glove rinsing. Inhalation exposure was measured via IOM-samplers equipped with glass fibre filters. The dosimeter samples were extracted and analysed for residues of imidacloprid by LC-MS/MS determination.
The product was applied with an application rate of 0.225 L product per unit of seeds (90 g imidacloprid/u). 12 operators were monitored during a complete working shift. Four operators (2 at each site) performed the mixing/loading and eight operators (4 at each site) were monitored while operating the coating equipment plus cleaning.

Description of the activities at each site:

1st Plant: Mereville

The mixing/loading was performed in an area separated from the coating area. Water was first loaded

into a vessel followed by the product and further components (inert material and the fungicide TACHIGAREN®). The mixture was stirred for about 45 minutes and then transferred into a 1000-L container.
One operator per shift conducted the seed coating (including supervision, maintenance and cleaning). In total 4 shifts were monitored (2 x 2 replicates on two consecutive days). The coating was performed during 2 hours in a drum coating system using two drums (A and B) in parallel both of which have a capacity of about 300 units of seeds per batch. The cleaning was performed after two coating cycles.
Cleaning was partially automated. At first, the drum was automatically rinsed with water. Operators finished drum cleaning using high-pressure water. They also cleaned the discharge hopper and filters. Some parts of the equipment were removed and washed in a sink.

2nd Plant: Nerac

The mixing/loading was conducted in a specific area close to the coating area. IMPRIMO® was pumped into a storage container using a plunger which was manually transferred from one container to the other. The empty product containers were rinsed with water. The rinsing water was transferred into the vessel used for preparing the mixture. Then TACHIGAREN® was added. At the end of mixing, the slurry was pumped into the working container.
Two operators per shift conducted the seed coating (including supervision, maintenance and cleaning). Two shifts were monitored. Coating was performed in a fluid bed system with 10 units of seeds per batch.The cleaning lasted around 1 hour. The equipment was manually cleaned with water and a sponge. Some parts of the equipment were removed and washed in a sink.

The following Personal Protective Equipment (PPE) was worn at each site:

Mereville:

Mixing/loading:	Tyvek®, above long sleeved shirt and working trousers, nitrile gloves and a respirator with replaceable filters (half face mask).
Coating:	Tyvek®, nitrile gloves when working in the treatment area, visor during cleaning the drums, disposable filtering facemask during sampling and adjusting the height of spraying nozzles.

Nerac:

Mixing/loading:	Tyvek®, nitrile gloves, half facemask respirator and goggles
Coating:	Working trousers and jacket, disposable nitrile gloves according to their usual practice. Goggles only during cleaning N.b.: operators frequently did not use protective gloves when getting into contact with contaminated surfaces or treated seeds

Results and discussions

Individual measurements are presented in Table B.6.4-5. No corrections for recovery were necessary since field recoveries were between 82 to 101 %.

Table B.6.4-5: Individual exposure to imidacloprid using Imprimo in sugar beet seed treatment

Operator	Working time [min]	kg as	Potential dermal exposure [µg/task]	Actual dermal exposure [µg/task] *	Inhalation exposure [µg/task] **
Mixing/loading					
1 (Imprimo)	97	60.8	234940	1013	12.2
2 (Imprimo)	93	60.8	24207	254	6.7
3 (Imprimo)	83	182	85917	374	7.2
4 (Imprimo)	78	211	192216	1096	32.4

Operator	Working time [min]	kg as	Potential dermal exposure [µg/task]	Actual dermal exposure [µg/task] *	Inhalation exposure [µg/task] **
Seed coating					
1 (Imprimo)	437	109	128027	1794	195.9
2 (Imprimo)	386	98	137652	1110	93.9
3 (Imprimo)	414	102	31594	1046	41.9
4 (Imprimo)	397	105	20253	1015	142.0
5 (Imprimo)	370	68	74322	4283 ***	22.3
6 (Imprimo)	373	68	39043	1890 ***	20.2
7 (Imprimo)	381	68	54903	5266 ***	13.1
8 (Imprimo)	270	43	59060	7023 ***	81.1
* inner clothing + face + hand wash ** based on a default breathing rate of 1.25 m^3/h *** no Tyvek, gloves worn during cleaning only					

Conclusion:

The study results represent exposure from treatment of sugar beet seed in professional plants. The level of PPE clearly affects the extent of exposure.

