Renewal Assessment Report

beta-cyfluthrin

Volume 3 – B.7 Residue data

07 March 2017

Rapporteur Member State: Germany

Co-Rapporteur Member State: Hungary

Version history

When	What
18.01.2017	Changes following comments of co-RMS.

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B.7 Residue data

Cyfluthrin, an isomeric mixture of four diastereomers, was evaluated in the framework of Council Directive 91/414/EEC with Germany designated as Rapporteur Member State (RMS). It was included in its Annex I by Directive 31/2003/EC. In accordance with Commission Implementing Regulation (EU) No 540/2011, cyfluthrin was approved under Regulation (EC) No 1107/2009, repealing Council Directive 91/414/EEC.
Cyfluthrin belongs to the pyrethroid group and acts as an insecticidal contact and stomach poison with pronounced neurotoxic effects.

Identity of beta-cyfluthrin

The pyrethroid beta-cyfluthrin is identical to cyfluthrin in chemical structure containing three stereochemical centres resulting in eight possible isomers: Four diastereomeric pairs (I-IV), each pair consisting of two enantiomers.
The active substance beta-cyfluthrin is a specific mixture of these four diastereomeric pairs of enantiomers and differs in this respect to the active substance cyfluthrin. The isomeric mixture of beta-cyfluthrin has a higher insecticidal activity due to enrichment of cis- and trans-diastereomers II and IV.
The chemical structure of cyfluthrin and beta-cyfluthrin is:

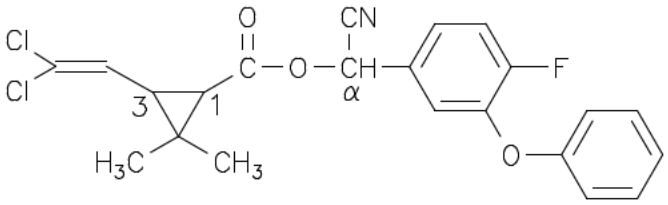


Table B.7-1: Isomeric mixture of cyfluthrin and beta-cyfluthrin

Diastereomers			Ratio of isomers	
			Cyfluthrin (%)*	beta-Cyfluthrin (%)
I	1R - 3R - αR + 1S - 3S - αS = 1:1	Cis	23-27	≤2
II	1R - 3R - αS + 1S - 3S - αR = 1:1	Cis	17-21	30-40
III	1R - 3S - αR + 1S - 3R - αS = 1:1	Trans	32-36	≤3
IV	1R - 3S - αS + 1S - 3R - αR = 1:1	Trans	21-25	57-67

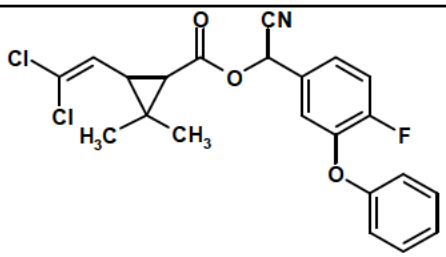
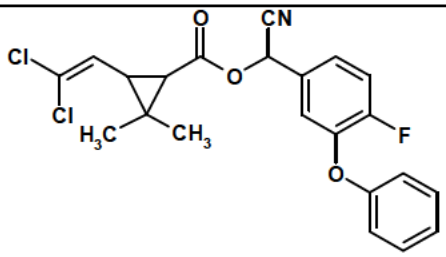
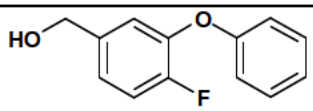
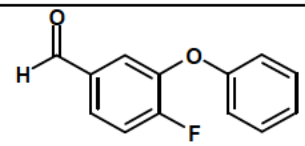
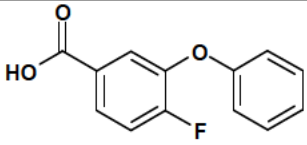
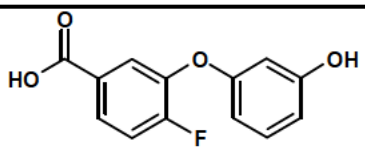
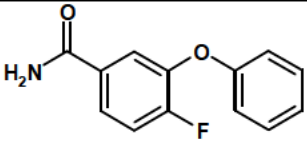
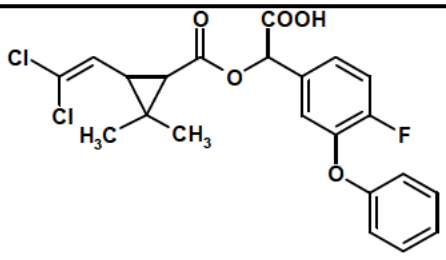
Studies of cyfluthrin and beta-cyfluthrin can be both interchangeably used to support the authorisation of either active substance.
As regards toxicity, it can be shown that both active substances share the same toxicological profile, with beta-cyfluthrin exhibiting an approximately 2-5 times higher acute toxicity than cyfluthrin and comparable values in subacute and subchronic endpoints. The full toxicological case is presented in Vol. 3, B.6.
Regarding residues, it can be shown in field trials that isomerisation starts immediately upon application of beta-cyfluthrin resulting in a change of the isomeric composition towards equilibrium. The interconversion of isomers proceeds over a mean calculated period of 74 days (±32 d) to achieve full equilibrium of isomeric pairs (average ratio of diastereomers I+III: II+IV). The full residue assessment of isomeric changes observed in residue trials is presented in B.7.2.1.9.

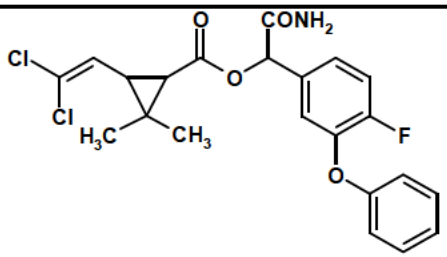
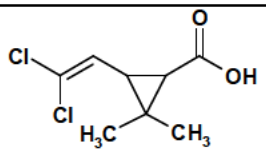
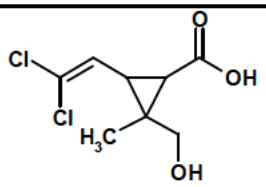
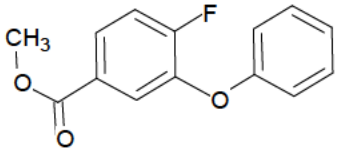
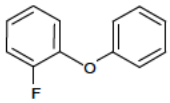
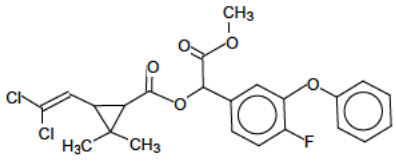
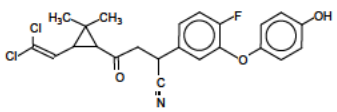
In an animal study (hen), no significant changes of isomer ratios were recorded from administered equilibrium towards preference of II+IV (beta-cyfluthrin type) or I+III (see **Figure B.7.2-3**).
It is therefore concluded that studies performed with cyfluthrin can be used to supplement the beta-cyfluthrin data base for all types of residue studies.
An initial evaluation and EU peer-review of metabolism and field residue data was performed in the framework of assessment under Directive 91/414/EEC without the contribution of EFSA (Monograph, 1996, ASB2010-10436; Addendum 1, 2002: ASB2014-9599), and in the framework of MRL assessments under Regulation (EC) 396/2005 (EFSA 2010, ASB2013-13744). Analysis of available plant and animal metabolism studies concluded on full acceptability of metabolism studies to elucidate the metabolic pathway of cyfluthrin (even for seed treatment uses without suitable data) and on a general residue definition for monitoring and risk assessment.
The data already evaluated in the process of Annex 1 listing under Directive 91/414/EEC and for MRL setting under Reg. (EU) 396/2005 are summarised and re-evaluated in this assessment report according to current standards and data requirements of COM Reg. (EU) 283/2013.
New residue and metabolism data are presented to cover the following assessment points:

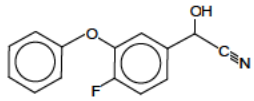
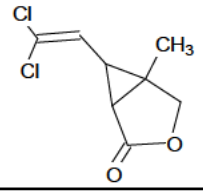
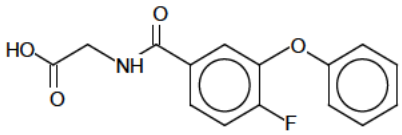
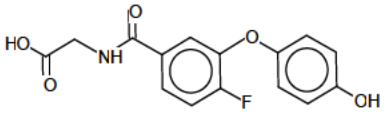
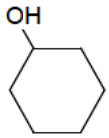
- Metabolism in sugar beets after seed treatment (B.7.2.1.8; ASB2014-7887; ASB2014-7886)
- Metabolism in goat (B.7.2.3; ASB2014-7899)
- Metabolism in rainbow trout (B.7.2.5; ASB2014-7897)
- Crop residue data in sugar beet after seed treatment (B.7.3.1; ASB2014-7883; ASB2012-4627)
- tomato after foliar treatment (B.7.3.2; ASB2014-7711)
- potato after foliar treatment (B.7.3.3; RIP2003-272, ASB2014-6706, ASB2014-7858, ASB2014-6718)
- wheat after foliar treatment (B.7.3.4; RIP2003-275, ASB2014-6714)
- Simulated hydrolysis (B.7.5.1; ASB2014-6710)
- Processing in tomatoes (B.7.5.3; ASB2014-7712)
- Field rotational crop (B.7.6.2; ASB2014-7884)

A list of metabolites and structures is provided in the table below.

Table B.7-2: Substances and metabolites (structures, codes, synonyms)

Substance name and code number	Chemical name [CAS Number]	Compound occurs in	Structure
Beta-cyfluthrin FCR 4545 30 – 40 % Isomer II (AE 1421342) 57 – 67 % Isomer IV (AE 1421344)	3-(2,2-dichloro-vinyl)-2,2-dimethyl-cyclopropane-carboxylic acid cyano-(4-fluoro-3-phenoxy-phenyl)-methyl ester [CAS 68359-37-5] (unstated stereochemistry)	Crop (sugar beet) Livestock (goat) Rat Fish Soil Water Sediment	
Cyfluthrin FCR 1272 23 – 27 % Isomer I (AE 1421341) 17 – 21 % Isomer II (AE 1421342) 32 – 36 % Isomer III (AE 1421343) 21 – 25 % Isomer IV (AE 1421344)	(R,S)-alfa-cyano-4-fluoro-3-phenoxy-benzyl (1RS,3RS; 1RS,3SR)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylate [CAS 68359-37-5] (unstated stereochemistry)	Crop (cotton, wheat, apple, tomato, potatoes, soybeans) Livestock (cow, hen) Rat Soil Water Sediment	
FPB alcohol FCR 1261	4-Fluoro-3-phenoxybenzyl alcohol [CAS 68359-53-5]	Crop Livestock Rat	
FPB aldehyde FCR 1260	4-Fluoro-3-phenoxybenzaldehyde [CAS 68359-57-9]	Crop Livestock Fish Rat Sediment	
FPB acid COE 5(3)38/78 FCR 2899	4-Fluoro-3-phenoxybenzoic acid [CAS 77279-89-1]	Crop Livestock Fish Rat Soil Water Sediment	
4-OH-FPB acid FCR 3145	3(4'-Hydroxyphenoxy)-4-fluorobenzoic acid [CAS not available]	Crop Livestock Fish Rat	
FPB amide FCR 2947	4-Fluoro-3-phenoxybenzoic acid amide [CAS 77279-89-1]	Crop Rat	
COOH-cyfluthrin Acid-cyfluthrin FCR 2728	+,-(R,S)-alfa-Carboxy-[3-phenoxy-4-fluoro]benzyl-1-(R,S)-trans-3-(2',2'-dichloroethen-1'-yl)-2,2-dimethylcyclo-propanecarboxylic acid ester [CAS not available]	Crop Livestock Fish Rat	

Substance name and code number	Chemical name [CAS Number]	Compound occurs in	Structure
$CONH_2$-cyfluthrin FCR 2978	+,-(R,S)-alfa-Carboxamido-[3-phenoxy-4-fluoro]benzyl-1-(R,S)-trans-3-(2,2-dichloroethen-1-yl)-2,2-dimethyl-cyclopropane-carboxylic acid ester [CAS 92731-61-8]	Crop (cell culture) Livestock Rat	
DCVA Permethric acid	3-(2',2'-Dichloroethen-1'-yl)-2,2-dimethyl-cyclopropane-carboxylic acid [CAS 55701-03-6]	Crop Livestock Fish Mouse Soil Water Sediment	
DCVA-OH FCR 4088	cis-3-(2,2-dichlorovinyl)-trans-2-hydroxymethyl-cis-2-methylcyclopropane-1-carboxylic acid	Livestock	
COE 263/78 Me-FPB acid	Me-FBP acid	Wheat Soybean Plant cell suspensions	
FCR 3030 FPB	1-fluoro-2-phenoxybenzene	Potato Soybean	
FCR 2956 Me-cyfluthrin	α-methoxycarbonyl-α-[4-fluoro-3-phenoxy phenyl]-methyl-3-[2,2-dichlorovinyl]-2,2-dimethylcyclo-propane-carboxylate (Me-cyfluthrin)	Artefact of acid hydrolysis in wheat	
FCR 4150	*trans*-3-(2,2-dichlorovinyl)-*cis*-2-hydroxymethyl-*trans*-2-methylcyclopro-pane-1-carboxylic acid lactone	Hen	

Substance name and code number	Chemical name [CAS Number]	Compound occurs in	Structure
FCR 1271 α-hydroxy FPB ACN (common metabolite to flumethrin)	4-fluoro-α-hydroxy-3-phenoxybenzene acetonitrile	Hen Goat [postulated intermediate in plants]	
FCR 4093		Hen	
FCR 3343 Hippuric acid		Goat	
OH-FCR 3343		Goat	
Sulphate and gluc. conjugate of phenol	Phenol	Goat	
FCR 4896	(3-(4´-hydroxyphenoxy)-4-fluorobenzylalcohol)	Hen	
FCR 3137	(3-(4´-hydroxyphenoxy)-4-fluorobenzaldehyde)	Hen	
FCR 4209	3-hydroxy-4-fluorobenzoic acid	Hen	

Preliminary remark on Good Laboratory Practice (GLP) requirements

In COM Reg. (EU) No. 283/2013, setting out the data requirements for active substances, the following considerations are made with regard to the GLP status of submitted studies (Annex, Introduction: Information to be submitted, its generation and its presentation):

"3. Good laboratory practice (GLP):

3.1 Tests and analyses shall be conducted in accordance with the principles laid down in Directive 2004/10/EC of the European Parliament and of the Council where testing is done to obtain data on the properties or safety with respect to human or animal health or the environment.

3.2. By way of derogation from point 3.1:

3.2.1. …
3.2.2. …
3.2.3. Studies conducted before the application of this Regulation, although not fully compliant with GLP requirements or with current test methods, may be integrated into the assessment, when accepted by the competent authorities as scientifically valid, thereby removing the need for repeating animal tests, especially for carcinogenicity and reprotoxicity studies. This derogation applies to studies on all vertebrate species."

It is the interpretation of the RMS that for all studies relevant for the assessment of active substances according to Reg. (EU) No 283/2013 the GLP requirements at the time of the first submission of a study apply. The lack of GLP status therefore does not necessarily mean that a study is not acceptable. However, missing GLP certificate and a lacking or undocumented quality system of study management controls is considered as a weakness of the study performance.
This interpretation should be confirmed by EFSA and COM.

The scientific assessment of every submitted study is indicated in the conclusion of the respective study evaluation.

B.7.1 Storage stability of residues

The existing and proposed residue definition for dietary risk assessment and monitoring for plants and livestock animals is cyfluthrin (sum of isomers; see Vol. 1, 2.7.3). All storage stability studies were performed with cyfluthrin covering adequately the residue spectra of beta-cyfluthrin.
These studies were originally submitted for Annex I inclusion and are already described in the Monograph of beta cyfluthrin (1996, ASB2010-10436). They are summarised and re-evaluated according to current standards below.

Table B.7.1-1: Summary of food related storage stability data for cyfluthrin[a]

Commodity category	Test commodity	Stability (months)	Study
Plant matrices			
High water content	Tomato Apple (peel) Head lettuce Corn, wheat (green) Apple, melon, tomato, cucumber, sugar cane raw, molasse	not acc. not acc. 26 26 38	Delk 1988 (RIP9401051) Minor and Freeseman 1989 (RIP9401053) Minor and Freeseman 1992 (RIP9401054, ASB2009-1208) Lenz and Lemke 1996 (ASB2009-1323) [b]

Commodity category	Test commodity	Stability (months)	Study
High oil content	Cotton seed Cotton seed Soybean Soybean Corn oil	not acc. not acc. not acc. not acc. not acc.	Grace 1989 (RIP9401052) Minor and Freeseman 1989 (RIP9401053) Grace 1989 (RIP9401052) Minor and Freeseman 1989 (RIP9401053) Lenz and Lemke 1996 (ASB2009-1323) [b]
High protein content	-	-	-
High starch content	Potato Potato leaves Corn, potato, wheat [c]	not acc. not acc. 38	Delk 1988 (RIP9401051) Minor and Freeseman 1989 (RIP9401053) Lenz and Lemke 1996 (ASB2009-1323) [b]
High acid content	Orange [c]	not acc.	Lenz and Lemke 1996 (ASB2009-1323) [b]
Miscellaneous	Hops Peanut shells	not acc. 38	Grace 1989 (RIP9401052) Lenz and Lemke 1996 (ASB2009-1323) [b]
Animal matrices			
Ruminant	Liver (fortified)	12 1	Lemke 1987 (RIP9401049) Shaw 1983 (ASB2009-1452)
	Liver (incurred)	3 [d]	Shaw 1983 (ASB2009-1452)
	Kidney (incurred)	1 [e]	Shaw 1983 (ASB2009-1452)
	Muscle (incurred)	5	Shaw 1983 (ASB2009-1452)
	Fat (incurred)	5	Shaw 1983 (ASB2009-1452)
	Milk (incurred)	11 39	Shaw 1983 (ASB2009-1452) Minor and Freeseman 1993 (RIP9401069)

not acc.: non-acceptable study
[a] covering storage stability of beta-cyfluthrin
[b] comprising reports RIP9401055, RIP9401056 and ASB2009-1322
[c] raw and processed
[d] significant instability (<70 % recovery) for next sampling point (7 months)
[e] significant instability (<20 % recovery) for later samplings (6 months)

B.7.1.1 Storage stability in plant matrices

Data point:	KCA 6.1 /12
Report:	Delk, J. L. (1988): Baythroid - Storage stability of residues in various frozen crops Mobay Chemical Corporation, Stilwell, KS, USA Bayer CropScience, Report No.: MR98334, M-049821-01-1 RIP9401051
Guideline(s):	US EPA Ref: 171-4(e) Storage Stability.
Deviations:	None
GLP:	No
Acceptability:	Not acceptable

Potato and tomato samples were spiked with cyfluthrin and its metabolites (DCVA, FPB acid, FPB alcohol, FPB aldehyde) at levels of 1 mg/kg and analysed for residues after approximately 35 months of frozen storage (-7 °C). Corn dry forage and soybean green forage samples spiked with cyfluthrin metabolites were analysed through approximately 8 months of frozen storage.

The following analytical methods were applied:
88937 (FPB acid, alcohol and aldehyde; FPB alcohol and aldehyde derivatised to the acid)
88702 (DCVA)
85823 (parent)

Poor storage recovery of cyfluthrin and its metabolites was partly observed, indicating instability of cyfluthrin in potatoes and tomatoes stored for longer than 2 months and 8 months under tested conditions.

Method 85823 is considered as valid with regard to the investigations performed in this study (see Vol.3, B.5.1.2). Reported concurrent recoveries are within acceptable limits and ranged from 70 % to 107 %.

The study is not acceptable due to the following reasons:

- Non GLP
- Storage at insufficient temperature (-7 °C)
- Storage recoveries cannot be verified (chromatograms not readable, cannot be attributed to reported results)
- Concurrent recoveries cannot be verified (no sample description, chromatograms partly not readable, no recovery calculation provided; number of procedural recoveries too low compared to treated sample analyses)
- Analytical methods 88937 and 88702 not validated (see Vol. B.5.1.2)
- Insufficient reporting (see requirements for reporting expressed in OECD 506)

Table B.7.1-2: Concurrent recovery of cyfluthrin and its metabolites in various crop matrices

Sample	Spiking level (mg/kg)	Analyte	Recovery (%)
Potatoes	1.0	Cyfluthrin	107
			100
			88
			85
	1.0	DCVA	86
			71
	1.0	FPB aldehyde	94
			72
Tomato	1.0	Cyfluthrin	82
			89
			98
			82
	1.0	DCVA	83
			88
	1.0	FPB aldehyde	74
			84
Dry corn forage	1.0	DCVA	70
			94
	1.0	FPB aldehyde	85
			71
			82
Soybean green forage	1.0	DCVA	71
			70
		FPB aldehyde	77
			81
			94

Table B.7.1-3: Summary of average percent recovery of cyfluthrin and its metabolites in various crop matrices

Sample	Analyte	Interval (months)	% recovery
Potatoes	Cyfluthrin	2	91 1
		4	42 1
		8	55 1
		37	33 2
	DCVA	2	90 1
		4	75 1
		8	92 2
		38	88 2
	FPB acid	8	54 1
		38	100 2
	FPB alcohol	2	83 1
		8	97 1
		38	88 2
	FPB aldehyde	2	56 1
		8	69 1
		38	81 2
Tomatoes	Cyfluthrin	2	85 1
		4	96 1
		8	82 1
		37	56 2
	DCVA	2	77 1
		4	67 1
		8	82 0
		38	42 2
	FPB acid	2	42 1
		8	72 1
		38	85 2
	FPB alcohol	2	92 1
		8	90 1
		38	59 2
	FPB aldehyde	2	56 1
		8	34 1
		38	21 2

Sample	Analyte	Interval (months)	% recovery	
Corn, dry forage	DCVA	2	78	1
		5	82	1
		8	63	1
	FPB acid	2	74	1
		4	66	1
		8	45	1
	FPB alcohol	2	99	1
		4	35	1
		8	47	1
	FPB aldehyde	2	100	1
		4	35	1
		8	89	1
Soybean, green forage	DCVA	2	73	1
		5	80	1
		8	82	1
	FPB acid	2	100	1
		4	41	1
		8	66	1
	FPB alcohol	2	63	1
		4	50	1
		8	37	1
	FPB aldehyde	2	100	1
		4	97	1
		8	68	1

0 single analysis
1 average of duplicate analysis
2 average of triplicate analysis

Data point: KCA 6.1 /11

Report: Grace, T.J. (1989): Freezer storage stability of cyfluthrin in hops
Mobay Chemical Corporation, Stilwell, KS, USA
Bayer CropScience,
Report No.: 99203, Edition Number: M-049817-01-1
RIP9401052

Guideline(s): US EPA Ref: 171-4(e) Storage Stability.