Data point: KCP 7.2.1

Report: Determination of operator exposure to imidacloprid during treatment of sugar beet seeds with suspensions containing imidacloprid; Brennecke, R., 2007, Report No. MR-06/178, Study ID P666 04 1700, ASB2011-5997

Guideline(s): OECD guidance document for the conduct of studies of occupational exposure to pesticides during agricultural application, Series on Testing and Assessment No. 9, 1997

Deviations: No

GLP: Yes

Acceptability: Yes

Materials and methods

The exposure study was conducted in a professional seed treatment facility in Germany. Two different products were applied for the coating of sugar beet seeds: Akteur FS 190, containing 150 g/L imidacloprid and 40 g/L tefluthrin, and Imprimo, containing 400 g/L imidacloprid and 17.8 g/L tefluthrin. Akteur was applied at an application rate of 66.67 mL product or 10 g imidacloprid per unit seed, Imprimo was applied at a rate of 225 mL product or 90 g imidacloprid per unit seed.
The operators were monitored while performing the mixing/loading task, the seed coating process (including supervision, maintenance, cleaning (one replicate only)) and the storage logistic tasks. For each of the task 3 replicates were monitored for a usual working shift. Mixing/loading of the seed coating suspension was performed 5 to 6 times per working shift, one operation lasted on average 39 min. Coating was done simultaneously in 10 batch treaters. A treatment cycle in one treatment chamber took about 45 min. The whole coating process was highly automated. The potential treatment capacity per hour in the whole plant was about 450 units of seed.
Potential and actual dermal exposure was measured by whole body dosimetry. The operators were dressed in long work trousers, a long-sleeved work jacket and a long-sleeved shirt as outer dosimeter

and long underpants and a long-sleeved T-shirt as inner dosimeter. In addition, the operators wore a disposable coverall during mixing/loading or cleaning. During both tasks the operators also wore gloves continuously, while during the other tasks gloves were only used when the operators got into contact with contaminated surfaces or had to handle treated seeds. Hand exposure was determined by washing the hands and the gloves and analysing the washing liquids whereas exposure to the head was measured by wiping face/neck of the operators. Inhalation exposure was monitored with personal air samplers with glass fibre filter located in the breathing zone of the operators.
Samples were analysed by extracting imidacloprid from the matrix and analysing the content with liquid gas chromatography using electrospray MS/MS detection.

Results and discussions

The results of the measurements are shown in the table below. No corrections for field recovery were made since the field recoveries were between 83 to 107 %.

Operator	Working time [min]	kg as	Potential dermal exposure [µg/task]	Actual dermal exposure [µg/task] **	Inhalation exposure [µg/task] ***
Mixing/loading					
1 (Akteur)	353	39	3906	1312	5.3
2 (Imprimo)	344	287	32811	1558	68.7
3 (Imprimo)	393	431	10638	510.0	24.0
Seed coating					
1 (Akteur)	427	39	925.8	295.0	2.5
2 (Imprimo) *	431	310	4968	497.1	18.6
3 (Imprimo)	451	332	1156	174.0	11.0
Storage logistics					
5 (Akteur)	334	41	547.3	128.0	5.2
6 (Imprimo)	386	548	1251	232.3	16.6
7 (Imprimo)	377	679	1069	220.2	6.9

* cleaning included in task
** inner clothing + face + hand wash
*** based on a default breathing rate of 1.25 m^3/h

Conclusion

The study presents exposure for operators during sugar beet seed treatment in a professional plant. Highest exposures were observed for the mixer/loaders being in direct contact with the product.

Risk assessment for inhalation exposure:

Montur Forte FS 230 will be applied at a rate of 0.1 L product or 8 g beta-cyfluthrin per unit seed. The products in the studies were applied at higher rates (Imprimo: 80 g imdicloprid per unit; Akteur: 10 g imdiclaprid per unit), therefore, the study results can be considered as a worst case for Montur Forte FS 230. Exposure was measured during a usual work shift; no adjustment for working duration or work rate is considered necessary.
Table B.6.4-6 presents the maximum values or the 75th percentile (in case of more than 10 replicates) for the respective task from both studies. For the risk assessment a body weight of 60 kg is assumed.

Table B.6.4-6: Summary of inhalation exposure

	Inhalation exposure [µg/task]	Inhalation exposure [mg/kg bw/day]	% inhal. AOEL	% inhal. AOEL (RPE*)
Mixing/loading				
max. value	68.7	0.001145	471	47.1
Seed coating				
max. value	195.9	0.003265	1344	134
75th percentile	87.5	0.001458	600	60.0
Storage logistics				
max. value	16.6	0.000277	114	11.4

* FFP2, P2 or similar (reduction factor: 10 %; acc. to EFSA guidance (EFSA Journal 2014;12(10):3874))

According to the study data a safe use for beet seed treatment in professional plants can be demonstrated for Montur Forte FS230 if RPE is used during the tasks which are performed by different operators.