Deviations: No

GLP: No

Acceptability: Not acceptable

Field treated samples of kiln dried hops which were analysed for cyfluthrin. Subsamples were held in storage at room temperature for 6 months and at <-20 °C for an additional period of 22 months, and re-analysed.
The following analytical method was applied: 85823 (modified).

The mean recovery of cyfluthrin in 5 samples of kiln dried hops was 96 % (n=5; RSD 25 %). Concurrent recoveries were 99 % (n=4; RSD 6 %) for initial analysis of field samples and 103 % (n=4; RSD 3 %) for stored samples. Method 85823 is considered as valid with regard to the investigations performed in this study (see Vol.3, B.5.1.2).

Additional results were reported for so called control samples with residues at beginning (end) of the study of 1.48 mg/kg (2.59 mg/kg) and 1.24 mg/kg (<1.0 mg/kg). The role and treatment of these samples is not reported.
Results of all samples indicate, that at the same time, degradation and concentration processes due to weight loss (storage at room temperature for 6 months) have occurred. Both processes have opposing effects on the residue level.

Supplemental information is provided on stability of cyfluthrin residues in cotton and soybean fractions for periods of frozen storage (-23 °C) ranging from 105-234 days, apparently originating from metabolism reports (RIP9400822 and RIP9400835). However, these data are not clearly referenced, not supported by sufficient experimental information and raw data, and are therefore not summarized here.

The study is not acceptable due to the following reasons:
- Non GLP
- Storage conditions (subsequently room temperature and frozen state) do not allow for conclusions on frozen storage stability
- Residue data for initial analysis cannot be verified (only chromatograms of the standards are reported)
- Recovery analyses were not performed together with treated/stored sample analyses
- Supplemental data on cotton and soybean are not supported by detailled information.
- Role of control samples is unclear (difference to recovery samples regarding source, treatment and storage conditions)
- Insufficient reporting (see requirements for reporting expressed in OECD 506)

Table B.7.1-4: Summary of average percent recovery of cyfluthrin in hops, soybean and cotton

Commodity	Matrix	Interval (months)	Initial residue	Residue after storage	% uncorrected recovery	Mean (RSD)
Hops	Kiln dried	28	2.05 8.34 20.6 7.15 28.5	2.47 8.11 24.5 4.96 21.2	120 97 119 69 74	96 % (25 %)

Data point: KCA 6.1 /01

Report: Minor, R. G.; Freeseman, P. L. (1989): Freezer storage stability of cyfluthrin in apples, cotton, potatoes and soybeans
Mobay Chemical Corporation, Stilwell, KS, USA, Bayer CropScience,
Report No.: 99631,
Edition Number: M-049792-01-1
RIP9401053

Guideline(s): US EPA Ref: 171-4(e) Storage Stability.

Deviations: No

GLP: No

Acceptability: Not acceptable

One part of the study refers to samples originating from metabolism studies: RIP9400827 for analyses on soybean, RIP9400836 for analyses on potato and RIP9400838 for analyses on apple.

Tissues from [^{14}C]cyfluthrin plant metabolism studies are presented (apple peels, potato leaves, and soybean leaves). Samples were stored under freezer conditions (-18 to -23 °C) for up to 7 years and repeatedly extracted with acetone/chloroform (2:1) or methanol/water (4:1). After partitioning, cyfluthrin was determined in the extract by thin-layer chromatography (TLC) and compared to the original analyses.
No decomposition of cyfluthrin residue was observed in potato leaf samples (92 % of TRR as cyfluthrin on day 0; 94 % TRR on day 2436). In soybean leaf samples, residue declined from 53 % TRR (day 0) to 43 % TRR (day 164) to 38 % TRR (day 2512; equivalent to 72 % recovery).

Additionally, stability experiments were performed, where soybean dry vines, beans and cotton seeds were fortified at 1 mg/kg [^{14}C]cyfluthrin and stored for 63 months (1888-1895 days). Sample homogenates were repeatedly extracted by acetonitrile and partitioned into hexane. Final extracts were radioassayed and subjected to TLC.

Table B.7.1-5: Storage stability of ^{14}C-cyfluthrin under frozen conditions

Commodity	Matrix	Interval (days)	Recovery (mg/kg)	Mean recovery (mg/kg)	Recovery (%)
Soybean	Beans	0	1.06, 1.03, 1.01	1.03	-
		96	0.98, 1.03	1.01	98
		187	1.02, 1.06	1.04	101
		1895	0.92, 0.97	0.94	91
Soybean	Dry vines	0	1.10, 1.06, 1.09	1.08	-
		91	0.99, 1.11	1.05	97
		182	0.97, 0.94	0.96	89
		1890	1.00, 0.93	0.96	89
Cotton	Seeds	0	1.11, 1.08, 1.00	1.06	-
		89	1.04, 1.07	1.06	100
		180	1.06, 1.10	1.08	102
		1888	1.11, 1.24	1.18	111

Presented data indicate stability of cyfluthrin residues over the investigated time span in all matrices investigated (recovery >70 % is reported).

- The study is not acceptable due to the following reasons:
- The study is not compliant to GLP.
- The analytical method is not sufficiently validated to support stability of cyfluthrin.

Data point: KCA 6.1 /02

Report: Minor, R. G.; Freeseman, P. L. (1989): Freezer storage stability of cyfluthrin in corn green forage, head lettuce, and wheat green forage
Bayer Corporation, Kansas City, MO, USA
Bayer CropScience,
Report No.: 102608; 102608-1, Edition Number: M-022101-02-1
RIP9401054 (amended by KCA 6.1 /10; ASB2009-1208)

Guideline(s): US EPA Ref: 171-4(e) Storage Stability.

Deviations: No

GLP: Yes

Acceptability: Partly acceptable

Materials and methods

Homogenised samples of corn green forage, head lettuce and wheat green forage were fortified with [phenoxy-UL-^{14}C]cyfluthrin (radiochemical purity: 96 %) at a level of 4 mg/kg and stored under freezer conditions at -24 °C for 783 days (26 months; RIP9401054). For duplicate samples of head lettuce, an additional storage interval was tested (2079 days; 69 months). No significant temperature alterations were observed throughout the study period.

Triplicate (day 0) or duplicate samples (intervals up to 783 days) were extracted by acetone/chloroform mixture (2:1), evaporated to dryness and dissolved in ethyl acetate. A change of solvent was done for the 2079 day sample, where residues were extracted with methanol to enhance extraction efficiency. Cyfluthrin was determined in the extract by radio-TLC (normal and reverse-phase, co-chromatography with non-radiolabelled standard).). No separate procedural recoveries were run.

Results

Linearity of the response of the radio TLC analyzer for ^{14}C-cyfluthrin was demonstrated over the range of radioactivity applied (3400 to 170000 dpm; correlation coefficient 0.996).
Recovery of radioactivity from all samples ranged from 93 to 108 % of theoretically applied ^{14}C. The radioactivity was found to co-chromatograph almost entirely with the standard of cyfluthrin, with only traces being found at the TLC origin.

Storage recoveries were all within 87 and 103 % of initial fortifications.

Conclusion

Sufficient evidence is provided for storage stability of cyfluthrin in matrices of high water content for a period of at least 26 months (783 days). The impact of the change of extraction method on recovery of cyfluthrin cannot be assessed. Therefore, no conclusion can be drawn on stability over periods exceeding 26 months.

Table B.7.1-6: Storage stability data for [phenoxy-UL-^{14}C] cyfluthrin in various crops

Sample	Storage interval (month) [3]					
	0 [2]	1	6	12	26	69
Head lettuce						
Treated (mg/kg)	4.12 4.26 3.68	3.92 3.71	3.93 3.97	3.50 3.56	3.88 3.90	3.93 3.73
Mean recovery (mg/kg)	4.02	3.82	3.95	3.53	3.89	3.83
Mean recovery (%) [1]	101	96	99	88	97	96
Mean recovery (%) [2]	100	95	98	88	97	95
Corn (green forage)						
Treated (mg/kg)	4.05 n.a. 3.92	4.02 4.13	4.02 4.13	4.02 4.11	3.95 3.92	n.a.

Mean recovery (mg/kg)	3.98	4.08	4.08	4.06	3.94	
Mean recovery (%) [1]	100	102	102	102	99	
Mean recovery (%)	100	103	103	102	99	
Wheat (green forage)						
Treated (mg/kg)	4.37 4.22 4.22	4.38 3.99	4.23 4.28	3.87 3.90	3.42 3.99	n.a.
Mean recovery (mg/kg)	4.27	4.18	4.26	3.88	3.70	
Mean recovery (%) [1]	107	105	107	97	93	
Mean recovery (%)	100	98	100	91	87	

[1] nominal
[2] standardised to 100 % at day 0
[3] Storage intervals expressed as nominal months; actual days varied between matrices

Data point: KCA 6.1 /03

Report: Wiedmann, J. L.; Amato, S. L.; Koch, D. A. (1992): Storage stability of cyfluthrin in crops and processing fractions
Miles Inc., Agriculture Division, Kansas City, MO, USA
Bayer CropScience, Report No.: 103821, M-136649-01-1
RIP9401055

Guideline(s): US EPA Ref: 171-4(e) Storage Stability. Study conducted according to later EC data requirements (OECD Test Guideline 506) in all relevant points.

Deviations: None

GLP: Yes

Acceptability: Acceptable (for all matrices except those of high acid and fat content)

Data presented in this report cover the interval up to 7 months storage. Assessment is provided below for the full data set under ASB2009-1323 (KCA 6.1 /09).

Data point: KCA 6.1 /07

Report: Wiedmann, J. L.; Amato, S. L.; Koch, D. A. (1994): Storage stability of cyfluthrin in crops and processing fractions
Miles Inc., Agriculture Division, Kansas City, MO, USA
Bayer CropScience, Report No.: 103821-1, M-051312-01-1
RIP9401056

Guideline(s): US EPA Ref: 171-4(e) Storage Stability.
Study conducted according to EC data requirements (OECD Test Guideline 506) in all relevant points.

Deviations: No

GLP: Yes

Acceptability: Acceptable (for all matrices except those of high acid and fat content)

Data presented in this addendum cover the period of 13-20 months of frozen storage. Assessment is provided below for the full data set under ASB2009-1323 (KCA 6.1 /09).

Data point:	KCA 6.1 /08
Report:	Wiedmann, J. L.; Amato, S. L.; Koch, D. A. (1994): Storage stability of cyfluthrin in crops and processed products Miles Inc., Agriculture Division, Kansas City, MO, USA Bayer CropScience, Report No.: 103821-2, M-051307-01-1 ASB2009-1322
Guideline(s):	US EPA Ref: 171-4(e) Storage Stability.
Deviations:	Not applicable
GLP:	Yes (by referencing to RIP9401055)
Acceptability:	Acceptable (for all matrices except those of high acid and fat content)

This study is an amendment of Wiedmann et al. (1992), RIP9401055 (correcting calculation error).

Data point:	KCA 6.1 /09
Report:	Lenz, C. A.; Lemke, V. J. (1996): Addendum 3 - Storage stability of cyfluthrin in crops and processed products data for 38-months Bayer CropScience AG, Report No.: MR103821-3, M-051281-01-1 ASB2009-1323 Report includes Trial Nos.: 103821 (6.1/03, RIP9401055), 103821-1 (6.1/07, RIP9401056), 103821-2 (6.1/08, ASB2009-1322)
Guideline(s):	US EPA Ref: 171-4(e) Storage Stability Study conducted according to EC data requirements (OECD Test Guideline 506) in all relevant points.
Deviations:	None
GLP:	Yes
Acceptability:	Acceptable (for all matrices except those of high acid and fat content)

Materials and methods

Storage stability of cyfluthrin residues in different crops (processed and unprocessed) was tested over a 38 months period. Homogenised samples of the matrix categories “water”, “starch”, “oil”, and “acid” were fortified at levels of 1 mg/kg cyfluthrin (100 mg/kg for processed fraction wheat dust) and stored in glass jars at -23 °C. Sporadic short-time temperature deviations in the range of hours were recorded during the study, with no impact on the frozen state and integrity of samples. Aliquots were analysed at day 0, and at nominal intervals of 1, 2, 3, 7, 13, 19-20, 24-25, and 38 months.

The following raw samples were tested: Apples, cantaloupe melon, corn, cucumbers, oranges, potatoes, sugar cane, tomatoes, wheat.
Processed samples were: Corn oil, corn starch, orange juice, orange dry pulp, peanut shells, potato granules, potato chips, potato dry peels, wet potato peels, wheat bran, wheat dust and wheat flour.

The following analytical method was applied: 85823. This method is considered as valid with regard to the investigations performed in this study, except for acidic matrices (orange; orange juice; see Vol.3, B.5.1.2).

Apples, oranges, orange dry pulp, peanut shells, potato tubers, sugarcane, wheat bran, wheat flour, and wheat grain were extracted using acetone:chloroform (2:1). Beginning with the 18-month samples, it was also used for peanut shells, potato tubers, sugarcane, wheat bran, and wheat grain. The extract was evaporated, the aqueous residue partitioned with acetone:chloroform (2:1), and the organic phase

evaporated to dryness.
Corn oil, corn starch, orange juice, and molasses were transferred directly to a separatory funnel with water, partitioned with (2:1) chloroform:acetone and the organic phase evaporated to dryness.
Corn, corn oil, oranges, dry orange pulp, and potato chips were partitioned between hexane and acetonitrile, with the acetonitrile portion evaporated to dryness. With the change of extraction solvent, this step was added for peanut shells, sugarcane, wheat bran, and wheat grain.
The organic phase from each of the above steps was redissolved for column cleanup using alumina or Florisil column chromatography prior to GC analysis on a gas chromatograph equipped with an electron capture detector.
Wheat dust was extracted by shaking with acetone for one hour, then filtered and run directly on the gas chromatograph.

Due to continued difficulty with the analysis of molasses and the resulting poor recoveries, it was determined at 32 months to try some further modifications to the procedure. As a result of the improved recoveries obtained with this procedure, it was decided to apply it to the analysis of all matrices for the 3 year interval. For the 36 month interval, most crop samples were therefore blended in methanol:water (4:1), filtered, the methanol evaporated, and the aqueous phase partitioned with acetone:chloroform (1:2).

Validation sets were run for all of the matrices used in the study to verify that the analytical procedure would give acceptable results and to determine that the control sample to be used had no serious background residue. Validation levels were 0.3 mg/kg and 1.0 mg/kg, and were either run as one of each or as a pair of each. Wheat dust was validated over the 2 to 400 mg/kg range for another study.
No quantitative differentiation was possible for split peaks of cyfluthrin (apparently diastereomeric pairs).

Validation data for all 22 Matrices ranged from 67 to 123 % recovery of cyfluthrin.
Concurrent recovery data were produced for at least one sample per storage period and sample type at a level of 1 mg/kg (100 mg/kg for wheat dust).

Results

The validity of analytical method is verified for dry matrices and those of high water content. A summary of the concurrent recoveries obtained for cyfluthrin is presented in Table B.7.1-7.

The results of the storage stability recoveries for different matrices are summarised in Table B.7.1-8.
Recoveries are not corrected for concurrent recoveries or for residues in the control sample. Results at the different samplings are presented in comparison to nominal and effective fortification levels at day zero, the latter being considered as relevant measure for stability. Samples (unprocessed and processed) are grouped into matrix categories according to OECD 506, if applicable.

After storage of 38 months at -23 °C, mean recovery values in crops belonging to the category of high water and high starch content were >70 % (Figure B.7.1-1 to Figure B.7.1-3). The high oil content matrix also gave recoveries >70 %, however, the analytical method is not sufficiently validated.
Crops belonging to the matrix group of high acid content were apparently stable over 25 month, while longer storage formally showed slight signs of instability (mean recovery 63 %). However, the analytical method is not sufficiently validated.
Peanut shells (recovery >70 %) are not covered by any OECD 506 matrix category.

Stability of residues in sample extracts are covered by analyses of freshly fortified samples for concurrent recovery determination, which were handled and stored in parallel. No signs of degradation in sample extracts are observed.

Residues in some control samples exceeded 0.01 mg/kg. This refers mostly to intermediate samples, with no impact on the final conclusions about storage stability. However, within the acid matrix group, systematic contamination of orange whole fruit and dry pulp samples was observed (14 out of 16

control samples >0.01 mg/kg cyfluthrin).
Additional consideration of residues in controls for recovery calculation (subtraction and recalculation) has no impact on the conclusions about stability or instability in any sample.

Conclusion

Investigations on storage stability were performed with homogenised, processed and unprocessed samples over a period of 38 months. Formally, stability of cyfluthrin residues was demonstrated over 38 months for commodities belonging to the matrix groups of high water, high starch and high oil content, as well as for peanut shells (no matrix group). Storage stability for samples belonging to the group of high acid content is apparently shown for a period of 25 months. However, the slope of recovery over time and scattering of acid matrix recoveries could be interpreted as plateau levelling at around 70 % beginning with 7 months of storage. Procedural recoveries or residues in control samples do not explain reduced storage recoveries.

The analytical method 85823 is not sufficiently validated for acidic and high fat matrices, thus stability data for these matrices are not considered acceptable for regulatory decisions.

A slight (regulatory insignificant) degradation within the acceptable level of 30 % is observed for all matrix groups. Moreover, a widespread scattering of data is also observed for all crop groups, where more than one commodity was tested for storage stability. In the main commodities (starch, acid, water), individual recoveries were below the acceptable level of 70 %, even after short study durations (e.g. matrix of high water content: 2 out of 5 samples after 2 months). It is therefore recommended to analyse field samples in future residue trials shortly after sampling.

Analytical methods employed for storage stability investigations are considered scientifically valid and regulatory acceptable except for acidic and high fat matrices, where conclusions are tentatively.
No quantitative differentiation between the individual isomers is possible.

The following major deficiency is noted:
Validation data of the analytical method is considered insufficient for acidic and high fat matrices.

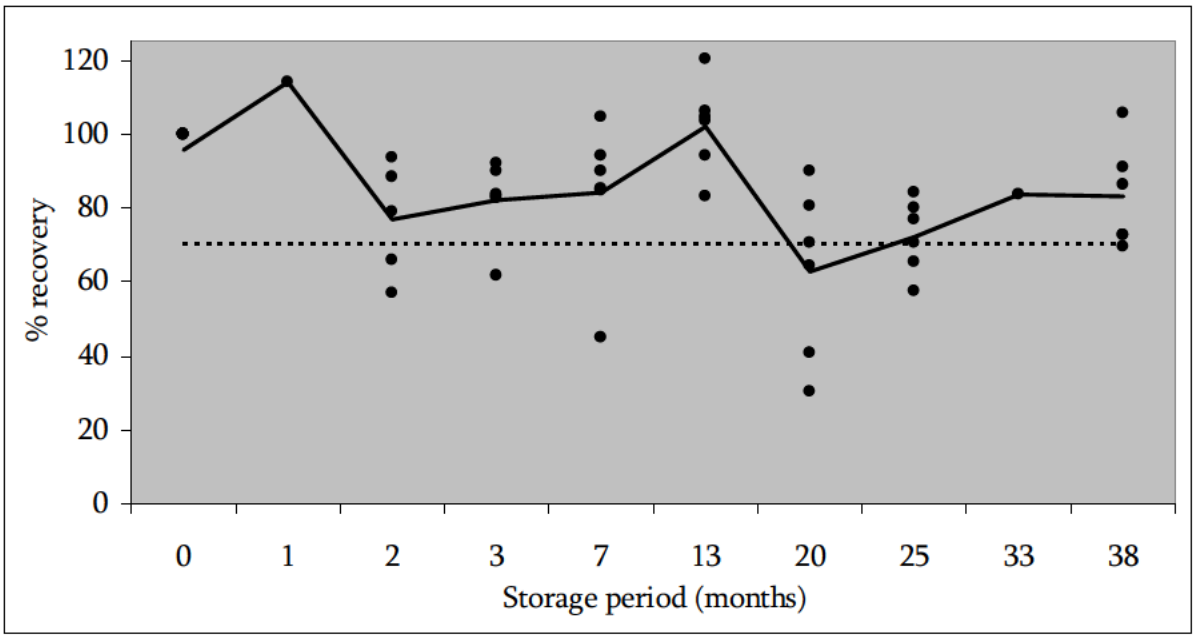


Figure B.7.1-1: Recovery of cyfluthrin after frozen storage in matrices of high water content (apple; melon; tomato; cucumber; sugar cane raw and molasse)

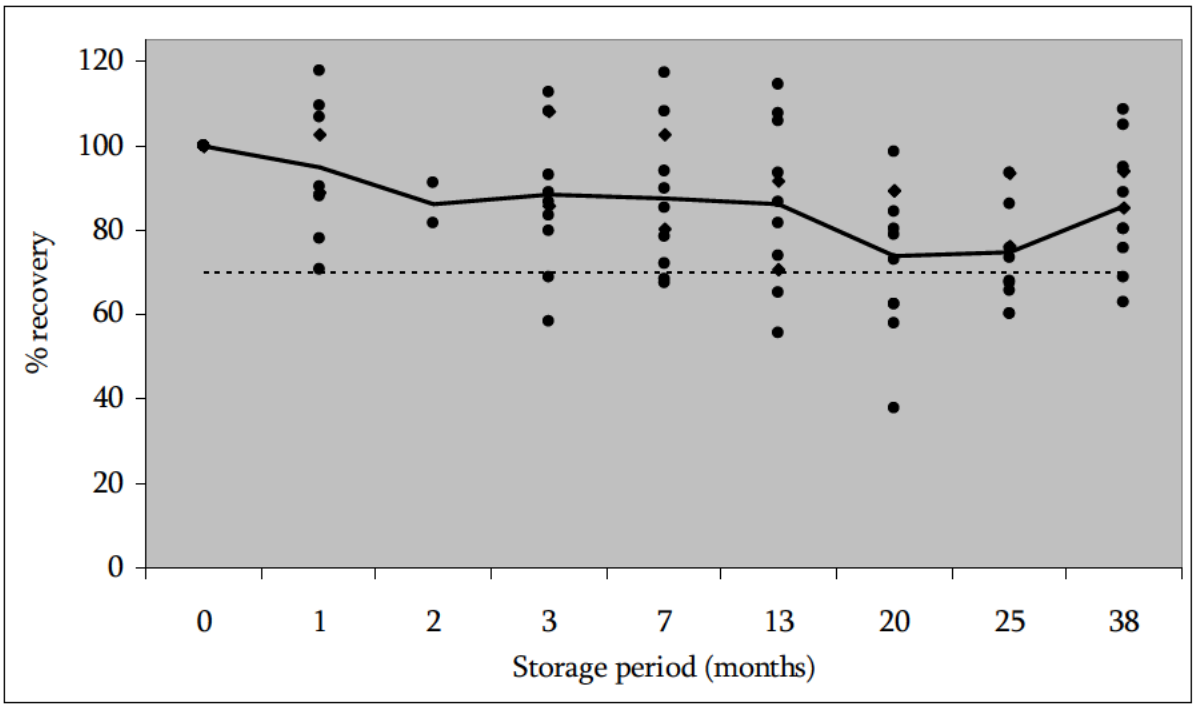


Figure B.7.1-2: **Recovery of cyfluthrin after frozen storage in matrices of high starch content (corn, potato, wheat: all raw and processed)**

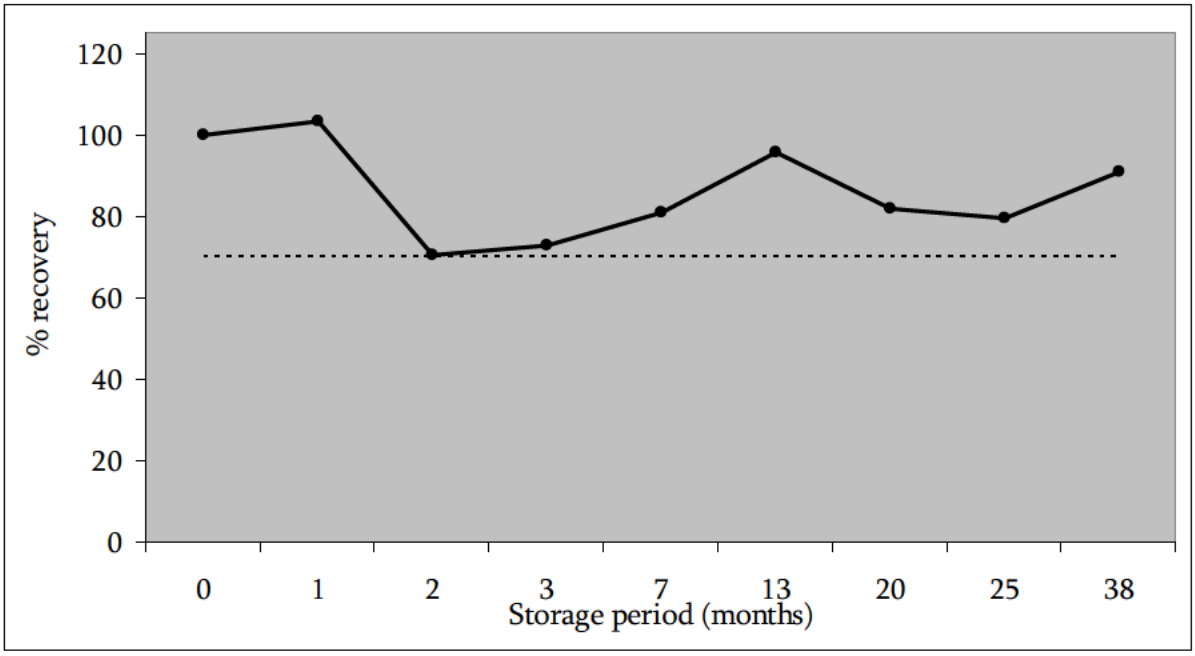


Figure B.7.1-3: **Recovery of cyfluthrin after frozen storage in corn oil (matrix of high oil content)**

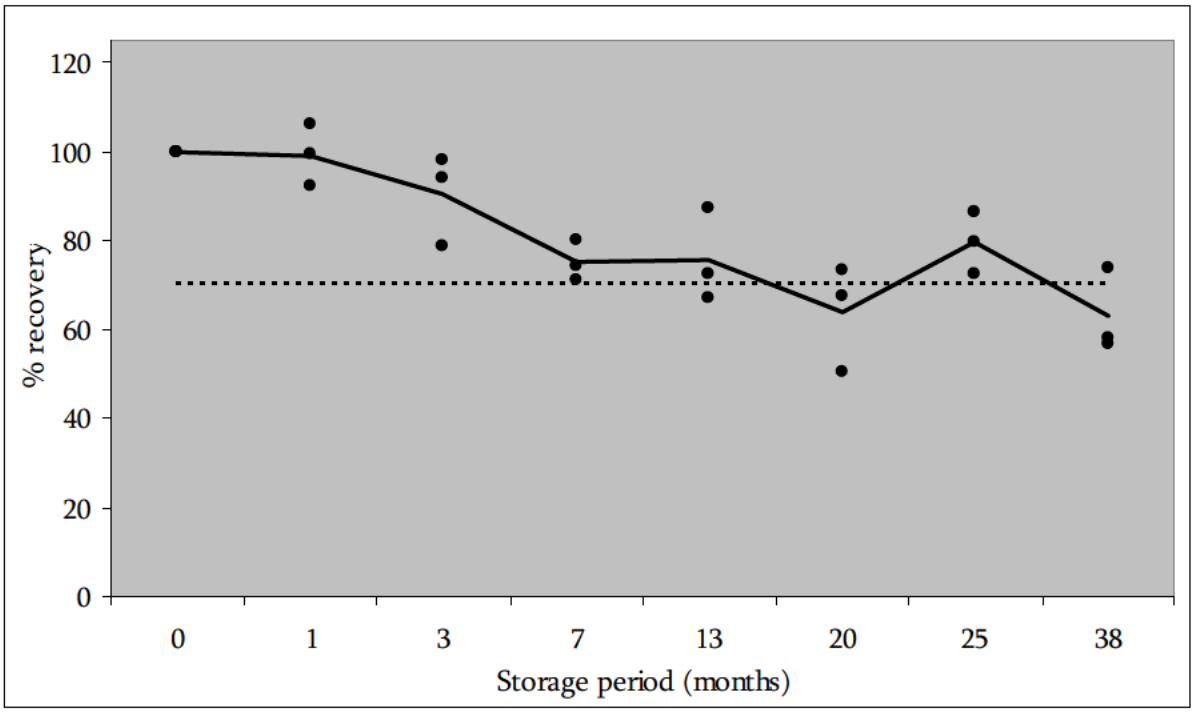


Figure B.7.1-4: Recovery of cyfluthrin after frozen storage in matrices of high acid content (orange, raw and processed)

Table B.7.1-7: Summary of concurrent recovery data of cyfluthrin from various crop matrices

Sample	Storage interval (month)[1]									
	0[2]	**1**	**2**	**3**	**7**	**13**	**20**	**25**	**33**	**38**
Apple	106	71	-	70	100	94	80	101	-	92
Cantaloupe	74	-	87	82	98	103	78	98	-	77
Corn grain	77	94	-	89	99	99	71	79	-	87
Corn oil	112	127	73	66	84	95	75	81	-	80
Corn Starch	119	91	-	82	103	91	86	95	-	87
Cucumber	72	-	88	95	84	103	72	71	-	76
Orange whole fruit	96	122	-	108	80	100	72	95	-	77
Orange juice	104	98	-	72	79	91	79	97	-	78
Orange dry pulp	101	114	-	91	87	91	102	100	-	80
Peanut shells	85	74	-	72	85	95	95	78	-	77
Potato tuber	100	75	-	93	83	81	86	95	-	85
Potato chip	71	86	-	100	89	80	80	73	-	87
Potato granules	71	96	-	66	88	91	83	87	-	94
Dry potato peel	89	-	71	73	82	91	67	83	-	75
Wet potato peel	97	-	70	78	73	73	74	86	-	67
Sugarcane	90	-	67	69	70	85	81	80	-	80
Sugarcane molasses	123	-	92	86	85	97	85	84	78[3]	90
Tomato whole fruit	108	-	72	106	95	103	92	94	-	80
Wheat grain	81	90	-	85	85	73	95	94[3]	-	83
Wheat bran	82	81	-	78	93	73	91	92	-	88
Wheat flour	121	93	-	86	92	95	77	87	-	80
Wheat dust	102	90	-	106	102	101	118	111	-	99

[1] Storage intervals expressed as nominal months; actual days varied between matrices.
[2] Validation samples done at zero time (average of samples amended with 1.0 mg/kg cyfluthrin for all matrices except wheat dust which were amended with 100 mg/kg cyfluthrin).
[3] Average of samples analysed from two intervals.

Table B.7.1-8: Results of storage stability experiments with cyfluthrin in crops (uncorrected values; assessment based on recoveries standardised to 100 % at day 0)

Sample		Storage interval (month)[a]									
		0	**1**	**2**	**3**	**7**	**13**	**20**	**25**	**33**	**38**
		% concurrent recovery									
Apple	Control (mg/kg)	0.003	0.326	-	0.002	0.002	0.008	0.001	0.005	-	0.000
(water matrix)	Treated (mg/kg)	0.926 0.989 0.778	- 1.05 1.00	- - -	- 0.71 0.79	- 0.90 0.98	- 0.93 0.95	- 0.34 0.39	- 0.71 0.73	- - -	- 0.84 0.79
	Mean recovery (mg/kg)	0.898	1.025	-	0.750	0.940	0.940	0.365	0.720	-	0.815
	Mean recovery (%) [1]	90	103	-	75	94	94	37	72	-	82
	Mean recovery (%) [2]	**100**	**114**	**-**	**84**	**105**	**105**	**41**	**80**	**-**	**91**
Cantaloupe	Control (mg/kg)	0.005	-	0.000	0.006	0.002	0.000	0.001	0.001	-	0.003
(water matrix)	Treated (mg/kg)	0.949 1.058 1.124	- - -	- 0.88 0.96	- 0.73 0.99	- 0.90 0.88	- 1.04 0.92	- 0.67 0.67	- 0.76 0.84	-	- 0.72 0.80
	Mean recovery (mg/kg)	1.044	-	0.920	0.860	0.890	0.980	0.670	0.800	-	0.760
	Mean recovery (%) [1]	104	-	92	86	89	98	67	80	-	76
	Mean recovery (%) [2]	**100**	**-**	**88**	**82**	**85**	**94**	**64**	**77**	-	**73**
Sugar cane	Control (mg/kg)	0.009	-	0.003	0.000	0.000	0.007	0.001	0.000	-	0.000
(water matrix)	Treated (mg/kg)	0.784 0.769 0.792	-	- 0.70 0.76	- 0.72 0.69	- 0.68 0.79	- 0.98 0.90	- 0.69 0.72	- 0.66 0.66	-	- 0.84 0.81
	Mean recovery (mg/kg)	0.782	-	0.730	0.705	0.735	0.940	0.705	0.660	-	0.825
	Mean recovery (%) [1]	78	-	73	71	74	94	71	66	-	83
	Mean recovery (%) [2]	**100**	**-**	**93**	**90**	**94**	**120**	**90**	**84**	**-**	**106**

[a] Nominal value (mean based on reported days; deviating from reported periods in months); storage period in days varies between matrices

Sample		Storage interval (month)[a]									
		0	**1**	**2**	**3**	**7**	**13**	**20**	**25**	**33**	**38**
		% concurrent recovery									
Sugar cane molasses (water matrix)	Control (mg/kg)	0.000	-	0.000	0.000	0.001	0.000	0.002	0.000	0.000	0.02
	Treated (mg/kg)	0.944 0.757 1.145	-	- 0.51 0.57	- 0.77 0.40	- 0.28 0.43	- 0.64 0.79	- 0.27 0.29	- 0.51 0.62	0.83 0.77 0.81 0.81	- 0.83 0.82
	Mean recovery (mg/kg)	0.951	-	0.540	0.585	0.430	0.790	0.290	0.620	0.797	0.820
	Mean recovery (%) [1]	95	-	54	59	43	78	29	62	80	82
	Mean recovery (%) [2]	**100**	**-**	**57**	**62**	**45**	**83**	**30**	**65**	**84**	**86**
Tomato whole fruit (water matrix)	Control (mg/kg)	0.000	-	0.000	0.000	0.000	0.000	0.000	0.002	-	0.000
	Treated (mg/kg)	1.023 0.994 1.043	-	- 0.67 0.67	- 0.86 1.02	- 0.97 0.87	- 0.95 1.16	- 0.83 0.81	- 0.50 0.67	-	- 0.68 0.80
	Mean recovery (mg/kg)	1.020	-	0.670	0.940	0.920	1.055	0.820	0.585	-	0.740
	Mean recovery (%) [1]	102	-	67	94	92	106	82	59	-	74
	Mean recovery (%) [2]	**100**	**-**	**66**	**92**	**90**	**103**	**80**	**57**	**-**	**73**
Cucumber (water matrix)	Control (mg/kg)	0.002	-	0.000	0.000	0.001	0.010	0.001	0.001	-	0.001
	Treated (mg/kg)	0.894 0.858 0.901	- - -	- 0.69 0.71	- 0.74 0.73	- 0.73 0.77	- 0.96 0.92	- 0.64 0.61	- 0.61 0.64	-	- 0.63 0.60
	Mean recovery (mg/kg)	0.884		0.700	0.735	0.750	0.940	0.625	0.625	-	0.615
	Mean recovery (%) [1]	88	-	70	74	75	94	63	63	-	62
	Mean recovery (%) [2]	**100**		**79**	**83**	**85**	**106**	**71**	**71**	**-**	**70**

Sample		Storage interval (month)[a]									
		0	**1**	**2**	**3**	**7**	**13**	**20**	**25**	**33**	**38**
		% concurrent recovery									
Corn grain	Control (mg/kg)	0.000	0.000	-	0.083	0.005	0.001	0.001	0.000	-	0.000
(starch matrix)	Treated (mg/kg)	0.911 1.006 0.924	- 0.82 0.89	-	- 0.84 0.92	- 0.93 0.85	- 0.87 0.77	- 0.57 0.61	- 0.57 0.57	-	- 0.75 0.77
	Mean recovery (mg/kg)	0.947	0.855	-	0.880	0.890	0.820	0.590	0.570	-	0.760
	Mean recovery (%) [1]	95	86	-	88	89	82	59	57	-	76
	Mean recovery (%) [2]	**100**	**90**	**-**	**93**	**94**	**87**	**62**	**60**	**-**	**80**
Corn Starch	Control (mg/kg)	0.001	0.003	-	0.000	0.001	0.000	0.001	0.000	-	0.000
(starch matrix)	Treated (mg/kg)	1.048 1.118 1.097	- 0.80 0.74	- - -	- 0.76 0.51	- 0.85 0.86	- 0.81 0.80	- 0.51 0.31	- 0.65 0.66	- - -	- 0.78 0.87
	Mean recovery (mg/kg)	1.088	0.770	-	0.635	0.855	0.805	0.410	0.655	-	0.825
	Mean recovery (%) [1]	109	77	-	64	86	81	41	66	-	83
	Mean recovery (%) [2]	**100**	**71**	**-**	**58**	**79**	**74**	**38**	**60**	**-**	**76**
Potato tuber	Control (mg/kg)	0.001	0.000	-	0.000	0.000	0.000	0.003	0.000	-	0.000
(starch matrix)	Treated (mg/kg)	1.010 0.810 0.932	- 0.72 0.71	-	- 0.62 0.64	- 0.66 0.66	- 0.59 0.61	- 0.66 0.68	- 0.62 0.63	-	- 0.64 0.62
	Mean recovery (mg/kg)	0.917	0.715	-	0.630	0.660	0.600	0.670	0.625	-	0.630
	Mean recovery (%) [1]	92	72	-	63	66	60	67	63	-	63
	Mean recovery (%) [2]	**100**	**78**	**-**	**69**	**72**	**65**	**73**	**68**	**-**	**69**

Sample		Storage interval (month)[a]									
		0	**1**	**2**	**3**	**7**	**13**	**20**	**25**	**33**	**38**
		% concurrent recovery									
Potato chip	Control (mg/kg)	0.001	0.002	-	0.000	0.001	0.000	0.000	0.003	-	0.000
(starch matrix)	Treated (mg/kg)	0.752 0.668 0.815	- 0.82 0.81	-	- 0.876 0.80	- 0.86 0.89	- 0.79 0.79	- 0.63 0.63	- 0.56 0.57	-	- 0.79 0.83
	Mean recovery (mg/kg)	0.745	0.815	-	0.838	0.875	0.790	0.630	0.565	-	0.810
	Mean recovery (%) [1]	75	82	-	84	88	79	63	57	-	81
	Mean recovery (%) [2]	**100**	**109**	**-**	**112**	**117**	**106**	**85**	**76**	**-**	**109**
Potato granules	Control (mg/kg)	0.011	0.003	-	0.000	0.003	0.019	0.001	0.011	-	0.000
(starch matrix)	Treated (mg/kg)	0.833 0.699 0.812	- 0.85 0.82	-	- 0.62 0.63	- 0.67 0.66	- 0.84 0.84	- 0.50 0.73	- 0.57 0.58	-	- 0.90 0.74
	Mean recovery (mg/kg)	0.781	0.835	-	0.625	0.665	0.840	0.615	0.575	-	0.820
	Mean recovery (%) [1]	78	84	-	63	67	84	62	58	-	82
	Mean recovery (%) [2]	**100**	**107**	**-**	**80**	**85**	**108**	**79**	**74**	**-**	**105**

Sample		Storage interval (month)[a]									
		0	**1**	**2**	**3**	**7**	**13**	**20**	**25**	**33**	**38**
		% concurrent recovery									
Dry potato peel (starch matrix)	Control (mg/kg)	0.002	-	0.002	0.002	0.007	0.004	0.001	0.002	-	0.001
	Treated (mg/kg)	0.777 0.712 0.752	-	- 0.75 0.61	- 0.65 0.68	- 0.66 0.68	- 0.69 0.71	- 0.67 0.53	- 0.68 0.72	-	- 0.57 0.63
	Mean recovery (mg/kg)	0.747	-	0.680	0.665	0.670	0.700	0.600	0.700	-	0.600
	Mean recovery (%) [1]	75	-	68	67	67	70	60	70	-	60
	Mean recovery (%) [2]	**100**	**-**	**91**	**89**	**90**	**94**	**80**	**94**	**-**	**80**
Wet potato peel (starch matrix)	Control (mg/kg)	0.000	-	0.002	0.000	0.001	0.000	0.000	0.000	-	0.004
	Treated (mg/kg)	0.917 0.898 0.848	-	- 0.69 0.76	- 0.77 0.77	- 0.59 0.61	- 0.52 0.47	- 0.51 0.52	- 0.59 0.61	-	- 0.60 0.52
	Mean recovery (mg/kg)	0.888	-	0.725	0.770	0.600	0.495	0.515	0.600	-	0.560
	Mean recovery (%) [1]	89	-	73	77	60	50	52	60	-	56
	Mean recovery (%) [2]	**100**	**-**	**82**	**87**	**68**	**56**	**58**	**68**	**-**	**63**
Wheat grain (starch matrix)	Control (mg/kg)	0.003	0.002	-	0.003	0.000	0.001	0.002	0.000	-	0.000
	Treated (mg/kg)	0.943 0.880 0.833	- 0.74 0.77	-	- 0.79 0.64	- 0.54 0.63	- 0.70 0.70	- 0.84 0.85	0.84 <0.01[b] 0.73 0.75	-	- 0.75 0.77
	Mean recovery (mg/kg)	0.857	0.755	-	0.715	0.585	0.700	0.845	0.740	-	0.760
	Mean recovery (%) [1]	86	76	-	72	59	70	85	74	-	76
	Mean recovery (%) [2]	**100**	**88**	**-**	**83**	**68**	**82**	**99**	**86**	**-**	**89**