B.6.4.2 Bystander and resident exposure

B.6.4.2.1 Estimation of bystander and resident exposure

There are no validated exposure models for seed treatment; therefore, ‘surrogates’ were used. In Table B.6.4- the exposure models are given which were used for the estimation of bystander and resident exposure to beta-cyfluthrin. An attrition rate of 10 % is used as a worst case assumption. Nevertheless, according to data with the product from the Heubachfilter-test the attrition rate will be much lower and exposure for bystanders and residents can be considered as negligible. Outcome of the estimation is presented in Table B.6.4-. Detailed calculations are given in Appendix 1.

Table B.6.4-7: Exposure models for intended uses

Critical use	Loading/sowing of sugar beet seeds (max. 130 mL product/ha)
Models	Martin, S. et al. (2008) (available on http://www.bfr.bund.de/cm/343/schutz_von_nebenstehenden_und_anwohnern_v1.xls) [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.6.4-8: Estimated bystander and resident exposure for beta-cyfluthrin

Model data	Total absorbed dose (mg/kg/day)	% of systemic AOEL	Total inhaled dose (mg/kg/day)	% of inhalative AOEL
Bystanders (adult) Attrition rate: 10 % Body weight: 60 kg	0.0000379	0.38	0.0000258	10.6
Bystanders (children) Attrition rate: 10 %	0.0000646	0.65	0.0000551	22.7

Body weight: 16.15 kg				
Residents (adult) Attrition rate: 10 % Body weight: 60 kg	0.0000009	0.01	covered by bystander exposure	covered by bystander exposure
Residents (children) Attrition rate: 10 % Body weight: 16.15 kg	0.0000173	0.17	covered by bystander exposure	covered by bystander exposure

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

Estimated worker exposure to beta-cyfluthrin during loading and sowing was performed using Seed TROPEX data. The input parameters are shown in Table B.6.4-. Outcome of the estimation is presented in Table B.6.4-. Detailed calculations are shown in Appendix 1.

Table B.6.4-9: Input parameters for Seed TROPEX model

Working time per day:	8 hours
Worker body weight:	60 kg
Personal protective equipment (PPE):	In the Seed TROPEX studies workers wore coveralls and gloves during that task; therefore, the estimated actual dermal exposure value reflects this level of PPE.
Dermal absorption:	0.7 % for loading / sowing (worst-case)

Table B.6.4-10: Estimated worker exposure towards beta-cyfluthrin

Loading/sowing (8 hrs/d)			**% of systemic AOEL**	**% of inhalative AOEL**
Absorbed dose (mg/kg bw/day, dermal/inhalation):	0.00068	0.00248		1019.6
Absorbed dose (mg/kg bw/day, total):	0.0032		31.6	
Absorbed dose with RPE (mg/kg bw/day, dermal/inhalation):		0.00020		81.6

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 exposure estimations made with the Seed TROPEX model show that the total systemic exposure to beta-cyfluthrin will be below the systemic AOEL if gloves, coverall and respiratory protection are worn by the operators, but that the inhalative AOEL for beta-cyfluthrin will be exceeded for the intended use of Montur Forte FS 230 even if respiratory equipment is used. However, according to exposure data from two studies on beet seed treatment in professional plants in Europe a safe use could be demonstrated for operators. The data show that the inhalative AOEL will not be exceeded when RPE is used by the operators.
For workers, bystanders and residents no unacceptable risk was identified when the product is used as intended and provided that protective equipment is worn by workers. The equipment for workers comprises protective gloves, coverall and respiratory protection.
A summary of the critical use and the overall conclusion for beta-cyfluthrin in Montur Forte FS 230 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			Crops[1] and situation (e.g. growth stage of crop)	F/G or I[2]			
		Method/ Kind (incl. application technique	Max. number (min. interval between applications) a) per use b) per crop/ season	a) Amount product per 100 000 seeds b) Max. product per ha	kg as/ha a) beta-cyfluthrin b) imidacloprid	kg as/1000 kg seed[3] a) beta-cyfluthrin b) imidacloprid			Operator	Worker	Bystander	Residents
Beet	F	Seed treatment	a) 1 b) 1	a) 100 mL b) 130 mL	a) 0.0104 b) 0.0195	a) 8 b) 15	Seed TROPEX					
							Operator exposure studies on beet seed treatment					