[b] Sample apparently not fortified; not considered for storage stability assessment (chromatogram not reported)

Sample		Storage interval (month)[a]									
		0	**1**	**2**	**3**	**7**	**13**	**20**	**25**	**33**	**38**
		% concurrent recovery									
Wheat flour	Control (mg/kg)	0.004	0.040	-	0.000	0.002	0.005	0.001	0.004	-	0.000
(starch matrix)	Treated (mg/kg)	0.754 0.913 0.873	 0.95 1.04	-	 0.86 0.97	 0.93 0.90	 0.95 0.99	 0.52 0.54	 0.61 0.50	-	 0.82 0.79
	Mean recovery (mg/kg)	0.847	0.995	-	0.915	0.915	0.970	0.530	0.555	-	0.805
	Mean recovery (%) [1]	85	100	-	92	92	97	53	56	-	81
	Mean recovery (%) [2]	**100**	**118**	**-**	**108**	**108**	**115**	**63**	**66**	**-**	**95**
Wheat bran	Control (mg/kg)	0.004	0.004	-	0.003	0.006	0.001	0.002	0.001	-	0.004
(starch matrix)	Treated (mg/kg)	0.836 0.947 0.870	- 0.83 0.74	-	- 0.75 0.77	- 0.70 0.72	- 0.60 0.65	- 0.79 0.79	- 0.71 0.64	-	- 0.78 0.73
	Mean recovery (mg/kg)	0.884	0.785	-	0.760	0.710	0.625	0.790	0.675	-	0.755
	Mean recovery (%) [1]	88	79	-	76	71	63	79	68	-	76
	Mean recovery (%) [2]	**100**	**89**	**-**	**86**	**80**	**71**	**89**	**76**	**-**	**85**
Wheat dust	Control (mg/kg)	0.00	0.00	-	0.00	0.00	0.00	0.15	0.19	-	0.00
(starch matrix)	Treated (mg/kg)	120 105 98	105 116	-	116 117	111 110	98.3 99.2	95.8 96.4	99.8 101.1	-	101.1 101.5
	Mean recovery (mg/kg)	108	111	-	117	111	99	96	100	-	101
	Mean recovery (%) [1]	108	111	-	117	111	99	96	100	-	101
	Mean recovery (%) [2]	**100**	**103**	**-**	**108**	**103**	**92**	**89**	**93**	**-**	**94**

Sample		Storage interval (month)[a]									
		0	**1**	**2**	**3**	**7**	**13**	**20**	**25**	**33**	**38**
		% concurrent recovery									
Corn oil	Control (mg/kg)	0.000	0.008	0.011	0.000	0.001	0.009	0.001	0.000	-	0.000
(oil matrix)	Treated (mg/kg)	0.805 0.878 0.848	- 0.87 0.87	- 0.58 0.61	- 0.50 0.73	- 0.69 0.67	- 0.75 0.86	- 0.60 0.78	- 0.69 0.65	-	- 0.78 0.75
	Mean recovery (mg/kg)	0.844	0.870	0.595	0.615	0.680	0.805	0.690	0.670	-	0.765
	Mean recovery (%) [1]	84	87	60	62	68	81	69	67	-	77
	Mean recovery (%) [2]	**100**	**103**	**71**	**73**	**81**	**95**	**82**	**79**	**-**	**91**
Orange whole fruit (acid matrix)	Control (mg/kg)	0.025	0.017	-	0.021	0.020	0.018	0.004	0.011	-	0.018
	Treated (mg/kg)	1.003 1.019 1.104	- 1.14 1.07	- - -	- 1.04 1.00	- 0.77 0.71	- 0.92 0.90	- 0.76 0.77	0.86- 0.80	-	- 0.60 0.61
	Mean recovery (mg/kg)	1.042	1.105	-	1.020	0.740	0.910	0.765	0.830	-	0.605
	Mean recovery (%) [1]	104	111	-	102	74	91	77	83	-	61
	Mean recovery (%) [2]	**100**	**106**	**-**	**98**	**71**	**87**	**73**	**80**	**-**	**58**
Orange juice	Control (mg/kg)	0.001	0.000	-	0.000	0.002	0.004	0.000	0.000	-	0.001
(acid matrix)	Treated (mg/kg)	0.887 0.828 0.853	- 0.81 0.89	-	- 0.73 0.88	- 0.65 0.72	- 0.54 0.61	- 0.46 0.40	- 0.67 0.81	-	- 0.62 0.64
	Mean recovery (mg/kg)	0.856	0.850	-	0.805	0.685	0.575	0.430	0.740	-	0.630
	Mean recovery (%) [1]	86	85	-	81	69	58	43	74	-	63
	Mean recovery (%) [2]	**100**	**99**	**-**	**94**	**80**	**67**	**50**	**86**	**-**	**74**

Sample		Storage interval (month)[a]									
		0	**1**	**2**	**3**	**7**	**13**	**20**	**25**	**33**	**38**
		% concurrent recovery									
Orange dry pulp	Control (mg/kg)	0.026	0.020	-	0.033	0.021	0.026	0.005	0.016	-	0.024
(acid matrix)	Treated (mg/kg)	1.226 1.147 1.116	- 1.04 1.10	-	- 0.86 0.97	- 0.80 0.93	- 0.93 0.75	- 0.81 0.76	- 0.82 0.86	-	- 0.66 0.31 [c]
	Mean recovery (mg/kg)	**1.163**	**1.070**	**-**	**0.915**	**0.865**	**0.840**	**0.785**	**0.840**	**-**	**0.660**
	Mean recovery (%) [1]	**116**	**107**	**-**	**92**	**87**	**84**	**79**	**84**	**-**	**66**
	Mean recovery (%) [2]	**100**	**92**	**-**	**79**	**74**	**72**	**67**	**72**	**-**	**57**
Peanut shells	Control (mg/kg)	0.009	0.005	-	0.108	0.006	0.009	0.001	0.001	-	0.000
(matrix not attributed)	Treated (mg/kg)	0.645 0.750 0.781	- 0.81 0.78	-	- 0.72 0.74	- 0.73 0.76	- 0.94 0.85	- 0.87 0.94	- 0.66 0.67	-	- 0.59 0.43
	Mean recovery (mg/kg)	0.725	0.795	-	0.730	0.745	0.895	0.905	0.665	-	0.510
	Mean recovery (%) [1]	73	80	-	73	75	90	91	67	-	51
	Mean recovery (%) [2]	**100**	**110**	**-**	**101**	**103**	**123**	**125**	**92**	**-**	**70**

[1] nominal
[2] standardised

[c] Result of analysis stated to be invalid due to analytical mismatch ("*poor injection resulting in low value*"); statement cannot be verified.

B.7.1.2 Storage stability in animal matrices

Data point: KCA 6.1 /05

Report: [redacted] (1987): Storage stability of Baythroid in bovine liver MR94303, M-136845-01-1
RIP9401049

Guideline(s): EPA 171-4(c), Magnitude of residue – Storage stability

Deviations: None

GLP: No

Acceptability: Acceptable

Materials and methods

The stability of cyfluthrin was investigated in bovine liver under frozen conditions (-18 to -23 °C). Residues in liver samples fortified at 1 mg/kg with cyfluthrin were analysed with method 85883 (RIP9400740). After storage of 11, 42, 154 and 350 days, residues were 0.93, 0.88, 1.02 and 1.05 mg/kg.

Results

Stability for at least 350 days of storage is indicated. Further information on procedural recoveries or residues at day 0 is not available.

Table B.7.1-9: Stability of cyfluthrin in bovine liver during frozen storage at -18 to -23 °C

Matrix	Fortification level (mg/kg)	Storage time (days)	Residue (mg/kg)	Recovery (nominal in %)
Liver	1	11	0.93 0.92 0.94	93 92 94
		42	0.90 0.86 0.89	90 86 89
		154	1.00 1.04 1.02	100 104 102
		350	1.06 1.05 1.04	106 105 104

Conclusion

GLP status of the study is claimed by the applicant. However, current GLP requirements are not fulfilled by the study, and requirements at the time of study conduct (40 CFR Part 160) did not apply to the study. Therefore, the GLP status of the study is not given.
However, studies performed with vertebrates are integrated in the active substance assessment solely based on the scientific validity and apparent credibility of information contained in the report. Although this study type is not strictly a study with living animals, the derogation from GLP requirements of COM Reg. (EU) No. 283/2013, Annex 3.2, is extended to stability investigations.

Though overall the study is considered acceptable, the following deficiencies are noted:
- Information on procedural recoveries is not available.
- No control samples are reported.
- No GLP
- Analytical method 85883 not fully validated, but adequate to quantify residue levels ≥0.1 mg/kg
- Study results with fortified samples are not in concordance with investigations on storage stability of incurred residues (Shaw 1983; ASB2009-1452)

Data point: KCA 6.1 /04

Report: [redacted] (1983): The effect of frozen storage at 0 to -10 degree F on baythroid in bovine tissues and milk
86041, M-060765-01-1
ASB2009-1452

Guideline(s): None stated.

Deviations: -

GLP: No

Acceptability: Acceptable

Materials and methods

The stability of incurred cyfluthrin residues in liver, muscle, kidney, fat and milk collected from apparently the lactating cow metabolism study [redacted] 1983, RIP9400870) were analysed for parent cyfluthrin and acid cyfluthrin (FCR 2728; liver only) after storage of up to 342 days at -18 to -23 °C. Additionally, fortified liver samples were analysed after 21 days of storage for cyfluthrin. The method applied is 85883 (RIP9400740).

Results

Results are summarised in Table B.7.1-10, the results of the original metabolism study are presented in Table B.7.2-24, p.85. Apparently, cyfluthrin residues in milk are stable over 342 days, while significant degradation of cyfluthrin is reported for liver after 76 days of storage and kidney after 43 days of storage. In muscle and fat, presence of 99 and 96 % of TRR as parent indicate stability over at least 144 (muscle) and 158 days (fat).

It is noted in the report that liver samples with incurred residues were analysed for acid cyfluthrin (FCR 2728). Since in the metabolism study [redacted] (1983), where samples were derived from, metabolite FCR 2728 was not identified, the statement is interpreted that FCR 2728 was suspected as product of the observed degradation of parent compound. However, no further information is given in the study whether FCR 2728 was found or not.

Table B.7.1-10: Stability of cyfluthin in bovine tissues and milk after storage at -18 to -23 °C

Matrix	Fortification level (mg/kg)	% TRR	Storage time (days)	Residue (mg/kg)	Effective recovery (%)
Milk	(*incurred*)	98 98 98	0 315 342	0.055 0.055 0.055	100 100 100

Liver	2	-	0 21	1.86 1.82	93 91
	(*incurred*)	98 91 86 *62*	0 [b] 35 [b] 76 [b] *222* [b]	0.609 0.566 0.535 *0.386*	100 93 88 *63*
Muscle	(*incurred*)	99	144 [c]	0.021	n.a.
Fat	(*incurred*)	96	158 [c]	0.221	n.a.
Kidney	(*incurred*)	82 57 17	0 43 *189*	0.154 0.107 *0.032*	100 70 *21*

[a] mean recovery of day x divided by mean recovery of day 0
[b] in the report it is stated that liver was analysed for acid cyfluthrin, whereas the values presented are likely to be parent cyfluthrin
[c] interval from date of sacrifice

Conclusion

Based on incurred residues, degradation of the main residue cyfluthrin is demonstrated for storage periods exceeding 43 days (kidney) and 76 days (liver). Residues in milk are stable over at least 342 days. Parent residues in muscle and fat are stable for at least 144 and 158 days, respectively.

Though overall the study is considered acceptable, the following short-comings are noted:

- The source of samples is not clear; no cross reference reported; only indications are given, that the samples with incurred residues are from the metabolism study [redacted] 1983 (RIP9400870), very limited reporting, no further possibilities of comparison to metabolism study
- Procedural recoveries are not reported.
- Control samples were not analysed.
- Day 0 analyses for muscle and fat are not available.
- Unclear reporting (incurred residues of liver analysed for parent and/or FCR 2728?).
- FCR 2728 data missing.
- Results not in accordance to investigations with fortified samples ([redacted] 1987; RIP9401049), where stability of cyfluthrin is shown after 12 months of storage.
- No GLP, but this is not mandatory for studies with incurred residues.

Data point: KCA 6.1 /06

Report: [redacted] (1987): Storage stability of FPB aldehyde (Baythroid metabolite) in bovine liver
MR94304, M-069575-01-1
RIP9401050

Guideline(s): EPA 171-4(c), Magnitude of residue – Storage stability

Deviations: None

GLP: No

Acceptability: Acceptable

Material and methods

The storage stability of FPB aldehyde (FCR 1260) was investigated in bovine liver. Residues in liver samples fortified at nominal 1 mg/kg were analysed with method 86217 (RIP9400874). After storage of 0, 1, 3, 7, 14, 28, 106, 188 and 380 days, recovery of residues was >70 % for all individual samples (nominal and absolute).

Results

Stability for at least 380 days of storage is indicated for fortified liver samples.

Table B.7.1-11: Stability of FPB aldehyde (FCR 1260) in bovine liver during storage at -18 to -23 °C

Matrix	Fortification level (mg/kg)	Storage time (days)	Residue (mg/kg)	Recovery (nominal in %)	Recovery [a] (effective in %)
Liver	1	0	0.92 0.90 0.90	92 90 90	100
		1	0.93 0.88 0.84	93 88 84	97
		3	0.86 0.87 0.87	86 87 87	96
		7	0.89 0.83 0.89	89 83 89	96
		14	0.92 0.94 0.93	92 94 93	103
		28	0.91 0.86 0.81	91 86 81	95
		106	0.84 0.82 0.84	84 82 84	92
		188	0.96 0.94 0.94	96 94 94	104
		380	0.87 0.70 0.86	87 70 86	89

[a] mean recovery of day x divided by mean recovery of day 0

GLP status of the study is claimed by the applicant. However, current GLP requirements are not fulfilled by the study, and requirements at the time of study conduct (40 CFR Part 160) did not apply to the study. Therefore, the GLP status of the study is not given. However, studies performed with mammals are integrated in the active substance assessment solely based on the scientific validity and apparent credibility of information contained in the report. Although this study type is not strictly a study with living animals, the derogation from GLP requirements of COM Reg. (EU) No. 283/2013 is extended to stability investigations.

Conclusion

The study is considered acceptable although short-comings are noted. Metabolite FPB aldehyde (FCR 1260) is not proposed for inclusion into the residue definition.

Though overall the study is considered acceptable, the following deficiencies are noted:
- Information on procedural recoveries is not available
- No control samples are reported.
- No GLP
- Analytical method 86217 not fully validated, but adequate to quantify residue levels ≥0.1 mg/kg.

Additional data

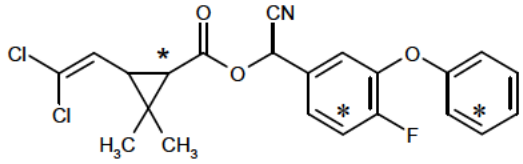
One more storage stability study for cyfluthrin (fortified) in animal matrices is described in the JMPR

evaluation of cyfluthrin (2007; Krebber 1999, MR-697/99). This study is not available to RMS. The study indicated stability over a period of 2 months in liver, kidney, muscle and fat, however, procedural recoveries reported for kidney and muscle were unacceptable.
In absence of the study report, the results of this study are not considered for assessment.

B.7.2 Metabolism, distribution and expression of residues

B.7.2.1 Plants

The data package submitted to address the plant metabolism of cyfluthrin after foliar application contains the already submitted studies on apple, tomatoes, potatoes, soybeans, cotton and wheat (Table B.7.2-1), which were performed with the 2 diastereoisomeric pairs of cyfluthrin, which are also contained in beta cyfluthrin in different amounts. The metabolism of beta-cyfluthrin is therefore inherently covered by these studies with cyfluthrin. The test compound in metabolism studies was labelled either in the cyclopropyl, fluorophenyl or phenyl ring position.



The above mentioned studies are re-evaluated according to current practice and data requirements.

Table B.7.2-1: Plant metabolism studies for cyfluthrin assessed within the peer-review process for initial Annex I setting (Monograph 1996, Addendum 1, 2002)

Crop	Application Method: Foliar	Reference
Tomato	[Fluorophenyl-UL-^{14}C]cyfluthrin, plant treatment, unknown rate	Wagner, K. and Neitzel, H., 1983, RIP9400821 GLP: No; KCA 6.2.1 /01
Apple	[Phenyl-UL-^{14}C]cyfluthrin 0.3 g as/L, direct fruit treatment	Minor, R.G. and Freeseman, P.L., 1985, RIP9400838, M-063640-01-1 GLP: No; KCA 6.2.1 /02
Potatoes	[Phenyl -UL-^{14}C]cyfluthrin 0.1 kg as/ha, plant treatment	Minor, R.G. and Ernst, V.J., 1983, RIP9400836, ASB2009-277, M-062850-01-1 GLP: No; KCA 6.2.1 /03
Soybeans	[Phenyl -UL-^{14}C]cyfluthrin 0.1 kg as/ha, plant treatment	Minor, R.G. and Ernst, V.J., 1983, RIP9400827, M-063915-01-1 GLP: No; KCA 6.2.1 /04
Plant cell cultures of soybean	[Phenyl -UL-^{14}C]cyfluthrin 5.2 mg as/L	
Cotton	[Phenyl -UL-^{14}C]cyfluthrin 0.1 kg as/ha, plant treatment	Minor, R.G. and Ernst, V.J., 1983, RIP9400835, M-064360-01-1 GLP: No; KCA 6.2.1 /05
Wheat	[Phenyl -UL-^{14}C]cyfluthrin 0.1 kg as/ha	Minor, R.G. et al., 1985, RIP9400840, M-136985-01-1 GLP: No; KCA 6.2.1 /06
	[Cyclopropyl-1-^{14}C]cyfluthrin 0.1 kg as/ha	

Crop	Application Method: Foliar	Reference
Plant cell cultures of apple, cotton, peanut, potato, carrot, wheat and tomato	[Fluoro-phenyl-U-^{14}C]cyfluthrin 40 mg as/L nutrient medium	Preiß, U., 1985, RIP9400837, M-064802-01-2 GLP: No; KCA 6.2.1 /07

To support the application via seed treatment two new plant metabolism studies in sugar beet are submitted.

Table B.7.2-2: Plant metabolism studies for beta-cyfluthrin after seed treatment (new submission)

Crop	Application Method: Seed treatment	Reference
Sugar beet	[Cyclopropane-1-^{14}C]beta-cyfluthrin in sugar beets after seed treatment	Bongartz, R. and Miebach, D., 2013 ASB2014-7887, M-468898-01-1 GLP: Yes; KCA 6.2.1 /10
Sugar beet	[Fluorophenyl-UL-^{14}C]beta-cyfluthrin in sugar beets after seed treatment	Bongartz, R., 2013 ASB2014-7886, M-468900-01-1 GLP: Yes; KCA 6.2.1 /11

B.7.2.1.1 Tomatoes (foliar application)

Data point: KCA 6.2.1 /01

Report: Wagner, K.; Neitzel, H. (1986): Studies on metabolism of cyfluthrin (FCR 1272) in tomatoes (revised 03/1986)
RIP9400821
Report No.: PF2578,
M-063323-01-2
MR85901

Guideline(s): None cited. Not compliant to OECD 501.

Deviations: Not applicable.

GLP: No.

Acceptability: Acceptable with limitations.

Material and methods

The test material labeled in the [fluorobenzene-^{14}C] ring was characterised by

- Radioactive purity >98 %;
- Specific activity 62 µCi/mg;
- Cyfluthrin content >97 %:
- Diastereoisomeric mixture the following isomers:
  - I_{cis}: 22.7 %,
  - II_{cis}: 19.7 %,
  - III_{trans}: 28.8 %,
  - IV_{trans}: 28.8 %

Greenhouse tomato plants were used as target crop 18 weeks after sowing. Tomato fruit and leaf surfaces were treated by a brush with an acetonic solution (35 mL) of the radiolabelled test item

(0.42 mg) and unlabelled cyfluthrin (1.7 mg), amounting to a concentration of 6.1 g as/hL (GAP: 1.75-3.5 g as/hL; 1.75-3.5 N rate refering to concentration).
Samples of mature tomatoes and leaves were taken between 1 and 35 days after treatment. Samples were repeatedly washed by acetone, the acetone concentrated and radioactivity measured by liquid scinitillation counting.
Washed fruits were macerated and extracted with acetone, filtered and the filtrate concentrated in a rotary evaporator, mixed with water and partitioned 3 times with dichloromethane (DCM). The DCM phase was dried and concentrated over sodium sulfate. Radioactivity was measured by TLC in organic and aqueous phase. Unextractable radioactivity was determined by combustion.
TLC analyses of DCM and aq phases were performed for identification of metabolites. Solvent systems were n-hexane:benzene:methanol (95:15:5) (I) and chloroform:methanol (9:1) (II). Radioactivity in the separated spots was determined by scintillation counting.
No information is given in the report on storage of samples.

Results

92.6 % of applied radioactivity were found in the acetone surface rinses. The relative amount of radioactivity in the rinses remained constant for all samples (86-96 % of sample radioactivity for fruits and 93-97 % for leaves). 97.8 % of applied radioactivity was recovered.

Cyfluthrin parent was the only residue compound identified. Amounts in acetone rinses of fruits and leaves were 91-93 % and 91-95 % of sample radioactivity for all samplings, respectively. Polar metabolites at the origin amounted to 2-4 % of sample radioactivity.

DCM and aqueous phases were only partly chromatographed due to the low radioactivity and matrix effects. However, while in the DCM extract, only unchanged parent was identified in fruits and leaves, one polar compound was found in the aqueous extract of tomato leaves (45 % of sample radioactivity; 0.12 % of applied radioactivity).