	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
[3] Thousand grain weight: 10 g/1000 seeds

B.6.6 References relied on

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
KCP 7.1.1 /01	[redacted]	2002	FCR 4545 80 FS & NTN 33893 150 (c.n.: beta-cyfluthrin; Imidacloprid) - Study for acute oral toxicity in rats [redacted] Bayer CropScience, Report No.: AT00174, Edition Number: M-073996-01-1 Date: 2002-12-17 GLP/GEP: yes, unpublished BVL-2633241, BVL-2633241, ASB2014-7871	Y	Y	data not submitted on EU level	Bayer CropScience
KCP 7.1.2 /01	[redacted]	2002	FCR 4545 80 FS & NTN 33893 150 (c.n.: beta-cyfluthrin, Imidacloprid) - Study for acute dermal toxicity in rats [redacted] Bayer CropScience, Report No.: AT00173, Edition Number: M-073993-01-1 Date: 2002-12-17 GLP/GEP: yes, unpublished BVL-2633242, BVL-2633242, ASB2014-7872	Y	Y	data not submitted on EU level	Bayer CropScience

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
KCP 7.1.3 /01	[redacted]	2002	FCR 4545 80 FS & NTN 33893 150 (Common-names: beta-cyfluthrin, Imidacloprid) - Study on acute inhalation toxicity in rats according to OECD no. 403 [redacted] Bayer CropScience, Report No.: AT00011, Edition Number: M-051182-01-1 Date: 2002-09-06 GLP/GEP: yes, unpublished BVL-2633243, BVL-2633243, ASB2014-7861	Y	Y	data not submitted on EU level	Bayer CropScience
KCP 7.1.4 /01	[redacted]	2002	Acute skin irritation test (patch test) of FCR 4545 80 FS & NTN 33893 150 in rabbits [redacted] Bayer CropScience, Report No.: R8259, Edition Number: M-075070-01-1 Date: 2002-07-22 GLP/GEP: yes, unpublished BVL-2633244, BVL-2633244, ASB2014-7859	Y	Y	data not submitted on EU level	Bayer CropScience
KCP 7.1.5 /01	[redacted]	2002	Acute eye irritation study of FCR 4545 80 FS & NTN 33893 150 by instillation into the conjunctival sac of rabbits [redacted] Bayer CropScience, Report No.: R8260, Edition Number: M-075080-01-1 Date: 2002-07-22 GLP/GEP: yes, unpublished BVL-2633245, BVL-2633245, ASB2014-7860	Y	Y	data not submitted on EU level	Bayer CropScience

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**
KCP 7.1.6 /01	[redacted]	2002	FCR 4545 80 FS & NTN 33893 150 - Study for the skin sensitisation effect in guinea pigs (guinea pig maximisation test according to Magnusson and Kligman) [redacted] Bayer CropScience, Report No.: AT00134, Edition Number: M-072841-01-1 Date: 2002-12-03 GLP/GEP: yes, unpublished BVL-2633246, BVL-2633246, ASB2014-7870	Y	Y	data not submitted on EU level	Bayer CropScience
KCP 7.2.1 /01	Brennecke, R.; Timmermann, C.	2007	Determination of operator exposure to Imidacloprid during treatment of sugar beet seeds with suspensions containing Imidacloprid MR-06/178 ! M-282685-01-1 ! P 666 04 1700 Bayer AG, Germany GLP: Yes Published: No BVL-2044005, BVL-2939180, ASB2011-5997	N	Y	data not submitted on EU level	Bayer CropScience
KCP 7.2.1 /02	Marcenac, F.	2006	Determination of operator exposure to Imidacloprid during treatment of sugar beet seeds with Imprimo in France - Amended final report 04B033 HI ! M-266526-02-1 ! MR-162/04 ! P666 04 1001 GLP: No (1) Yes (6) Published: No BVL-1966327, BVL-2142351, BVL-2218390, BVL-2226584, BVL-2484806, BVL-2939179, BVL-2963419, ASB2012-1715	N	Y	data not submitted on EU level	SeedTropex Steering Group

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**
KCP 7.2.1 /03	Anft, T.; Timmermann, C.	2015	Summary of measurements of occupational exposure and risk assessment for seed treatment of beet seeds and information for the plant protection product for Imidacloprid + beta-cyfluthrin (150 + 80 g/L) flowable concentrate for seed treatment Bayer CropScience Bayer CropScience, Report No.: M-537929-01-1, Edition Number: M-537929-01-1 Date: 2015-10-28 GLP/GEP: n.a., unpublished BVL-2963421, ASB2016-1480	N	Y	data not submitted on EU level	Bayer CropScience
KCP 7.3 /01	Odin, M.	2014	Montur Forte (CYB + IMD FS 80 + 150): [14C]-beta-cyfluthrin - In vitro dermal absorption study using human skin Bayer S.A.S., Bayer CropScience, Sophia Antipolis, France Bayer CropScience, Report No.: SA 13187, Edition Number: M-479592-01-1 Date: 2014-03-07 GLP/GEP: yes, unpublished BVL-2633247, BVL-2633247, ASB2014-7895	Y	Y	new data requirement	Bayer CropScience

Grey shaded Studies indicate Baseline Dossier Studies
Black Studies indicate Supplementary Dossier Studies

Appendix 1 Exposure calculations

A 1.1 Operator exposure (total systemic exposure)

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

Intended use:	Seed treatment		**AOEL-S:**	0.01	mg/kg bw/d
Concentration of as:	80	g/L or g/kg	**Body weight:**	70 / 60	kg/person
Application rate:	8	kg as/t seed	**Dilution factor:**	1	
Dermal absorption:	0.1	% for seed treatment	**Seeds treated:**	5	t/day
			M/L operations per day:	3	
	0.7	% for cleaning	**Mixing/loading system:**	Fast-couple	
Inhalation absorption:	100	%	**Working duration (bagging)**	8	h/d

Table A 2: Estimation of operator exposure towards beta-cyfluthrin during seed treatment (based on Seed TROPEX data), 70 kg body weight

	Generic dermal exposure [1) 2)] (mL/operation or h)	**Generic inhalation exposure [1)] (mL/operation or h)**	**Actual dermal exposure (mg as/operation or h)**	**Inhalation exposure (mg as/operation or h)**	**No. of operations / working duration (bagging; h)**
Calibration	0.0142	0.0014	1.1382	0.1105	1
Mixing/loading	0.0052	0.0001	0.4154	0.0082	3
Bagging	0.6976	0.054	0.6976	0.054	8
Cleaning	0.0834	0.0159	6.6691	1.2696	1
	Actual dermal exposure (mg as/d)	**Inhalation exposure (mg as/d)**	**Absorbed dose dermal (mg as/kg bw/d)**	**Absorbed dose inhalation (mg as/kg bw/d)**	**% AOEL-S**
Calibration	1.1382	0.1105	0.000016	0.001578	
Mixing/loading	1.2461	0.0245	0.000018	0.000350	
Bagging	5.5807	0.432	0.000080	0.006171	
Cleaning	6.6691	1.2696	0.000667	0.018137	
Total			**0.000781**	**0.026237**	**270.17**
Total (with RPE [3)] for cleaning)			**0.000781**	**0.009550**	**103.31**
Total (with RPE [3)] for all tasks)			**0.000781**	**0.002099**	**28.80**

[1)] values represent geometric mean of measured data; inhalation exposure during bagging represented by maximum measured value

[2)] workers wore gloves (except for bagging) and coverall

[3)] RPE with a protection factor of 0.08

Table A 3: Estimation of operator exposure towards beta-cyfluthrin during seed treatment (based on Seed TROPEX data), 60 kg body weight

	Generic dermal exposure [1) 2)] (mL/operation or h)	**Generic inhalation exposure [1)] (mL/operation or h)**	**Actual dermal exposure (mg as/operation or h)**	**Inhalation exposure (mg as/operation or h)**	**No. of operations / working duration (bagging; h)**
Calibration	0.0142	0.0014	1.1382	0.1105	1
Mixing/loading	0.0052	0.0001	0.4154	0.0082	3
Bagging	0.6976	0.054	0.6976	0.054	8

Cleaning	0.0834	0.0159	6.6691	1.2696	1
	Actual dermal exposure (mg as/d)	**Inhalation exposure (mg as/d)**	**Absorbed dose dermal (mg as/kg bw/d)**	**Absorbed dose inhalation (mg as/kg bw/d)**	**% AOEL-S**
Calibration	1.1382	0.1105	0.000019	0.001841	
Mixing/loading	1.2461	0.0245	0.000021	0.000408	
Bagging	5.5807	0.432	0.000093	0.007200	
Cleaning	6.6691	1.2696	0.000778	0.021160	
Total			**0.000911**	**0.030609**	**315.20**
Total (with RPE [3] for cleaning)			**0.000911**	**0.011142**	**120.53**
Total (with RPE [3] for all tasks)			**0.000911**	**0.002449**	**33.60**