Table B.7.2-3: Radioactivity determined in different sample fractions of cyfluthrin treated tomatoes (fruit and leaves)

DAT	Acetone surface rinses		DCM fruit/leaf extract		Aqueous fruit/ leaf extract		Solid phase		Total	
(sample weight in g)	% TRR[1]	% SR[2]	% TRR[1]	% SR[2]	% TRR[1]	% SR[2]	%TRR[1]	% SR[2]	%TRR	% SR[2]
Tomato fruit										
Day 1 (32 g)	1.31	94.9	0.06	4.3	0.01	0.7	<0.01	<0.7	1.38	100
Day 5 (42 g)	1.54	86.5	0.13	7.3	0.01	0.6	0.1	5.6	1.78	100
Day 7 (108 g)	2.11	96.3	0.06	2.7	0.01	0.5	0.01	0.5	2.19	100
Day 9 (37 g)	0.73	89.0	0.07	8.5	0.01	1.2	0.01	1.2	0.82	100
Day 14 (27 g)	0.54	79.4	0.11	16.2	0.01	1.5	0.02	2.9	0.68	100
Day 21 (39 g)	0.96	94.1	0.05	4.9	0.01	1.0	<0.01	<1.0	1.02	100
Day 28 (74 g)	1.62	96.4	0.02	1.2	0.03	1.8	0.01	0.6	1.68	100
Day 35 (912 g)	11.88	85.8	1.08	7.8	0.32	2.3	0.56	4.0	13.84	100

Tomato leaves										
Day 14 (6.2 g)	1.12	93.3 [3]	0.04	3.3	0.01	0.8	0.03	2.5	1.2	100
Day 28 (8.0 g)	1.54	94.5 [3]	0.04	2.5	0.01	0.6	0.04	2.5	1.63	100
Day 35 (299 g)	69.26	96.8 [3]	0.55	0.8	0.27	0.4	1.49	2.1	71.57	100
Total recovery	92.61		2.21		0.70		2.29		97.79	100

[1] TRR (total radioactive residue) is understood as total recovery of radioactivity throughout all samples
[2] % sample radioactivity calculated from reported % TRR data
[3] metabolite identification revealed 95 % parent, 4.29 % TRR polar material, 4 spots of 0.59-1.39 % TRR
[4] metabolite identification revealed 91 % parent, 1.57 % TRR polar material, 5 spots of 0.38-2.37 % TRR
[5] metabolite identification revealed 95 % parent, 1.78 % TRR polar material, 6 spots of 0.26-1.13 % TRR

Conclusion

This non-guideline study shows the low rate of metabolisation of cyfluthrin resulting in only one metabolite detected at low percentages in tomato leaves. A very low translocation of radioactivity (parent only) into the fruit was observed.

Key information on test item, test design and analysis is provided. While the study allows only semi-quantitative estimates of the residue situation, this is not considered to challenge the scientific validity of the study, since only parent compound was detected in fruits with no other metabolite being overlooked, while identification rate is acceptable (97.79 % of applied radioactivity). The minor metabolites in leaves are not considered relevant as candidates for risk assessment when discussing a global residue definition.

Overall, the study provides valuable and scientifically meaningful insights into the metabolism of cyfluthrin in tomatoes, that are in congruence to other plant metabolism data (GLP and non-GLP). The lack of storage information is not considered to challenge the reported results, as no major degradation product was identified in fruits and leaves.
The information in this non-GLP report is not questioned, although documentation is not traceable and methods applied are not according to current standards.

B.7.2.1.2 Apples (foliar application)

Data point: KCA 6.2.1 /02

Report: Minor, R.G. and Freeseman, P.L. (1985): Metabolism of [^{14}C] BAYTHROID in apples.
RIP9400838,
Report No.: 88833,
M-063640-01-1

Guideline(s): None cited. Not compliant to OECD 501.

Deviations: Not applicable.

GLP: No.

Acceptability: Acceptable with limitations.

Material and methods

The test material was prepared by dissolving 15 mg of [phenyl-U-^{14}C]cyfluthrin (radioactive purity 96 %; specific activity 21.74 mCi/mmol; mixture of isomers with cis:trans ratio of approx. 40:60) in 0.063 ml of blank formulation. The material was dissolved in 50 ml water to obtain the treatment

solution (113.5 g as/100 gal equivalent to 30 g as/hL; 9-17N rate referring to concentration and GAP of tomato). A surfactant (ortho-X77) was added at a rate of 226 g/hL. [Phenyl-U-^{14}C]cyfluthrin was applied in small droplets by spraying to the surface of outdoor apples (variety *Red Rome Beauty*). A canopy of polyethylene sheeting was used to protect the apple tree from rainfall. Ten apples were collected at each sampling occasion (0, 7, 14, 21 and 28 days post treatment).
No information is provided on storage of samples.

After sampling, apples were repeatedly washed with methanol:water (4:1). Rinses were combined and radioassayed. The rinses were then concentrated to near dryness and redissolved in 100 ml water. This solution was partitioned against chloroform:acetone (1:2). This phase was radioassayed and subjected to TLC. The aqueous phase was radioassayed and discarded.

The rinsed apples were peeled, peel and pulp homogenised and radioassayed. Peels were repeatedly extracted with chloroform:acetone (1:2), radioassayed and subjected to TLC.

TLC was performed in one dimension with toluene, reverse-phase TLC with acetonitrile/methanol/aq. sodium chloride (2:2:1). The following non-radioactive standards were co-chromatographed along with the apple extracts:

- COOH-cyfluthrin (FCR 2728),
- Me-cyfluthrin (FCR 2956),
- $CONH_2$-cyfluthrin (FCR 2978),
- FPB amid (FCR 2947),
- Me-FPB acid (COE 263/78),
- FPB acid (COE 538/78),
- FPB aldehyde (FCR 1260),
- FPB alcohol (FCR 1261),
- hydroxy FPB acid (FCR 3145),
- FPB (FCR 3030),
- FCR 4150,
- α-hydroxy FPB acetonitrile (FCR 1271).

Distribution of radioactivity in apples was determined by TLC.

Results

Preliminary note: Results are reported as total radioactive residues in terms of total recovery throughout all samples (combined radioactivity of rinses, peel and pulp).
The rinses contained decreasing levels of radioactivity from day zero (96 % TRR) to day 28 (16 % TRR), while the radioactivity in the peel increased by the same order of magnitude (Table B.7.2-4). The combined radioactivity is therefore constant throughout the investigated period of time and shows the low recovery of cyfluthrin residues in water affine matrices. Traces of radioactivity (2-4 % TRR) are attributed to cross-contamination during peeling. The distribution of radioactivity in the methanol:water rinses further underlines the non-polar nature of cyfluthrin residues.

Table B.7.2-4: Radioactivity determined in different sample fractions of cyfluthrin treated apples

Days after treatment	Methanol/water rinses (organosoluble:aqueous)	Peel	Pulp	Total
	% TRR [1]	% TRR [1]	% TRR [1]	% TRR [1]
0	96 (94:2)	2	2	100
7	44 (43:1)	52	4	100

14	23 (22:1)	73	4	100
21	22 (21:1)	74	4	100
28	16 (15:1)	80	4	100

[1] TRR is understood as total recovery of radioactivity throughout all samples

The nature of metabolites was investigated in rinses and peels (Table B.7.2-5). The majority of residues is comprised on cyfluthrin parent compound. FPB_{ald} was found at levels of 2 % of total recovery from day 0 up to final harvest (day 28). In terms of relative radioactivity, FPB_{ald} amounts up to 12.5 % of radioactivity in the day 28 rinses (equivalent to 18.2 % of parent).

Table B.7.2-5: Metabolites identified in sample fractions of cyfluthrin treated apples

	0 DAT		**7 DAT**		**14 DAT**		**21 DAT**		**28 DAT**	
	Rinse (%TRR[1])	**Peel (%TRR[1])**	**Rinse (%TRR[1])**	**Peel (%TRR[1])**	**Rinse (%TRR[1])**	**Peel (%TRR[1])**	**Rinse (%TRR[1])**	**Peel (%TRR[1])**	**Rinse (%TRR[1])**	**Peel (%TRR[1])**
Cyfluthrin	89	2	35	48	16	67	16	67	11	73
FPB_{ald} (FCR 1260)	2	-	2	-	2	-	1	-	2	-
FPB_{acid} (COE 538/78)	-	-	<1	-	<1	-	<1	-	<1	-
Other organosoluble	2	-	6	4	4	6	4	7	2	7
Non-organosoluble	2	-	1	-	1	-	1	-	1	-
Total	96	2	44	52	23	73	22	74	16	80

[1] TRR (total radioactive residue) is understood as total recovery of radioactivity throughout all samples (rinse + peel + pulp); no identification attempts for pulp (TRR data presented in Table B.7.2-4)

Conclusion

This non-guideline study shows the low rate of metabolisation of cyfluthrin resulting in only 2 metabolites detected at low percentages, the organosoluble character of all residue compounds, and the diffusion of unmetabolised cyfluthrin from outer surfaces into the peel.

The report reflects state-of-the-art of the time the study was conducted. Some key information on test item (specific activity; purity, isomeric composition), test design (application, sampling) and analysis (methods of analysis, radioactivity calculation) is provided. The lack of storage information is not considered to challenge the reported results, as no major degradation products were identified.

The study allows only semi-quantitative estimates of the residue situation and metabolites relevance for dietary risk assessment. The following deficiencies are noted:

- Unrepresentative study design (direct treatment of apples at known concentration, but unknown rate per area)
- Insufficient reporting of analytical results (no reporting of absolute amounts)
- Non-GLP
- No identification attempts in pulp.

Overall, the study provides valuable and scientifically meaningful insights into the metabolism of cyfluthrin in apples that are in congruence to other plant metabolism data (GLP and non-GLP). Therefore, the information in this non-GLP report is not challenged, although documentation is not traceable and methods applied are not according to current standards.

B.7.2.1.3 Potatoes (foliar application)

Data point:	KCA 6.2.1 /03
Report:	Minor, R.G. and Ernst, V.J. (1983): Metabolism of Baythroid TM in potatoes (revised 12/1986) MR86053, M-062850-01-1 ASB2009-277, RIP9400836
Guideline(s):	None cited. Not compliant to OECD 501.
Deviations:	Not applicable.
GLP:	No.
Acceptability:	Acceptable with limitations.

Material and methods

The test material was prepared by dissolving 20.1 mg of [phenyl-U-^{14}C]cyfluthrin (radioactive purity 99 %; specific activity 21.74 mCi/mmol; mixture of four diastereoisomeric pairs of enantiomers with cis:trans ratio of approx. 40:60) in 0.1 ml of blank formulation (EC). The material was dissolved in 19 ml water to obtain the treatment solution (40 g/10 gal/ac equivalent to 100 g as/ha in approx. 100 L; equivalent to 4N rate).

Seed potatoes planted and grown under greenhouse conditions were treated with the test solution by foliar spray 60 days after planting (BBCH 61). Soil surface was covered during the treatment.
Whole plants were collected 0, 42, 52, 80 and 98 days post treatment and divided into foliage and tubers and stored in a freezer.

Storage conditions are not reported in detail (storage temperature; study duration: 7 months).

Tubers and foliage were homogenised, repeatedly extracted by methanol:water (4:1) and filtered. Extracts of the 0, 42 and 52 DAT samples were directly radioassayed. After concentration, the residue was dissolved in methanol, radioassayed and subjected to TLC.
Methanol/water extracts of the 80 and 98 DAT samples were concentrated near dryness, water was added and the solution partitioned against two volumes of chloroform:acetone (1:2). The chloroform:acetone fraction was radioassayed, concentrated and subjected to TLC.
The aq phase was subjected to acid hydrolysis (1 hour reflux with 6M HCl), followed by chloroform/ acetone partitioning. The organic extract was radioassayed, concentrated and subjected to TLC.

One-dimensional TLC was performed with toluene or hexane/p-dioxane/acetone/acetic acid (80:30:2:1). Reverse phase TLC (1D) was performed with acetonitrile/methanol/0.5M sodium chloride (2:2:1).

The following non-radioactive standards were co-chromatographed along with the potato extracts:

- COOH-cyfluthrin (FCR 2728),
- Me-cyfluthrin (FCR 2956),
- $CONH_2$-cyfluthrin (FCR 2978),
- FPB amid (FCR 2947),
- Me-FPB acid (COE 263/78),
- FPB acid (COE 538/78),
- FPB aldehyde (FCR 1260),
- FPB alcohol (FCR 1261),
- hydroxy FPB acid (FCR 3145),
- FPB (FCR 3030),
- α-hydroxy FPB acetonitrile (FCR 1271).

Results

No significant residues were reported for potato tubers (<0.01 mg/kg TRR). Therefore, no further identification attempts were made on the tubers.
In potato foliage, increasing residue levels were determined with time, an effect that was attributed to drying processes. No individual metabolite exceeded the level of significance (10 % TRR). Extraction (96-100 %) and identification rates for all foliage samples were high (84-95 %). At 80 and 98 DAT samples, metabolite conjugates were released by acid hydrolysis at levels between 1-3 % TRR.

Conclusion

This non-guideline study shows the low rate of metabolisation and systemic translocation of cyfluthrin. No major metabolites are likely to be formed by potato plants.

Key information on test item, test design and analysis is provided. The study provides valuable and scientifically meaningful insights into the metabolism of cyfluthrin in potatoes that are in congruence to other plant metabolism data (GLP and non-GLP). The lack of storage information is not considered to challenge the reported results, as no major degradation products were identified.
The information in this non-GLP report is not questioned, although documentation is not traceable and methods applied are not according to current standards.

Table B.7.2-6: Metabolites identified in sample fractions of cyfluthrin treated potato leaves [1]

	0 DAT		**42 DAT**		**52 DAT**		**80 DAT**		**98 DAT**	
	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR [2]	mg/kg	% TRR [1]
Cyfluthrin	6.62	95	7.70	86	9.28	83	9.83	80	18.00	70
FPB_{ald} (FCR 1260)	0.00	0	0.09	1	0.11	1	0.12	1	0.51	2
FPB_{alc} (FCR 1261)	0.00	0	0.09	1	0.11	1	0.49	4 (2)	1.03	4 (2)
FPB_{acid} (COE 538/78)	0.00	0	0.09	1	0.11	1	0.25	2 (1)	0.26	1
4-OH-FPB_{acid}	0.00	0	0.00	0	0.00	0	0.49	4 (3)	0.77	3 (2)
FPB (FCR 3030)	0.00	0	0.00	0	0.00	0	0.12	1 (1)	0.77	3 (2)
Other organosoluble	0.35	5	0.90	10	1.34	12	0.98	8	3.09	12
Non-extractable	0.00	0	0.09	1	0.22	2	0.00	0	1.03	4
Total	6.97	100	8.95	100	11.18	100	12.29	100	25.72	99

[1] amounts in mg/kg for individual residue components or fractions calculated by RMS from relative amounts and TRR of samples
[2] in parenthesis: percent of total identified as conjugate

B.7.2.1.4 Soybean (foliar application)

Data point:	KCA 6.2.1 /04
Report:	Minor, R.G. and Ernst, V.J. (1983): Metabolism of Baythroid TM in soybeans (revised 05/1984) RIP9400827, M-063915-01-1 MR86049
Guideline(s):	None cited. Not compliant to OECD 501.
Deviations:	Not applicable.
GLP:	No.
Acceptability:	Acceptable with limitations.

Material and methods

The test material was prepared by dissolving 20.1 mg of [phenyl-U-^{14}C]cyfluthrin (radioactive purity 99 %; specific activity 21.74 mCi/mmol; mixture of four diastereoisomeric pairs of enantiomers with cis:trans ratio of approx. 40:60) in 0.1 ml of blank formulation (EC). The material was dissolved in 19 ml water to obtain the treatment solution (40 g/10 gal/ac equivalent to 100 g as/ha in approx. 100 L).

Soybeans sown and grown under greenhouse conditions were treated with the test solution by foliar spray 40 days after planting (BBCH 61). Whole plants were collected 4, 19, 33, 48, 62 and 84 days post treatment, while soybeans harvested 88 days after treatment were divided into leaves, stalks, pods and seeds and stored in a freezer. Storage period is unknown.

Soybean plants were homogenised, repeatedly extracted by methanol:water (4:1) and filtered. Extracts were directly radioassayed. After concentration, the residue was dissolved in methanol, radioassayed and subjected to TLC.

One-dimensional TLC was performed with toluene or hexane/p-dioxane/acetone/acetic acid (80:30:2:1). Reverse phase TLC (1D) was performed with acetonitrile/methanol/0.5M sodium chloride (2:2:1).

HPLC of soybean organic and aqueous extracts was combined with UV detector.

The methanol extracts of immature samples (4-84 DAT) were subjected to acid hydrolysis (1 hour reflux with 6M HCl), followed by chloroform/acetone (1:2) and chloroform partitioning. The organic extract was radioassayed, concentrated and subjected to TLC.

Methanol/water extract of the mature 88 DAT sample was concentrated near dryness, water was added and the solution partitioned against two volumes of chloroform:acetone. The chloroform:acetone fraction was radioassayed, concentrated and subjected to TLC. The aqueous phase was subjected to acid hydrolysis (1 hour reflux with 6M HCl), followed by chloroform/acetone (1:2) partitioning. The resulting organic extract was radioassayed, concentrated and subjected to TLC.

The following non-radioactive standards were co-chromatographed along with the soybean extracts:

- Cyfluthrin
- COOH-cyfluthrin (FCR 2728),
- Me-cyfluthrin (FCR 2956),

- $CONH_2$-cyfluthrin (FCR 2978),
- FPB amid (FCR 2947),
- Me-FPB acid (COE 263/78),
- FPB acid (COE 538/78),
- FPB aldehyde (FCR 1260),
- FPB alcohol (FCR 1261),
- hydroxy FPB acid (FCR 3145),
- FPB (FCR 3030),
- α-hydroxy FPB acetonitrile (FCR 1271).

Soybean cell suspension
Callus tissue of soybeans was prepared from root explants grown on tissue culture. After 14 days of growing, soybean cell suspensions were fortified with the radioactive labelled test substance. Samples were taken at 7, 19 and 32 days after treatment and centrifugated. The supernatant was decanted, cells washed with distilled water (see additional experiment below), and the solutions combined, radioassayed, and partitioned with chloroform/acetone (2:1). Soybean cells were homogenised in methanol/water (4:1), centrifugated, radioassayed and subjected to TLC.

Reductive pathway confirmation
To verify the potential of soybeans to reduce FPB_{ald} to FPB_{alc}, a study utilising watersoluble extracts of soybean callus tissue fortified with FPB_{ald} was performed. Watersoluble extracts of callus tissue were prepared from the filtrate of callus tissue homogenised in distilled water. These extracts were fortified with FPB_{ald} (0.1 mg/mL) and incubated at 30 °C for 7 days, followed by direct HPLC analysis.

Results

TRR values for leaves, stalks, pods (without seeds) and seeds are presented in Table B.7.2-7. The majority of applied radioactivity is found in the leaves (no mass balance possible; 61.04 mg/kg at final harvest stage), while only low amounts were found in the seeds (0.04 mg/kg TRR).

Major residue compound in soybean leaves, stalks and pods is parent (43-55 % TRR); eight metabolites were found in amounts ≤ 10 % TRR. Seeds were not analysed due to low levels of radioactivity (TRR < 0.05 mg/kg).

Identification and characterisation rate is acceptable (66-98 % of TRR).

For the individual identified compounds in the acid hydrolysis fraction, the report postulates a differentiation into their unconjugated or conjugated form. However, any efforts undertaken to qualify or quantify these amounts are not presented.

Soybean cell suspension
In vitro investigations indicated largely similarity of metabolite profiles with *in vivo* data: Parent is major compound, the metabolites identified comprised FPB_{acid}, 4-OH-FPB_{acid} and FPB_{alc}.