[1] values represent geometric mean of measured data; inhalation exposure during bagging represented by maximum measured value

[2] workers wore gloves (except for bagging) and coverall

[3] RPE with a protection factor of 0.08

A 1.2 Operator exposure (inhalation exposure only)

Table A 4: Input parameters considered for the estimation of operator exposure

Intended use:	Seed treatment		**AOEL-I:**	0.000243	mg/kg bw/d
Concentration of as:	80	g/L or g/kg	**Body weight:**	70 / 60	kg/person
Application rate:	8	kg as/t seed	**Dilution factor:**	1	
Dermal absorption:			**Seeds treated:**	5	t/day
			M/L operations per day:	3	
			Mixing/loading system:	Fast-couple	
Inhalation absorption:	100	%	**Working duration (bagging)**	8	h/d

Table A 5: Estimation of operator exposure towards beta-cyfluthrin during seed treatment (based on Seed TROPEX data), 70 kg body weight

	Generic dermal exposure [1] [2] (mL/operation or h)	**Generic inhalation exposure [1] (mL/operation or h)**	**Actual dermal exposure (mg as/operation or h)**	**Inhalation exposure (mg as/operation or h)**	**No. of operations / working duration (bagging; h)**
Calibration		0.0014		0.1105	1
Mixing/loading		0.0001		0.0082	3
Bagging		0.054		0.054	8
Cleaning		0.0159		1.2696	1
	Actual dermal exposure (mg as/d)	**Inhalation exposure (mg as/d)**	**Absorbed dose dermal (mg as/kg bw/d)**	**Absorbed dose inhalation (mg as/kg bw/d)**	**% AOEL-S**
Calibration		0.1105		0.0016	
Mixing/loading		0.0245		0.0003	
Bagging		0.432		0.0062	
Cleaning		1.2696		0.0181	
Total				**0.0262**	**10796.95**
Total (with RPE [3] for cleaning)				**0.0096**	**3930.21**
Total (with RPE [3] for all tasks)				**0.0021**	**863.76**

[1] values represent geometric mean of measured data; inhalation exposure during bagging represented by maximum measured value

[2] workers wore gloves (except for bagging) and coverall

[3] RPE with a protection factor of 0.08

Table A 6: Estimation of operator exposure towards beta-cyfluthrin during seed treatment (based on Seed TROPEX data), 60 kg body weight

	Generic dermal exposure [1] [2] (mL/operation or h)	**Generic inhalation exposure [1] (mL/operation or h)**	**Actual dermal exposure (mg as/operation or h)**	**Inhalation exposure (mg as/operation or h)**	**No. of operations / working duration (bagging; h)**
Calibration		0.0014		0.1105	1
Mixing/loading		0.0001		0.0082	3
Bagging		0.054		0.054	8
Cleaning		0.0159		1.2696	1
	Actual dermal exposure (mg as/d)	**Inhalation exposure (mg as/d)**	**Absorbed dose dermal (mg as/kg bw/d)**	**Absorbed dose inhalation (mg as/kg bw/d)**	**% AOEL-S**
Calibration		0.1105		0.0018	
Mixing/loading		0.0245		0.0004	
Bagging		0.432		0.0072	
Cleaning		1.2696		0.0212	
Total				**0.0306**	**12596.44**
Total (with RPE [3] for cleaning)				**0.0111**	**4585.24**
Total (with RPE [3] for all tasks)				**0.0025**	**1007.71**

[1] values represent geometric mean of measured data; inhalation exposure during bagging represented by maximum measured value

[2] workers wore gloves (except for bagging) and coverall

[3] RPE with a protection factor of 0.08

A 1.3 Bystander and resident exposure (total systemic exposure)

Table A 7: Input parameters considered for the estimation of bystander exposure

Intended use(s):	Seed sowing		**Attrition rate (AtR):**	10	% Deposition (% Attr.rate)
Application rate (AR):	0.0104	kg as/ha	**Exposed body surface area (BSA):**	1	m² (adults)
	1.04	mg/m²		0.21	m² (children)
Body weight (BW):	60	kg/person (adults)	**Specific Inhalation Exposure (I^*_A):**	0.148653	mg/person/8 h (adult) based on worker exp. acc. SeedTropex)
	16.15	kg/person (children)		0.085433	mg/person/8 h (children) based on worker exp. acc. SeedTropex)
Dermal absorption (DA):	0.7	% ('worst case')	**Area Treated (A):**	20	ha/d (based on Seed Treatment)
Inhalation absorption (IA):	100	%			
AOEL:	0.01	mg/kg bw/d	**Exposure duration (T):**	5	min

Table A 8: Estimation of bystander exposure towards beta-cyfluthrin

Adults			**Children**		
Bystander: Systemic dermal exposure during/after application (via spray drift)					
SDE_B = (AR x D x BSA x DA) / BW			SDE_B = (AR x D x BSA x DA) / BW		
(1.04 x 10 % x 1 x 0.7 %) / 60			(1.04 x 10 % x 0.21 x 0.7 %) / 16.15		
External dermal exposure	0.104	mg/person	External dermal exposure	0.02184	mg/person
External dermal exposure	0.001733	mg/kg bw/d	External dermal exposure	0.001352	mg/kg bw/d

Systemic dermal exposure	**0.000012**	**mg/kg bw/d**	**Systemic dermal exposure**	**0.000009**	**mg/kg bw/d**
Bystander: Systemic inhalation exposure during/after application (via spray drift)					
$SIE_B = (I^*_A$ x AR x A x T x IA) / BW			$SIE_B = (I^*_A$ x AR x A x T x IA) / BW		
(0.148653 / 480 x 5 x 100 %) / 60			(0.085433 / 480 x 5 x 100 %) / 16.15		
External inhalation exposure	0.001548	mg/person	External inhalation exposure	0.00089	mg/person
External inhalation exposure	0.000026	mg/kg bw/d	External inhalation exposure	0.000055	mg/kg bw/d
Systemic inhalation exposure	**0.000026**	**mg/kg bw/d**	**Systemic inhalation exposure**	**0.000055**	**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	0.002276	mg/person	Total systemic exposure	0.001043	mg/person
Total systemic exposure	**0.000038**	**mg/kg bw/d**	**Total systemic exposure**	**0.000065**	**mg/kg bw/d**
% of AOEL	**0.38**	**%**	**% of AOEL**	**0.65**	**%**

Table A 9: Input parameters considered for the estimation of resident exposure

Intended use(s):			**Attrition rate (AtR):**	10	% Deposition (% Attr.rate)
Application rate (AR):	0.0104	kg as/ha	**Transfer coefficient (TC):**	7300	cm^2/h (adults)
	0.000104	mg/cm^2		2600	cm^2/h (children)
Number of applications (NA):	1		**Turf Transferable Residues (TTR):**	5	%
Body weight (BW):	60	kg/person (adults)	**Exposure Duration (H):**	2	h
	16.15	kg/person (children)	**Airborne Concentration of Vapour (ACV):**	0	mg/m^3
Dermal absorption (DA):	0.7	% ('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 10: Estimation of resident exposure towards beta-cyfluthrin

Adults			**Children**		
Residents: Systemic dermal exposure after application (via deposits caused by spray drift)					
$SDE_R = (AR \times NA \times D \times TTR \times TC \times H \times DA) / BW$			$SDE_R = (AR \times NA \times D \times TTR \times TC \times H \times DA) / BW$		
(0.000104 x 1 x 10 % x 5 % x 7300 x 2 x 0.7 %) / 60			(0.000104 x 1 x 10 % x 5 % x 2600 x 2 x 0.7 %) / 16.15		
External dermal exposure	0.007592	mg/person	External dermal exposure	0.002704	mg/person
External dermal exposure	0.000127	mg/kg bw/d	External dermal exposure	0.000167	mg/kg bw/d
Systemic dermal exposure	**0.000001**	**mg/kg bw/d**	**Systemic dermal exposure**	**0.000001**	**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		
			(0.000104 x 1 x % x 5 % x 50 % x 20 x 20 x 2 x 100 %) / 16.15		
			External oral exposure	0.000208	mg/person
			External oral exposure	0.000013	mg/kg bw/d
			Systemic oral exposure	**0.000013**	**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		
			(0.000104 x 1 x % x 20 % x 25 x 100 %) / 16.15		
			External oral exposure	0.000052	mg/person
			External oral exposure	0.000003	mg/kg bw/d
			Systemic oral exposure	**0.000003**	**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	0.000053	mg/person	Total systemic exposure	0.000279	mg/person