Reductive pathway confirmation
From the study utilising watersoluble extracts of soybean callus tissue fortified with FPB_{ald}, after 7 days, both compounds (FPB_{ald} and FPB_{alc}) were detected in the culture extract. A control sample (water + FPB_{ald}) showed no formation of FPB_{alc}

Table B.7.2-7: Metabolites identified in sample fractions of [phenyl-U-^{14}C] cyfluthrin treated soybean samples

	4 DAT		19 DAT		33 DAT		48 DAT		62 DAT		84 DAT		88 DAT					
	Leaves		Leaves		Leaves		Leaves		Leaves		Leaves		Leaves		Stalks		Pods w/o seeds[1]	
	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg[6]	% TRR	mg/kg[6]	% TRR	mg/kg[6]	% TRR
Cyfluthrin	n.r.	92	n r.	81	n.r.	76	n r.	73	n.r.	59	n r.	61	*31.62*	43	*1.49*	51	*0.18*	55
FPB_{ald} (FCR 1260)	n.r.	1	n r.	4	n.r.	3	n r.	4	n.r.	5	n r.	4	*0.74*	1	*0.03*	1	*0.00*	0
4-OH-FPB_{acid} [2]	n.r.	n.a.[4]	n r.	<1	n.r.	<1	n r.	<1	n.r.	2	n r.	2	*3.68*	5	*0.06*	2	*0.00*	0
FPB_{acid} [2] (COE 538/78)	n.r.	n.a.[4]	n r.	3	n.r.	5	n r.	5	n.r.	7	n r.	8	*6.62*	9	*0.29*	10 [5]	*0.00*	0
FPB_{alc} [2] (FCR 1261)	n.r.	n.a.[4]	n r.	7	n.r.	8	n r.	8	n.r.	10	n r.	9	*4.41*	6			*0.00*	0
Me-FPB_{acid} [2] (COE 263/78)	n.r.	n.a.[4]	n r.	1	n.r.	1	n r.	1	n.r.	1	n r.	1	*3.68*	5	*0.00*	0	*0.00*	0
FPB_{amide} (FCR 2947)	n.r.	n.a.[4]	n r.	0	n.r.	0	n r.	0	n.r.	0	n r.	0	*2.21*	3	*0.06*	2	*0.00*	0
FPB (FCR 3030)	n.r.	n.a.[4]	n r.	0	n.r.	0	n r.	0	n.r.	0	n r.	0	*0.74*	1	*0.03*	1	*0.00*	0
$Cyfluthrin_{acid}$	n.r.	n.a.[4]	n r.	0	n.r.	0	n r.	0	n.r.	0	n r.	0	*0.00*	0	*0.12*	4	*0.00*	0
Other organosoluble	n.r.	n.a.[4]	n r.	2	n.r.	2	n r.	4	n.r.	8	n r.	3	*7.35*	10	*0.44*	15	*0.04*	11
Total	n.r.	93	n r.	98	n.r.		n r.		n.r.		n r.		61.04	83	2.51	86	0.22	66

[1] complementary residue level (TRR) in seeds is 0.04 mg/kg; no residue identification possible
[2] released from polar material after acid hydrolysis
[3] not reported (n r.)
[4] not analysed (n.a.)
[5] combined FPB_{acid} and FPB_{alc}
[6] values (mg/kg) for individual compounds calculated by RMS based on reported % TRR and total (in mg/kg)

Conclusion

This non-guideline study shows the low rate of metabolisation and systemic translocation of cyfluthrin. No individual metabolite in final harvest products exceeded the level of significance (10 % TRR). Most of radioactivity is located in foliar parts (61 mg/kg), in stalks (2.5 mg/kg) and pods (0.22 mg/kg), while TRR in seeds are low (0.04 mg/kg).
No information on absolute residue levels is provided for immature samples, however, relative shares of individual compounds on total radioactivity and high identification rate allow the assessment of metabolite relevance.

Key information on test item, test design and analysis is provided. The lack of storage information is not considered to challenge the reported results, as no major degradation products were identified.
The study provides valuable and scientifically meaningful insights into the metabolism of cyfluthrin in soybeans that are in congruence to other plant metabolism data (GLP and non-GLP). Therefore, the information in this non-GLP report is not challenged, although documentation is not traceable.

B.7.2.1.5 Cotton (droplet and spray application)

Data point:	KCA 6.2.1 /05
Report:	Minor, R.G. and Ernst, V.J. (1983): Metabolism of Baythroid in cotton MR86048 M-064360-01-1 RIP9400835
Guideline(s):	None cited. Not compliant to OECD 501.
Deviations:	Not applicable.
GLP:	No.
Acceptability:	Acceptable with limitations.

Material and methods

The [phenyl-UL-^{14}C] labelled test material was prepared by dissolving 20.1 mg of [phenyl-U-^{14}C]cyfluthrin (radioactive purity 97 %; specific activity 21.74 mCi/mmol; mixture of four diastereoisomeric pairs of enantiomers with cis:trans ratio of approx. 40:60) in 0.1 ml of blank formulation (EC). The material was dissolved in 19 ml water to obtain the treatment solution (40 g/10 gal/ac equivalent to 100 g as/ha or 88 g as/hL).
In a first experiment, the metabolism of cyfluthrin in cotton was investigated with [phenyl-UL-^{14}C]cyfluthrin applied by droplet application at rates of 0.1 kg as/ha over the surface of leaves. Plants were maintained in the greenhouse and leaves harvested at different times between 0 and 63 days post treatment.
A second set of plants were treated with formulated [^{14}C]-cyfluthrin and taken out of the greenhouse. Leaf samples were taken between 7 and 37 days after treatment.
In a third experiment, outer bolls of cotton plants representing different stages of maturity were sprayed with [^{14}C]-cyfluthrin and allowed for maturation under greenhouse conditions. At harvest cotton bolls were separated into gin trash, lint and seeds.
In a fourth experiment, cotton balls were removed from three mature plants and leaves were sprayed.

In a further translocation experiment a number of individual leaves of an immature cotton plant were treated with labelled cyfluthrin and untreated leaves sampled after 14 days.

Samples were stored in a freezer for a period not exceeding 15 months (begin and end of study). Samples were homogenised and extracted with methanol/water and the extracts analysed for

radioactivity. Components were identified using TLC and comparison of retention times with authentic standards. Lint samples were subject to Soxhlet extraction with chloroform/methanol. Residues in polar extracts were hydrolysed with 6N HCl.

The following non-radioactive standards were co-chromatographed along with the cotton extracts:

- Cyfluthrin
- COOH-cyfluthrin (FCR 2728),
- Me-cyfluthrin (FCR 2956),
- FPB amide (FCR 2947),
- Me-FPB acid (COE 263/78),
- FPB acid (COE 538/78),
- FPB aldehyde (FCR 1260),
- FPB alcohol (FCR 1261),
- 4-OH-FPB acid (FCR 3145),
- FPB (FCR 3030),
- $CONH_2$-cyfluthrin (FCR 2978)

Results

Extraction efficiency was high: 99 % of radioactivity in leaves and gin trash was rendered organosoluble after extraction and hydrolysis. Soxhlet extraction of lint samples was efficient with 91-94 % of radioactivity released.
Results of the different sample analyses are presented in Table B.7.2-8 for experiments with droplet application onto immature leaves and Table B.7.2-9 for experiments with mature plants. In all cases, paren tcyfluthrin is quantitatively the only relevant residue compound. No metabolite exceeds the level of relevance (10 % TRR).

Table B.7.2-8: Characterisation and identification of radioactivity in cotton leaves after droplet application of [phenyl-UL-^{14}C] cyfluthrin onto immature leaves at a rate of 88 g as/hL (experiment 1 and 2)

	% TRR at days after application									
	Greenhouse							**Outdoor**		
	0	7	14	21	35	49	63	7	22	37
MeOH extract	99	96	91	85	87	76	70	88	81	68
Cyfluthrin	99	96	91	82	84	69	64	88	75	61
FPBald	n.a.	n.a.	n.a.	3	3	7	6	n.a.	6	7
Polar material	n.a.	n.a.	n.a.	6	9	14	17	n.a.	11	17
FPBalc[a]				4	5	8	10		6	10
FPBacid[a]				1	2	4	5		3	5
Me-FPBacid[a]				1	1	1	1		1	1
4-OH-FPBacid[a]				0	1	1	1		1	1
Unidentified	n.a.	n.a.	n.a.	4	2	8	10	n.a.	6	11
Total	99	96	91	95	98	98	97	88	98	96

n.a. not analysed (polar material)
[a] released from polar material by acid hydrolysis

Table B.7.2-9: Characterisation and identification of radioactivity in cotton bolls and leaves after spray application of [phenyl-UL-^{14}C] cyfluthrin onto mature leaves or bolls at a rate of 88 g as/hL

	Leaves (85 d) [a]		**Cotton bolls (53 d)**				
	A	B	Gin trash		Lint		Seeds
	TRR (%)	TRR (%)	TRR (%)	TRR(mg/kg)	TRR (%)	TRR (mg/kg)	TRR (mg/kg)
MeOH extract [d]	79	75	85		69		
Cyfluthrin	73	70	83		68		
FPBald	6	1	2		1		
FPBalc		2 [c]					
FPBacid		2 [c]					
Polar material	8	6	7		n.a.		
FPBalc [b]	3	3	3				
FPBacid [b]	3	1	3				
Me-FPBacid [b]	1	1	<1				
4-OH-FPBacid[b]	1	1	1				
Other organosoluble	8	13	5		n.a.		
Total	95	94	97	52.3		0.1	0.03

[a] Extraction with methanol/water followed by acid hydrolysis (6N HCl) of polar material isolated from TLC plates (A) or with an acetone/chloroform/water partitioning (B)
[b] released from polar material after acid hydrolysis
[c] released without acid hydrolysis
[d] calculated from sum of cyfluthrin and metabolites not released from acid hydrolysis
n.a. not analysed

In the translocation experiment, no radioactivity was transferred to new growth or cotton boll components (gin trash, lint, seeds).

Conclusion

This non-guideline study shows the limited rate of metabolisation of cyfluthrin in cotton under the conditions of the study (droplet/spray application; indoor/outdoor). No individual metabolite in intermediate or final harvest products exceeded the level of significance (10 % TRR). The extraction efficiency and identification and characterisation rate is high for both experiments.

The study is reported in limited, but sufficient detail to allow for a scientific assessment. The study provides valuable and meaningful insights into the metabolism of cyfluthrin in cotton, that are in congruence to other plant metabolism data (GLP and non-GLP). The lack of storage information is not considered to challenge the reported results, as the observed little change of metabolite spectra and matrix association can be clearly attributed to maturation of crops.
The information in this non-GLP report is not challenged, although documentation is not traceable.

B.7.2.1.6 Wheat (foliar application)

Data point:	KCA 6.2.1 /06
Report:	Minor, R. G., Freeseman, P. L. and Ernst, V. J. (1985): Metabolism of Baythroid in wheat. MR88832 M-136985-01-1 RIP9400840
Guideline(s):	None cited. Not compliant to OECD 501.
Deviations:	Not applicable.
GLP:	No.
Acceptability:	Acceptable.

Material and methods

The metabolism of cyfluthrin in wheat was investigated with [phenyl-UL-^{14}C]cyfluthrin and [cyclopropyl-1-^{14}C] labelled cyfluthrin applied by foliar spray application at rates of 0.1 kg as/ha.

The [phenyl-UL-^{14}C] labelled test material was prepared by dissolving 20.1 mg of [phenyl-U-^{14}C]cyfluthrin (radioactive purity 97 %; specific activity 21.74 mCi/mmol; mixture of four diastereoisomeric pairs of enantiomers with cis:trans ratio of approx. 40:60) in 0.1 ml of blank formulation (EC). The material was dissolved in 19 ml water to obtain the treatment solution (40 g/10 gal/ac equivalent to 100 g as/ha in approx. 100 L).

The [cyclopropyl-1-^{14}C] labelled test material was prepared by dissolving 10.05 mg of [cyclopropyl-1-^{14}C] cyfluthrin (radioactive purity 98 %; specific activity 21.74 mCi/mmol; mixture of four diastereoisomers with cis:trans ratio of approx. 50:50) and 10.26 mg unlabelled active substance in 0.1 ml of blank formulation (EC). The material was dissolved in 19 ml water to obtain the treatment solution (40 g/10 gal/ac equivalent to 100 g as/ha in approx. 100 L).

Spring wheat plants were planted and maintained under greenhouse conditions. Two treatment regimes were applied:
In a first experiment, either labelled substance was applied at the rate of 100 g as/ha 4 times (eq. to 16N rate) with a one week interval to wheat plants in different plots (21d, 14 d, 7d, 1d pre-harvest); sampling occurred one day after final application. Harvest samples were divided into straw and heads.
In a second experiment, the first out of three foliar spray applications of [phenyl-UL-^{14}C] labelled test substance (100 g as/ha; 12N rate) occurred at 2-4 leaf stage (BBCH 12-14), a second one at the 4-6 leaf stage (BBCH 14-16) and a third application 21 days before harvest (BBCH unknown). Immature leaf samples were taken at the 4-6 leaf stage prior to the second treatment and at harvest (no growth stage reported). Harvest samples were divided into straw and heads.

All samples were stored in a freezer (storage temperature unknown). Samples were homogenised, repeatedly extracted by methanol:water (4:1) and filtered. Extracts were directly radioassayed. After evaporation of methanol, acetonitril was added. The residue was dissolved in 100 ml water and partitioned against chloroform:acetone (1:2). This phase was separated from water, radioassayed, concentrated and subjected to TLC.
The aqueous phase was radioassayed, combined with the filter cake and subjected to acid hydrolysis (6N HCl, reflux for 1 hr). The hydrolysate was filtered and partitioned against chloroform/acetone and radioassayed. Aliquots of the extracts were chromatographically separated by solvents of increasing polarity, radioassayed and subjected to TLC.

One-dimensional TLC was performed with toluene or hexane/p-dioxane/acetone/acetic acid

(80:30:2:1). Reverse phase TLC (1D) was performed with acetonitrile/methanol/0.5M sodium chloride (2:2:1).

The following non-radioactive standards were co-chromatographed along with the wheat extracts:

- Cyfluthrin
- COOH-cyfluthrin (FCR 2728),
- Me-cyfluthrin (FCR 2956),
- FPB amid (FCR 2947),
- Me-FPB acid (COE 263/78),
- FPB acid (COE 538/78),
- FPB aldehyde (FCR 1260),
- FPB alcohol (FCR 1261),
- 4-OH-FPB acid (FCR 3145),
- FPB (FCR 3030),
- DCVA
- FCR 4093
- DCVA-OH (FCR 4088)
- FCR 4150

Results

For the first experiment (4 x 100 g as/ha; PHI 1 day, cyclopropyl- and phenyl-^{14}C label), TRR values are presented in Table B.7.2-10 together with individual compounds data and fractions. Results for TRR, parent and common metabolites are comparable between labels, as well as for extraction profile. Parent is the major residue compound, with no individual metabolite exceeding 7 % of TRR. Metabolites were predominantly detected after acid hydrolysis. Methylated cyfluthrin (Me-cyfluthrin, FCR 2956) observed in both experiments is postulated as an artefact of acid hydrolysis, however, verification attempts after fortification and acid hydrolysis did not reproduce this assumption.

The results are in accordance to those from the second experiment (3 x 100 g as/ha; PHI 21 days, phenyl-^{14}C label; Table B.7.2-11) and with those from other plant metabolism studies.

The extraction efficiency and identification and characterisation rate is high for both experiments.

The metabolic pathway in wheat involves initial hydrolysis of the ester linkage to yield DCVA and FPB_{ald}. Even though α-OH-FPB-acetonitrile should be the initial hydrolysis product instead of FPB_{ald}, it is postulated that its instability precludes identification. FPB_{ald} can undergo oxidation to FPB_{acid} which is further hydroxylated to 4-OH-FPB_{acid}. Hydroxylation of the phenoxy moiety most probably occurred after initial hydrolysis. DCVA, FPB_{acid} and 4-OH-FPB_{acid} undergo conjugation in wheat.

Table B.7.2-10: Metabolite profile after foliar treatment of spring wheat with ^{14}C-cyfluthrin (4 x 100 g as/ha with sampling 1 day after last application) [4]

	[cyclopropyl-1-^{14}C]				**[phenyl-UL-^{14}C]**			
	Straw		Heads		Straw		Heads	
	mg/kg [1]	% TRR [1]	mg/kg [1]	% TRR [1]	mg/kg	% TRR [1,3]	mg/kg [1]	% TRR [1]
Cyfluthrin	*17.912 (1.343)*	80 (6)	*18.054 (1.593)*	68 (6)	*12.278 (1.473)*	75 (9)	*17.555 (3.566)*	64 (13)
COOH-cyfluthrin FCR 2728		0	*0 (1.328)*	0 (5)	*0 (0.164)*	0 (1)	*0 (0.274)*	0 (1)
Me-cyfluthrin FCR 2956	*0 (0.224)*	0 (1)	*0 (0.266)*	0 (1)	*0 (0.164)*	0 (1)	*0 (0.274)*	0 (1)

DCVA	*0.448 (0.448)*	2 (2)	*0.266 (1.593)*	1 (6)				
FPB aldehyde FCR 1260					*0 (0.164)*	0 (1)	*0.274*	1
FPB alcohol FCR 1261						traces		traces
FPB acid COE 538/78					*0 (0.164)*	0 (1)	*0 (0.274)*	0 (1)
4-OH-FPB acid FCR 3145					*0 (0.164)*	0 (1)	*0 (0.823)*	0 (3)
Unknown					*0.327 (0)*	2 (0)		1
Other organosoluble	*0.896 (0.672)*	4 (3)	*0.797 (1.328)*	3 (5)	*0.819 (0.327)*	5 (2)	*1.646 (1.646)*	6 (6)
Prior acid hydrolysis								
Organosoluble	*19.255*	86	*19.116*	72 [2]	*13.751*	84	*19.750*	72
Non-organosoluble	*2.015*	9	*4.779*	18	*1.964*	12	*4.389*	16
Solids	*1.120*	5	*2.655*	10	*0.655*	4	*3.292*	12
After acid hydrolysis (non-organosoluble and solid fraction)								
Organosoluble	*2.687*	12	*6.107*	23	*2.292*	14	*6.868*	25
Aq soluble	*0.448*	2	*1.328*	5	*0.327*	2	*0.823*	3
Total	22.39	100	26.55	100	16.37	100	27.43	100

[1] percentage in organosoluble fraction (in parenthesis: additional percentage as identified as conjugated/bound material released after acid hydrolysis)
[2] erroneously reported as 74 %
[3] mass balance not correctly reported: sum of organosoluble compounds/fraction prior to hydrolysis is 82 % instead of 84 %
[4] *italics*: mg/kg values for individual compounds or fractions calculated by RMS from reported values of total radioactivity (mg/kg) and percentages for individual compounds or fractions

Table B.7.2-11: Metabolite profile after foliar treatment of spring wheat with ^{14}C-cyfluthrin (3 x 100 g as/ha with sampling 21 days after last application)

	[phenyl-UL-^{14}C]		
	Forage	Straw	Heads
	% TRR	% TRR	% TRR
Cyfluthrin	64 (1)	68 (1)	47 (4)
COOH-cyfluthrin (FCR 2728)	Traces	Traces	0 (1)
Me-cyfluthrin (FCR 2956)	0 (1)	0 (1)	0 (3)
Me-FPB acid (COE 263/78)	0 (1)	0 (1)	0 (2)
FPB acid (COE 538/78)	0 (3)	3 (2)	0 (4)
4-OH-FPB acid (FCR 3145)	0 (5)	0 (4)	0 (5)
Unknown1	0 (1)	0 (1)	0 (1)
Unknown 2	0 (3)	0 (3)	1 (2)
Unknown 3	3 (1)	2 (1)	0 (3)
Other organosoluble	9 (3)	7 (3)	5(3)
Prior acid hydrolysis			
Organosoluble	76	78	53
Non-organosoluble	15	9	22
Solids	9	13	25
After acid hydrolysis (non-organosoluble and solid fraction)			
Organosoluble	19	17	28
Aq soluble	5	5	8
Solids	0	0	11
Total	100	100	100

[1] percentage in organosoluble fraction (in parenthesis: additional percentage as identified as conjugated/bound material released after acid hydrolysis)

Conclusion

This non-guideline study shows the limited rate of metabolisation of cyfluthrin. No individual metabolite in intermediate or final harvest products exceeded the level of significance (10 % TRR). The extraction efficiency and identification and characterisation rate is high for both experiments.

Sufficient information on test materials, study design and analytical efforts is available to allow the assessment of metabolite relevance under conditions probably representative for the intended use in cereals (21 d PHI, 3 instead of 2 applications), provided the final sampling is made at commercial harvest stage (no information provided).

The study provides valuable and scientifically meaningful insights into the metabolism of cyfluthrin in wheat, that are in congruence to other plant metabolism data (GLP and non-GLP). The lack of storage information is not considered to challenge the reported results, as no major degradation products were identified. The information in this non-GLP report is not challenged, although documentation is not traceable.

B.7.2.1.7 Plant cell suspensions

Data point:	KCA 6.2.1 /07
Report:	Preiss, U. (1985): Metabolism of Baythroid in cultured plant cells. RIP9400837 M-064802-01-2
Guideline(s):	None cited.
Deviations:	Not applicable.
GLP:	No.
Acceptability:	Scientifically robust. Supporting information.

Material and methods

The metabolism of cyfluthrin in cell cultures (tomato, cotton, apple, potato, carrot, peanut, wheat) was investigated with [fluoro-phenyl-U-^{14}C]cyfluthrin labelled cyfluthrin (specific activity 62 µCi/mg, radiochemical purity >98 %) diluted with unlabelled cyfluthrin, resulting in a concentration of 40 mg as/L nutrient medium.

Results

The degradation in cell cultures resulted in the formation of glycosides of FCR 1261 and COE 538/78. The only exceptions were that the COE 538/78 was not found in apple cultures and that in peanut cultures FCR 1261 was also found in its free form. In tomato, small amounts of FCR 2978 were also found. After about 10 days the concentration of cyfluthrin increased, which is attributed to the formation of COE 263/78.

Conclusion

The study shows a comparable metabolic pattern compared to soybean cell investigations (RIP9400827) and to studies on intact plants.

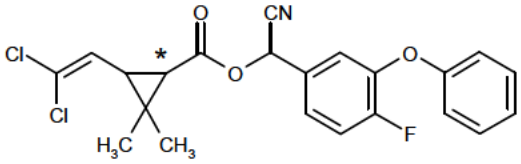
The study is considered as of additional information.

B.7.2.1.8 Sugar beets (seed treatment)

Two new metabolism studies of beta-cyfluthrin as seed treatment were submitted. These studies were performed with [cyclopropane-1-^{14}C] and [fluorophenyl-UL-^{14}C] beta-cyfluthrin.