Total systemic exposure	**0.000001**	**mg/kg bw/d**	**Total systemic exposure**	**0.000017**	**mg/kg bw/d**
% of AOEL	**0.01**	**%**	**% of AOEL**	**0.17**	**%**

A 1.4 Bystander exposure (inhalative route only)

Table A 11: Input parameters considered for the estimation of bystander exposure

Intended use(s):	Seed sowing		**Attrition rate (AtR):**		
Application rate (AR):	0.0104	kg as/ha	**Exposed body surface area (BSA):**		
	1.04	mg/m^2			
Body weight (BW):	60	kg/person (adults)	**Specific Inhalation Exposure (I^*_A):**	0.148653	mg/person/8 h (adult) based on worker exp. acc. SeedTropex)
	16.15	kg/person (children)		0.085433	mg/person/8 h (children) based on worker exp. acc. SeedTropex)
Dermal absorption (DA):			**Area Treated (A):**	20	ha/d (based on Seed Treatment)
Inhalation absorption (IA):	100	%			
AOEL-I:	0.000243	mg/kg bw/d	**Exposure duration (T):**	5	min

Table A 12: Estimation of bystander exposure towards beta-cyfluthrin

Adults			**Children**		
Bystander: Systemic inhalation exposure during/after application (via spray drift)					
$SIE_B = (I^*_A$ x AR x A x T x IA) / BW			$SIE_B = (I^*_A$ x AR x A x T x IA) / BW		
(0.148653 / 480 x 5 x 100 %) / 60			(0.085433 / 480 x 5 x 100 %) / 16.15		
External inhalation exposure	0.001548	mg/person	External inhalation exposure	0.00089	mg/person
External inhalation exposure	0.000026	mg/kg bw/d	External inhalation exposure	0.000055	mg/kg bw/d
Systemic inhalation exposure	**0.000026**	**mg/kg bw/d**	**Systemic inhalation exposure**	**0.000055**	**mg/kg bw/d**
% of AOEL	**10.62**	**%**	**% of AOEL**	**22.68**	**%**

A 1.5 Worker exposure (total systemic exposure)

Table A 13: Input parameters considered for the estimation of worker exposure

Intended use:	Seed loading / sowing		**Inhalation absorption:**	100	%
Concentration of as:	80	g/Lg	**AOEL-S:**	0.01	mg/kg bw/d
Dermal absorption:	0.7	% for loading/sowing	**Body weight:**	60	kg/person
			Working duration	8	h/d

Table A 14: Estimation of worker exposure towards beta-cyfluthrin during seed loading/sowing (based on Seed TROPEX data)

	Generic dermal exposure [1) 2)] (mg as/h)	**Generic inhalation exposure [1)] (mg as/h)**	**Working duration (h/d)**	**Actual dermal exposure (mg as/d)**	**Inhalation exposure (mg as/d)**
Loading/sowing	0.7331	0.0186	8	5.8647	0.1487
	Absorbed dose dermal (mg as/kg bw/d)	**Absorbed dose inhalation (mg as/kg bw/d)**	**Absorbed dose total (mg as/kg bw/d)**	**% AOEL-S**	
Loading/sowing	**0.000684**	**0.002478**	**0.003162**	**31.62**	

[1)] values represent geometric mean of measured data

[2)] workers wore gloves (except for bagging) and coverall

A 1.6 Worker exposure (inhalation exposure only)

Table A 15: Input parameters considered for the estimation of worker exposure

Intended use:	Seed loading / sowing		**Inhalation absorption:**	100	%
Concentration of as:	80	g/Lg	**AOEL-I:**	0.000243	mg/kg bw/d
Dermal absorption:			**Body weight:**	60	kg/person
			Working duration	8	h/d

Table A 16: Estimation of worker exposure towards beta-cyfluthrin during seed loading/sowing (based on Seed TROPEX data)

	Generic dermal exposure [1) 2)] (mg as/h)	**Generic inhalation exposure [1)] (mg as/h)**	**Working duration (h/d)**	**Actual dermal exposure (mg as/d)**	**Inhalation exposure (mg as/d)**
Loading/sowing		0.0186	8		0.1487
	Absorbed dose inhalation (mg as/kg bw/d)	**% AOEL-S**	**Absorbed dose total (RPE) (mg as/kg bw/d)**	**% AOEL-S (RPE)**	
Loading/sowing	**0.002478**	**1019.57**	**0.000198**	**81.58**	

[1)] values represent geometric mean of measured data

[2)] workers wore gloves (except for bagging) and coverall