Data point:	KCA 6.2.1 /10
Report:	Bongartz, R., Miebach, D. (2013): Metabolism of [cyclopropane-1-^{14}C] beta-cyfluthrin in sugar beets after seed treatment. ASB2014-7887 M-468898-01-1
Guideline(s):	OECD 501, Metabolism in Crops US EPA OCSPP Residue Chemistry Test Guideline OPPTS 860.1300: Nature of the Residue – Plants, Livestock EPA Ref.: 712-C-96-172, JAP FAMIC-ACIS Annex 2.4.1 to Notification No. 12 Nousan 8147: Studies of metabolic fate in plants
Deviations:	None
GLP:	Yes
Acceptability:	Acceptable

Materials and methods

CAS Name	(RS)-alpha-cyano-4-fluoro-3-phenoxybenzyl(1RS,3RS;1SR)-3-(2,2)-(dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate
Chemical structure	 * position of the radiolabel
Common name	Beta-cyfluthrin
Empirical formula	$C_{22}H_{18}Cl_2FNO_3$
Molar mass	434.29
Labelling	[cyclopropane-1-^{14}C]
Specific activity	3.27 MBq/mg (88.4 µCi/mg)
Chemical Purity	> 98 % (sum of isomers, determined by HPLC)
Radiochemical purity	> 98 % (HPLC and TLC, sum of isomers)
Isomer ratio	39.5 % isomer II 1.3 % isomer III 59.2 % isomer IV (all determined by HPLC)

Seed treatment
The supplied radiolabelled test compound [cyclopropane-1-^{14}C]beta-cyfluthrin was dissolved in toluene yielding the stock solution. Suitable aliquots of the stock solution were concentrated and adjusted with toluene to the final application concentration for the 1N (10 g as/ha) and the 10N (100 g as/ha) application rate. The seed treatment was performed by addition of the application solution directly to each seed during sowing. A volume of 49 µL application solution (corresponding to 0.328 MBq) was added to each seed of the 1N application rate and a volume of 47 µL (corresponding to 3.289 MBq) to each seed of the 10N overdose application rate.
The actual application rate was calculated from the amount of radioactivity applied to the seeds and the specific radioactivity of the test compound. As a result, 10.0 g as/ha (1N) and 100.6 g as/ha were applied (10N).
The stability check of the test compound in the application solutions was performed before and after treatment by HPLC. No degradation was observed. The purity of the test compound was determined after seed treatment and amounted to 99.1 % for both experiments.

The ratio of the isomers was determined by HPLC and amounted to 39.5 % for isomer II, 1.3 for isomer III and 59.2 % for isomer IV.

Planting and sampling
The experiments were performed indoors in a planting container filled with soil. Sugar beets were sown at a density of 10 seeds/m² and cultivated under artificial temperature and light conditions.
1N rate: Mature samples (leaves, roots) were harvested at BBCH 49, homogenised and subjected to extraction and analysis.
10N rate: Intermediate (leaves; BBCH 45, 56 days after sowing) and mature samples (leaves, roots; BBCH 49; 119 days after sowing) were homogenised and subjected for extraction and analysis.
Soil particles on the roots were removed by hand and washed with water. The radioactivity in the wash water was determined by LSC.

Extraction
Each sample (except sugar beet leaves of the 1X experiment) was extracted three times with methanol/water (8/2; v/v). The TRR of each RAC was calculated. A second extraction was performed with sugar beet leaves (intermediate, 10X) for the quantitation of metabolites and with sugar beet roots (10X) for an additional characterisation of metabolites.
The combined conventional extract of each RAC was concentrated to a volume suitable for profiling of metabolites by HPLC. In addition the extract of sugar beet roots (10X rate) was analysed by TLC.

Analytical Methodology
The measurement of the radioactivity in the liquid samples was carried out by liquid scintillation counting (LSC). Solid samples were combusted, released $^{14}CO_2$ absorbed and determined. Parent compound and metabolites were analysed by three different HPLC methods:
Method 1: Stability and purity check of the test compound in the application solution.
Method 2/3: Profiling and identification of parent compound and metabolites.
The methods are based on a reverse phase system with an acidic acetonitrile/water gradient coupled to a radioactivity detector with a glass scintillator cell (method 1) or liquid scintillator (methods 2/3; difference only by the column used).
The 10X root samples were analysed by 1-D TLC using a silica gel TLC plate and two solvent systems (SS1: trichloromethane/methanol/ammonia solution 65/28/8 (v/v/v); SS2: pure toluol).
GC/MS-EI was performed with GC spectrometer.

Identification and characterisation
The first profiling of parent compound and metabolites was performed by HPLC using method 2. Parent and metabolites were quantified by HPLC based on method 3. The identification of parent and metabolites was performed in the extract of sugar beet roots (10N rate) by HPLC and TLC. Further attempts to characterise metabolites were made by treatment of the extract with 5 N hydrochloric acid for approx. 1 h at 100 °C. The acidic extract was adjusted with sodium hydroxide to pH 6 and investigated with chromatographic methods.

Storage stability
Detailed evidence was provided in the report to show that the quantified pattern of parent compound and metabolites adequately reflected the residue components at harvest. The samples were extracted approx. one month after sampling. A second extraction of sugar beet leaves (intermediate) and roots at maturity (both at 10N rate) was performed approx. five and four months after sampling, respectively. The mg/kg values, which were determined during the second extraction, were similar compared to the values (mg/kg) of the first extraction.

Results

Recovery and distribution of radioactivity
Sugar beet roots and leaves (intermediate and maturity) of the 1N rate and roots of the 10Nrate were extracted with mixtures of methanol/water (8/2, v/v). The extraction rates are given in Table B.7.2-12 and Table B.7.2-13.

It is stated that negligible amounts of radioactivity were found in the wash waters.

Table B.7.2-12: Distribution of the residues in sugar beet roots after application of [cyclopropane-1-^{14}C]beta-cyfluthrin at 10.0 g as./ha (1N application rate)

	Sugar beet roots (1x application rate)	
	TRR = 0.014 mg/kg	
	% of TRR	mg/kg
Extractable*	77.6	0.011
Unextractable (PES**)	22.4	0.003
Accountability	100.0	0.014

* 3 x methanol/water (8/2; v/v)
** post extraction solids

Table B.7.2-13: Distribution of the residues in sugar beet roots after application of [cyclopropane-1-^{14}C]beta-cyfluthrin at 100.6 g as./ha (10N application rate)

	Sugar beet leaves (intermediate, 10N application rate) ***		Sugar beet leaves at maturity (10N application rate)		Sugar beet roots at maturity (10N application rate)	
TRR [mg/kg]	TRR = 0.022 mg/kg		TRR = 0.011 mg/kg		TRR = 0.110 mg/kg	
	% of TRR	mg/kg	% of TRR	mg/kg	% of TRR	mg/kg
Extractable*	97.5	0.022	92.1	0.010	94.0	0.103
Unextractable (PES**)	2.5	0.001	7.9	0.001	6.0	0.007
Accountability	100.0	0.022	100.0	0.011	100.0	0.110

* 3 x methanol/water (8/2; v/v)
** post extraction solids
*** Values are based on the second extraction. The TRR and the extraction rate calculated after the second extraction are similar compared to the first extraction.

A summary of the distribution of parent compound and metabolites is given in Table B.7.2-14.
Only traces of parent compound (0.004 mg/kg, 3.5 % of the TRR) were detected in sugar beet roots (10N rate). Metabolite DCVA (trans-isomer), which is specific for the cyclopropane label, was detected in all extracts at levels <10 % of TRR. DCVA was identified by HPLC co-chromatography with the radiolabelled reference compound.

Four conjugates were detected in the extracts and amounted to in sum of 58-84 % of TRR (individually 0-44 % TRR; 0.001-0.004 mg/kg in 1N sugar beet roots). These compounds as well as parent could be cleaved by acid hydrolysis to DCVA (mainly the trans-isomer), but not by enzymatic treatment (ß-Glucosidase). A further characterisation of the conjugates and a differentiation between conjugation with parent compound or with DCVA was not performed, due to the very low residue level of each single. Conjugation of parent compound could not be excluded.

The hydrolysis compound DCVA was identified in the hydrolysis solution of the extract of sugar beet roots (10N rate) after the second extraction by TLC co-chromatography with the radiolabelled reference compounds (trans- and cis-isomer).

Conclusions

Based on the metabolites identified the metabolic route given in Figure B.7.2-1 is proposed. Unconjugated parent is found in traces, metabolite DCVA is a minor compound in all samples (<10 %

TRR, <0.01 mg/kg at 1N and 10N rate). Conjugates represent the largest part of radioactivity (sum 58-83 % TRR), however, the low absolute amounts (<0.01 mg/kg in roots under 1N conditions) do not qualify these metabolites as candidates for the residue definition.

It is noted that conjugates were not identified in the parallel study with the fluorophenyl label. As cleavage was not demonstrated there, no conclusion can be made on whether conjugation in this cyclopropyl-label study occurred prior or post ester cleavage.

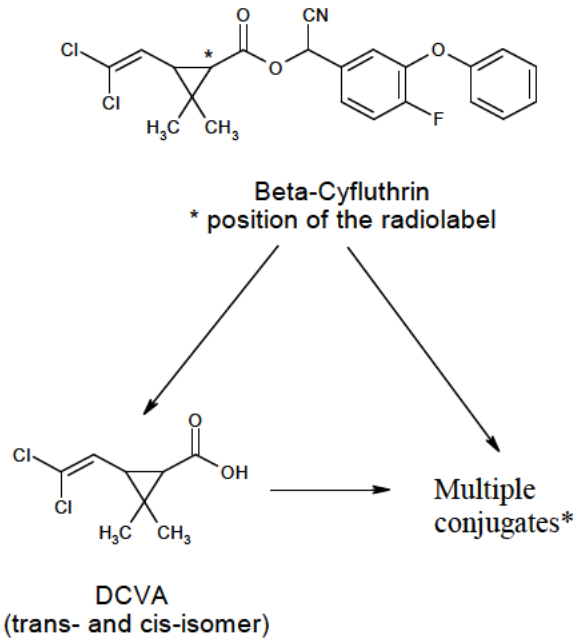


Figure B.7.2-1: Proposed metabolic pathway of [cyclopropane-1-^{14}C] beta-cyfluthrin in sugar beet

* 4 conjugates characterised

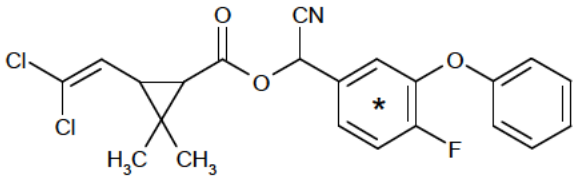
Table B.7.2-14: Distribution of parent compound and metabolites in sugar beet after application of [cyclopropane-1-^{14}C]beta-cyfluthrin

	Sugar beet roots (maturity, 1N rate)		**Sugar beet leaves** (intermediate, 10N rate)*		**Sugar beet leaves** (maturity, 10N rate)		**Sugar beet roots** (maturity, 10N rate)	
	% of TRR	mg/kg	% of TRR	mg/kg	% of TRR	mg/kg	% of TRR	mg/kg
Extract (3x methanol/water)								
Parent	---	---	---	---	---	---	3.5	0.004
DCVA (trans-isomer)	8.0	0.001	9.4	0.002	5.7	0.001	5.1	0.006
Conjugate 1**	---	---	8.6	0.002	14.5	0.002	3.0	0.003
Conjugate 2**	25.6	0.004	16.4	0.004	16.3	0.002	44.3	0.048
Conjugate 3**	24.5	0.004	42.5	0.010	33.9	0.004	36.1	0.040
Conjugate 4**	8.4	0.001	16.1	0.004	14.7	0.002	---	---
Unknown	11.2	0.002	4.4	0.001	7.1	0.001	2.0	0.002
Sum of conjugates 1-4	58.4	0.008	83.6	0.019	79.3	0.008	83.4	0.091
Characterised metabolite*	11.2	0.002	4.4	0.001	7.1	0.001	2.0	0.002
Total extracted	77.6	0.011	97.5	0.022	92.1	0.010	94.0	0.103
Unextractable (PES)	22.4	0.003	2.5	0.001	7.9	0.001	6.0	0.007
TRR	100.0	0.014	100.0	0.022	100.0	0.011	100.0	0.110

* Values are based on the second extraction. The TRR and the extraction rate calculated after the second extraction are similar compared to the first extraction.
** characterised as conjugate after acid hydrolysis

Data point:	KCA 6.2.1 /11
Report:	Bongartz, R. (2013): Metabolism of [fluorophenyl-UL-^{14}C] beta-cyfluthrin in sugar beets after seed treatment. ASB2014-7886 M-468900-01-1
Guideline(s):	OECD 501, Metabolism in Crops US EPA OCSPP Residue Chemistry Test Guideline OPPTS 860.1300: Nature of the Residue – Plants, Livestock EPA Ref.: 712-C-96-172, JAP FAMIC-ACIS Annex 2.4.1 to Notification No. 12 Nousan 8147: Studies of metabolic fate in plants
Deviations:	None
GLP:	Yes
Acceptability:	Acceptable

Materials and methods

Chemical structure	 * position of the radiolabel
Labelling	[fluorophenyl-UL -^{14}C]
Specific activity	4.36 MBq/mg (117.9 µCi/mg)
Chemical Purity	> 99 % (HPLC, sum of isomers)
Radiochemical purity	> 99 % (HPLC and TLC, sum of isomers)
Isomer ratio	39.7 % isomer II 60.3 % isomer IV (all determined by HPLC)

Seed treatment
The supplied radiolabelled test compound [fluorophenyl-UL -^{14}C]beta-cyfluthrin was dissolved in toluene yielding the stock solution. Suitable aliquots of the stock solution were concentrated and adjusted with toluene to the final application concentration for the 1N (10 g as/ha) and the 10N (100 g as/ha) application rate. The seed treatment was performed by addition of the application solution directly to each seed during sowing. A volume of 50 µL application solution (corresponding to 0.449 MBq) was added to each seed of the 1X application rate and a volume of 56 µL (corresponding to 4400 MBq) to each seed of the 10X overdose application rate.
The actual application rate was calculated from the amount of radioactivity applied to the seeds and the specific radioactivity of the test compound. As a result, 10.0 g as/ha (1N) and 100.6 g as/ha were applied (10N).
The stability check of the test compound in the application solutions was performed before and after treatment by HPLC. No degradation was observed. The purity of the test compound was determined after seed treatment and amounted to 99.6 % for both experiments.
The ratio of the isomers was determined by HPLC and amounted to 39.5 % for isomer II, 1.3 for isomer III and 59.2 % for isomer IV.

The objective of this study was to provide data on the metabolism of beta-cyfluthrin in the sugar beet after seed treatment. This study was designed to investigate the metabolic fate of the fluorophenyl-part

of beta-cyfluthrin and the test substance was therefore labelled in the fluorophenyl moiety.

Planting and sampling
The experiments were performed indoors in a planting container filled with soil. Sugar beets were sown at a density of 10 seeds/m² and cultivated under artificial temperature and light conditions.
1N rate: Mature samples (leaves, roots) were harvested at BBCH 49, homogenised and subjected to extraction and analysis.
10N rate: Intermediate (leaves; BBCH 45, 56 days after sowing) and mature samples (leaves, roots; BBCH 49; 117 days after sowing) were homogenised and subjected for extraction and analysis.
Soil particles on the roots were removed by hand and washed with water. The radioactivity in the wash water was determined by LSC.

Extraction
Each sample (except sugar beet leaves of the 1N experiment) was extracted three times with methanol/water (8/2; v/v). The TRR of each RAC was calculated. A second extraction was performed with sugar beet leaves (intermediate, 10N) for the quantitation of metabolites and with sugar beet roots (10N) for an additional characterisation of metabolites.
The combined conventional extract of each RAC was concentrated to a volume suitable for profiling of metabolites by HPLC.

The residues in the remaining solids after conventional extraction were digested with cellulase at pH 6. The radioactivity in the digestion solution was further characterised by partition against ethyl acetate. The radioactivity in the PES (post-extraction solids) was determined by combustion of aliquots followed by LSC.

An aliquot of the homogenised sugar beet roots (10 x overdose application rate) sample was extracted according to the residue methods 00922, S19 (00086/M088) and 00255. The residues were extracted 1x with acetone/water (2/1; v/v). Afterwards the extract was concentrated to a volume, suitable for the determination of the TTR (Total Toxic Residue, expressed in % of TRR and mg/kg) by HPLC using method 3.

Analytical Methodology

Radioactivity Measurement
The measurement of the radioactivity in the liquid samples was carried out by liquid LSC. Solid samples were combusted in an oxygen atmosphere using an oxidiser. The released $^{14}CO_2$ was absorbed in an alkaline scintillation cocktail and the radioactivity was determined by LSC.

HPLC
Parent compound and metabolites in the application solution and the extracts were analysed by three different HPLC methods. The HPLC-method 1 was used for the stability and purity check of the test compound in the application solution. The HPLC-methods 2 and 3 were used for the profiling and identification of parent compound and metabolites. The methods are based on a reverse phase (RP) system with an acidic acetonitrile/water gradient coupled to a radioactivity detector with a glass scintillator cell (method 1) or liquid scintillator (method 2 and method 3). The HPLC chromatograms (= metabolite profiles) were integrated for quantification of compounds.
To ensure the quantitative elution of the injected radioactivity from the HPLC-column, the eluent of the first profiling run of RACs from sugar beet was collected and measured for radioactivity by LSC. The radioactivity collected from the run was compared to the amount injected.

Gas Chromatography-Mass Spectrometry
GC/MS analysis in the electron impact mode (EI) was performed with a TSQ Quantum GC spectrometer.

Identification and characterisation
The first metabolite profile of the conventional extract of sugar beet roots (10N application rate) was

recorded immediately after extraction and sample preparation by HPLC with method 2. In addition the extract was analysed by HPLC with method method 3, which was developed for the separation of the isomers of beta-cyfluthrin.
Parent compound was identified in the extract of sugar beet roots by HPLC co-chromatography with the radiolabelled test compound based on method 3and assigned to the reference compound based on HPLC method 2.
All other metabolites (R1 to R4) were not further investigated, due to their very low amount of radioactivity. These metabolites were characterised as smaller polar compounds based on their extraction and chromatographic behaviour.

Storage stability
All RACs were stored at temperatures ≤ -18 °C before sample preparation and analysis. The sample for sugar beet roots (10N application rate) was extracted one month after sampling. Within one day after extraction, the first profile and quantitation of metabolites were obtained from the conventional extract by HPLC using the profiling method 2.
The stability of parent compound in sugar beet roots (10N application rate) could be demonstrated for a time period of 3 month based on the results of the determination of the extraction efficacy according to the conditions of the residue methods.
Therefore, it was concluded that the results of this study were not influenced by storage effects.

Results

Recovery and distribution of radioactivity
The total residues of the 1N rate application (10.3 g as/ha) were very low in sugar beet leaves and roots (all TRRs <0.01 mg/kg), even in sugar beet leaves of the overdose application rate. Sugar beet roots of the 10N rate application amounted to 0.05 mg/kg.
Sugar beet roots (10N rate) were extracted with mixtures of methanol/water (8/2, v/v). Results are given in Table B.7.2-15. PES were not further investigated, due to the very low amount of radioactivity.

The first metabolite profile of the conventional extract of sugar beet roots was recorded immediately after extraction and sample preparation by HPLC with method 2. In addition the extract was analysed by HPLC with method 3, which was developed for the separation of the isomers of beta-cyfluthrin.

Parent compound amounted to 43.1 % (0.021 mg/kg) of the TRR for sugar beet roots (10 x application rate) based on the first profiling method 2. The ratio of the isomers of beta-cyfluthrin was determined with HPLC method 3 and amounted to 52.4 % for isomer II, 4.3 % for isomer III and 43.3 % for isomer IV
Parent compound was identified in the extract of sugar beet roots by HPLC co-chromatography with the radiolabelled test compound based on method 3 and assigned to the reference compound based on HPLC method 2.

Cellulose is a part of the cell walls of plants and can be digested with the enzyme cellulase to smaller fragments. Approx. 22.4 % (0.011 mg/kg) of the TRR for sugar beet roots (10N application rate) were released from the cell matrix during the enzymatic digestion of the cellulose. One portion (12.2 % (0.006 mg/kg) of the TRR) of the released radioactivity was characterised as polar radioactivity based on its partition behaviour. The other portion (10.2 % (0.005 mg/kg) of the TRR) could be partitioned into the organic phase and was characterised as non-polar.
Further investigations were not performed, due to the low amount of radioactivity in the phases.

However these results give a strong indication that residues of beta-cyfluthrin are bound to or incorporated as natural compounds into the plant matrix.

A summary of the distribution of parent compound and metabolites for the 10x application rate is given in Table B.7.2-15

Table B.7.2-15: Distribution of parent compound and metabolites in sugar beet roots after application of [fluorophenyl-UL-^{14}C] beta-cyfluthrin at 100.9 g as/ha (10N application rate)

	Sugar beet roots (10N application rate)	
	% of TRR	mg/kg
Conventional extract		
Parent compound (sum of isomers) ratio of isomer IV / II / III is 43.3 / 52.4 / 4.3	43.1	0.021
unknown 1 (R1)	9.3	0.004
unknown 2 (R2)	4.2	0.002
unknown 4 (R4)	7.0	0.003
Identified metabolite	43.1	0.021
Characterised metabolite*	20.5	0.010
Iodentified + characterised metabolites	63.5	0.030
Cellulase digestion solution		
characterisation by partition against ethyl acetate:		
- aqueous phase (polar)	12.2	0.006
- organic phase (non-polar)	10.2	0.005
Total extracted	85.9	0.041
Unextractable (PES)	14.1	0.007
Accountability	100.0	0.048

* The unidentified metabolite is characterised by their extraction and chromatographic behaviour.

Extraction efficiency using the residue methods
Sugar beet roots (10N application rate) were extracted with acetone/water (2/1, v/v) according to the conditions of the residue methods 00922, S19 (00086/M088) and 00255 approx. three months after the first extraction. The extraction rate for parent compound (sum of isomers) amounted to 51.5 % of TRR (0.027 mg/kg).
The extraction efficiency was calculated by comparison of the results obtained during the metabolism investigation with the results after extraction according to the residue methods. The extraction efficiency of the TTR amounted to 102.5 %. Details are summarised in Table B.7.2-16

Table B.7.2-16: Extraction efficacy of the residue methods and recovery of parent for sugar beet roots (10N application rate)

	Extraction used in the metabolism investigations [a]		Extraction according to residue methods [b]	
	% of TRR	mg/kg	% of TRR	mg/kg
Total extractable	63.5	0.030	51.5	0.027
Parent compound (isomer IV / II / III)	40.1 (43.2/52.4/4.3)	0.019 (0.008/0.010/0.001)	41.1 (43.8/56.2/0)	0.022 (0.009/0.012/0)
Solids	36.5	0.017	48.5	0.026
Sum TRR	**100.0**	**0.048**	**100.0**	**0.053**

[a] Extraction with 3x methanol/water (8/2; v/v)
[b] Extraction with acetone/water (2/1; v/v)

The TRR's of sugar beet leaves and roots of the 1N application rate were <0.01 mg/kg. Therefore

sugar beet roots from the 10x overdose experiment were used to characterise the nature of the residues of beta-cyfluthrin. Parent compound was the major part of the radioactive residue and only three minor metabolites (all ≤0.004 mg/kg) were detected. These minor metabolites were only characterised, due to their very low amount of radioactivity.
After conventional extraction of sugar beet roots additional radioactivity could be solubilised from the solids by digestion with cellulase. The solubilised radioactivity could be characterised as polar and non-polar fraction by partitioning. Both fractions amounted to ≤0.006 mg/kg and were not further investigated. However, solubilisation of radioactivity by cellulase gives an indication for potential incorporation of residues in natural compounds or strong binding of residues to plant matrix.

Conclusion

Parent compound was the main compound, which was identified in sugar beet roots of the 10N application rate. Three minor metabolites (all ≤ 0.004 mg/kg) were detected. These minor metabolites were only characterised, due to their very low amount of radioactivity.
Based on these results a depiction of the metabolic pathway was not presented.

B.7.2.1.9 Information on isomerisation of beta-cyfluthrin in plant matrices

Data point:	KCA 6.2.1 /12
Report:	Bonarius, T. (2004): Isomerisation of beta-cyfluthrin - Re-evaluation of residue trials. M-241664-01-2 ASB2014-7873
Guideline(s):	Not applicable. Expert statement on meta-analysis of residue data.
Deviations:	Not applicable.
GLP:	Not applicable.
Acceptability:	Provisionally acceptable.

Preliminary remark of RMS:
The expert statement addressing the potential for isomerisation of beta-cyfluthrin was submitted by the applicant dated 2004. It does not contain information from scientific literature from the last 10 years as required by Regulation (COM) 283/2013, Annex 1.4, and Part A, Section 9. The information contained therein is therefore, irrespective of its scientific value, incomplete and not fully adequate to satisfy regulatory needs.

Introduction
The re-evaluation of beta-cyfluthrin residue trials was performed to demonstrate the isomerisation process of beta-cyfluthrin on plant surfaces (limited systemicity after foliar application; see e.g. plant metabolism data from tomatoes [Table B.7.2-3] and apples [Table B.7.2-4]).

Isomerisation of cyfluthrin has been reported earlier and was experimentally demonstrated in a GLP hydrolysis study in an artificial system (CHE2005-47; conversion of diastereomer II → I and IV → III in aqueous buffer solution independent on pH before hydrolysis starts).
Those findings were stated to be confirmed in a mesocosm study for natural systems [4]. However, this study is not available to BfR.

[4] Heimbach 1989: Biological effects and fate of FCR 4545 EC 025 (Bulldock) in experimental ponds; Bayer file HBF/VT01

A peer-reviewed study from open literature (Leicht 1996[5]) showed that isomerisation activates the less efficient isomers I and III and lowers the efficacy of II and IV. The test results were derived analytically and by bioassay. Evidence for the isomerisation on plant surfaces was also found in several field residue trials.

It is demonstrated that the molecular aspects of the isomerisation process can be understood on the basis of the chemical properties of cyfluthrin. When exposed to protic solvents, the *alpha* carbon atom can, due to its C-H acidic properties, undergo a deprotonation - protonation cycle. This reaction step involves a planar configuration of the alpha carbon anion. In the course of the reaction, the carbanion can be attacked by the proton from above or below the plane. Accordingly, racemisation is observed.

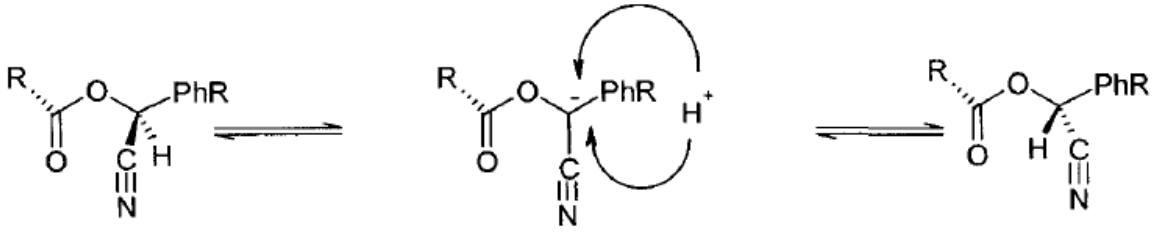


Figure B.7.2-2: Racemisation of the α-carbon

Materials and methods

To investigate the isomerisation of beta-cyfluthrin in residue trials, several cyfluthrin and beta-cyfluthrin trials were scanned for the following criteria:
1. The quality of chromatographic separation should allow of differentiation of the diastereomers.
2. The trials should result in beta-cyfluthrin residues well about the limit of quantification (LOQ), i.e. approximately > 0.05 mg/kg in most cases.
3. To monitor the kinetics of the isomerisation process on the plant, samples beginning from the day of application (DALT) should be available. At least DALT=0 and a later sample date are required for a data set.
4. To compare the residue behaviour with cyfluthrin side-by-side, a corresponding set of trials should exist in the cyfluthrin database.

In total eight trials were found for which the re-evaluations of the chromatograms were done. Table B.7.2-17 gives an overview over the used trials.

Table B.7.2-17: Selected residue trials (foliar spray to alfalfa and barley close to commercial harvest stage)

Trial and study No.	Act. substance	Crop	Year	Location
0429-96; ASB2009-2706; GLP compliant; 3x foliar spray, BBCH 41-65; samples analysed with validated analytical method 00255/E004	beta-cyfluthrin	alfalfa	1996	Italy
0067-96; ASB2009-2706; GLP compliant; 3x foliar spray, prior BBCH 65; samples analysed with validated analytical method 00255/E004	beta-cyfluthrin	alfalfa	1996	Spain

[5] Leicht, W., Fuchs, R., Londershausen, M. (1996): Stability and biological activity of cyfluthrin isomers. Pestic. Sci., 48 (1996), pp. 325–332.

R 2000 / 00308; RIP2003-273; GLP compliant; 2x foliar spray, BBCH 84-87; samples analysed with validated analytical method 00255	beta-cyfluthrin	barley	2000	France
R 2000 / 02270 RIP2003-273; GLP compliant; 2x foliar spray, BBCH 77-85; samples analysed with validated analytical method 00255	beta-cyfluthrin	barley	2000	Italy
R 2000 / 02289 RIP2003-273; GLP compliant; 2x foliar spray, BBCH 65; samples analysed with validated analytical method 00255	beta-cyfluthrin	barley	2000	Spain
R 2000 / 00502; RIP2003-267, GLP compliant; 2x foliar spray, BBCH 87-89; samples analysed with validated analytical method 00255/E011	cyfluthrin	barley	2000	France
R 2000 / 02440; RIP2003-267, GLP compliant; 2x foliar spray, BBCH 85-93; samples analysed with validated analytical method 00255/E011	cyfluthrin	barley	2000	Italy
R 2000 / 02459 ; RIP2003-267, GLP compliant; 2x foliar spray, BBCH 65-90; samples analysed with validated analytical method 00255/E011	cyfluthrin	barley	2000	Italy

Archived chromatograms of the respecting trials were digitised by a commercially available standard software tool (Corel draw®) and re-evaluated by estimating the peak height (h).
The peaks of the isomers were identified by comparing their retention time with those of standards. Since the elution order of the pure isomers is unknown, it was not possible to assign single peaks to specific isomers. Instead, the peaks were classified in groups "II + IV", i.e. peaks only present the beta-cyfluthrin samples or "I + III", i.e. those peaks present in cyfluthrin samples except peaks "II + IV".
Since the detector response for each specific isomer is unknown, the peak height reflects a change in concentration between groups "I+III" and "II+IV" only. Therefore, only the relative, not the absolute concentration or percentages of an isomer present the sample was calculated, using the following equations:

Relative concentration $c_{I+III} = \{ h_{I+III} / (h_{I+III} + h_{II+IV}) \} * 100$
Relative concentration $c_{II+IV} = \{ h_{II+IV} / (h_{I+III} + h_{II+IV}) \} * 100$

Results

Beta-cyfluthrin
The isomer ratio for cyfluthrin and beta-cyfluthrin for the different samplings is summarised in Table B.7.2-18. Relative concentrations of isomers I+III and II+IV demonstrate time-dependency of the ratio of isomers. While the amount of isomers I+III ioncreases with time, isomers II+IV decrease in the same order of magnitude. Additional influence on isomer ratio is indicated by humidity (in alfalfa trial 0067-96, where only 31 mm of rainfall were recorded, hardly any isomerisation was observed within 7 days).

Cyfluthrin
In contrast to the beta-cyfluthrin trials, the relative concentration of the isomers during degradation remained unchanged. This behaviour seemed also to be independent from sample date, season, location, or sample material. Cyfluthrin residues consisted of isomers I+III and II+IV in a 50:50 ratio during the monitored degradation period.

Table B.7.2-18: Relative concentation of isomers II+IV and I+III of beta-cyfluthrin and cyfluthrin in alfalfa and barley samples

Trial No.	Active Substance	Crop	DALT	Concentration of isomers	
				II+IV	I+III
0429-96	beta-cyfluthrin	alfalfa green material	0	98	2
			3	89	11
			7	91	9
0067-96	beta-cyfluthrin	alfalfa green material	0	98	2
			3	97	3
			7	97	3
R 2000/00308	beta-cyfluthrin	barley straw	0	83	11
			21	68	20
			28	69	19
R 2000/00308	beta-cyfluthrin	barley grain	0	89	11
			21	80	20
			28	81	19
R 2000/02270	beta-cyfluthrin	barley straw	0	87	13
			0	90	10
			21	74	26
			28	73	27
R 2000/02270	beta-cyfluthrin	barley grain	0	87	13
			0	90	10
			21	80	20
			28	80	20
R 2000/02289	beta-cyfluthrin	barley straw	0	93	7
			0	92	8
			21	82	18
			28	80	20
R 2000/02289	beta-cyfluthrin	barley grain	0	93	7
			0	92	8
			21	82	18
			28	82	28
R 2000/00502	Cyfluthrin	barley straw	0	48	52
			21	50	50
			28	50	50
R 2000/00502	cyfluthrin	barley grain	0	49	51
			21	51	49
			28	51	49
R 2000/02440	cyfluthrin	barley straw	0	47	53
			0	48	52
			21	50	50
			28	49	51

Trial No.	Active Substance	Crop	DALT	Concentration of isomers	
				II+IV	I+III
R 2000/ 02459	cyfluthrin	barley straw	0	49	51
			0	49	51
			21	51	49
			28	50	50
R 2000/ 02459	cyfluthrin	barley grain	0	49	51
			0	49	51
			21	51	49
			28	51	49

Given a sufficient separation of all four diastereomers in the samples analysed, the residue studies in barley and alfalfa demonstrate isomerisation of beta-cyfluthrin on plant surfaces. For the relative concentration of isomers I and III, a positive correlation with the days after the last application can be established.
As the comparison with the cyfluthrin residue trials indicate, the isomerisation process reaches equilibrium. The re-evaluation of those trials showed, that an isomer ratio of 50:50 (isomers I+III:II+IV) remains constant during the monitoring period of 28 days. It can be therefore assumed, that also the isomerisation process of beta-cyfluthrin on plants would have reached equilibrium with the same final ratio. As an estimation of the isomerisation period needed to reach such equilibrium, an isomerisation period of approximately 74 d (+/- 32 d) can be extrapolated on the basis of the examined residue trials.

Conclusions

Results are only considered indicative due to the low number of studies assessed, the limited number of crops, limited application pattern (foliar spray), short observation range (7-28 days) and the impact of environmental conditions (e.g. humidity; unknowns). Moreover, the assessment does not consider literature studies from 2004 onwards. The tools for re-assessment of residue trials are at best qualitative (visual inspection and digitalisation by commercially available standard software tool).

The data provide indications on the isomerisation of beta-cyfluthrin that probably tends to equilibrium within larger timeframes for the investigated trials with applications close to harvest. The work therefore supports the bridging approach that beta-cyfluthrin residue data can supplement cyfluthrin trials and vice versa.

B.7.2.1.10 Information on isomerisation of beta-cyfluthrin in animal matrices

Additional data on isomerisation of cyfluthrin in animal species (hen) is presented within the assessment of poultry metabolism (Eben et al. 1987, TOX9401851).

B.7.2.1.11 Poultry

Data point:	KCA 6.2.2 /08
Report:	[redacted] (1983): The distribution and metabolism of Baythroid in laying hens. MR-86044, M-054113-01-1 RIP9400869
Guideline(s):	None stated. Not compliant to OECD 503.
Deviations:	Not applicable.
GLP:	No.
Acceptability:	Additional information Not considered acceptable as a stand-alone-study.

Materials and methods

The test material was prepared by dissolving 55.2 mg of [phenyl-U-^{14}C]cyfluthrin (radiochemical purity >99 %; specific activity 21.74 mCi/mmol) and 115.93 mg unlabelled cyfluthrin (94.3 % chemical purity) in 7.5 ml ethanol. Each dose was adsorbed to lactose and encapsulated in gelatine. The specific activity was therefore reduced to 7.24 mCi/mmol by mixing.

Five laying hens were treated orally with gelatin capsules containing the phenyl-UL-^{14}C-labelled cyfluthrin in a dose of 5 mg/kg body weight per day for 5 successive days (530 N rate; see

Table B.7.4-5). The doses were given in the morning of each day and the birds were sacrificed 2 hours after the final treatment. Samples of tissues, organs and eggs (collected at 24 hour intervals) were analysed for total radioactive residue (TRR) and for metabolites. No analyses were done on the excreta.

Samples were stored at -10 °C for a period not exceeding 13 months (sacrifice to date of study issue; exact storage time is not reported).

For TRR determination, samples were combusted and radioassayed.
Composite samples (5 hens) of eggs, kidney, liver, heart, skin, muscle (breast, leg and thigh) and gizzard (without contents and lining) were homogenised and extracted with 250 ml acetone/chloroform (2:1) and 2 ml concentrated HCl and filtered. The filter cake was re-extracted twice with acetone/chloroform (2:1). Extracts were combined, evaporated to dryness, and taken up in hexane/acetonitrile (1:1) and partitioned in a separatory funnel. The acetonitrile fraction was repeatedly drained off into a separatory funnel containing hexane saturated with acetonitrile. The contents were again partitioned and the ACN fraction drained of and filtered. ACN extracts were combined, as well as hexane fractions.

Fat samples (renal, omental, subcutaneous) were homogenised in hexane, filtered, and the filter cake repeatedly extracted by ACN. Hexane and ACN extracts were combined and partitioned in a separatory funnel. ACN extracts were combined.

Hexane and ACN extracts were subjected to TLC. Solid residues were combusted and radioassayed.
The filter cakes were also refluxed with 6N HCl for 2 hours. The hydrolysate was extracted 3 times with diethyl ether or chloroform/acetone (2:1). The organic extract was dried, radioassayed and subjected to TLC analysis.

Organosoluble residues were resolved by TLC (normal and reverse-phase). TLC was performed in one dimension with hexane/p-dioxane/acetone/acetic acid (80:30:2:1) and toluene/diethyl ether/acetic acid (100:5:1), reverse-phase TLC with acetonitrile/methanol/0.5N sodium chloride (2:2:1).

The extracts were applied along with the following non-labelled reference standards:

- cyfluthrin (FCR 1272),
- COOH-cyfluthrin (FCR 2728),
- Me-cyfluthrin (FCR 2956),
- $CONH_2$-cyfluthrin (FCR 2978),
- FPB amid (FCR 2947),
- Me-FPB acid (COE 263/78),
- FPB acid (COE 538/78),
- FPB aldehyde (FCR 1260),
- FPB alcohol (FCR 1261),
- hydroxy FPB acid (FCR 3145),
- FPB (FCR 3030),
- α-hydroxy FPB acetonitrile (FCR 1271).

Reference compounds were identified on TLC plates by UV light, radioactive spots were located by autoradiography. Quantification was done by separating the spots and LSC.

Enzymatic hydrolysis of residues from the TLC origin was attempted using β-glucuronidase arylsulfatase and protease.

Results

The sample radioactivity and its distribution between the different solvent fractions and post-extraction solid is shown in Table B.7.2-19. Highest residues are found in liver and kidney, while residues in eggs are very low. However, it is noted that plateau was not formed in eggs throughout the

administration period.

The organo-extractable fraction of combined ACN and hexane extracts amounts from 60 % (liver and kidney) to 86 % (gizzard). Strong acid hydrolysis of the post-extraction solids did not solubilise significant portions of radioactivity (Table B.7.2-20).

Between 33 % and 80 % of the total radioactivity recovered could be identified. Besides the unchanged parent compound which accounted for 9-75 % of TRR, COE 538/78 and FCR 3145 were found as main metabolites, the highest levels being found in muscles, gizzard, skin and heart. FCR 2728 was only found in eggs (6 %) and in liver, kidney and fat (only in traces). Up to 40 % of the total radioactivity was not extractable. Acid hydrolysis released small portions of COE 538/78 and FCR 3134.

From enzymatic hydrolysis of the polar residues at the TLC origin, no detectable release of any aglycone was observed.

Table B.7.2-19: Radioactivity determined in different tissue and egg fractions after treatment with phenyl-UL-^{14}C-labelled cyfluthrin at 5 mg/kg bw/day (530N rate)

Tissue	**Acetonitrile**		**Hexane**		**Solids**		**Total**	
	% TRR	**mg/kg [1]**	**% TRR**	**mg/kg [1]**	**% TRR**	**mg/kg [1]**	**mg/kg**	**% TRR**
Liver	53	1.59	7	0.21	40	1.20	3.0 [3]	100
Kidney	54	2.54	7	0.33	39	1.83	4.7	100
Gizzard	85	1.36	1	0.02	14	0.22	1.6	100
Breast muscle	81	0.16	0	0	19	0.04	0.2	100
Skin	76	0.30	3	0.01	21	0.08	0.4	100
Leg/thigh muscle	82	0.25	0	0	18	0.05	0.3	100
Heart	79	0.32	2	<0.01	19	0.08	0.4	100
Fat Renal Subcut. Omental	80	- [2]	3	- [2]	17	- [2]	- [2] 0.2 0.1 0.2	100
Eggs [4] 24 hrs 48 hrs 72 hrs 96 hrs	60	0.03	15	<0.01	25	0.01	<0.01 (5 x <0.01) 0.01 (<0.01-0.01) 0.02 (<0.01-0.04) 0.05 (0.02-0.13)	100

[1] Calculated by RMS based on reported values for whole sample TRR (in mg/kg) and reported values for TRR in extracts (in %)

[2] Cannot be calculated, since TRR (in mg/kg) are given for each subsample, while TRR (in %) are reported on average

[3] average for five hens based on triplicate analyses for composite samples

[4] average; in brackets: range of residue levels

Table B.7.2-20: Radioactive residue distribution after acid hydrolysis (6N HCl) of solid fraction and partitioning against diethyl ether or chloroform/acetone (2:1) and identification of residues in organosoluble fraction

				% TRR			
			Organic		**Aqueous**	**Solids**	**Total**
	Total	**FPB_{acid} (COE 538/78)**	**4-OH-FPB_{acid} (FCR 3145)**	**TLC origin**	**Total**	**Total**	**Total**
Liver	4	<1	2	1	3	33	40
Kidney	5	1	2	2	7	27	39
Gizzard	4	1	1	2	1	10	15
Breast muscle	3	1	1	1	5	11	19
Skin	3	1	1	1	5	13	21
Leg/thigh muscle	3	1	1	<1	3	12	18
Eggs (96 hrs)	5	1	3	1	n.d.	n.d.	25

n.d. not determined

Table B.7.2-21: Distribution of radioactivity in organosoluble fractions (hexane and ACN extracts) from tissues and eggs of laying hens treated with phenyl-UL-^{14}C-labelled cyfluthrin in a dose of 5 mg/kg bw/d (530 N rate) for 5 successive days

	Liver	**Kidney**	**Gizzard**	**Breast**	**Skin**	**Leg/thigh**	**Heart**	**Fat**	**Eggs (96 hrs)**
	% TRR	% TRR	% TRR	% TRR	% TRR	% TRR	% TRR	% TRR	% TRR
Cyfluthrin	12	9	40	39	28	21	16	75	56
FPB_{acid} (COE 538/78)	12	11	13	15	19	21	26	3	4
4-OH-FPB_{acid} (FCR 3145)	10	12	11	11	13	20	19	0	7
COOH-cyfl. (FCR 2728)	1	1	0	0	0	0	0	2	6
Identified	35	33	64	65	60	62	61	80	73
Unknown 1	6	12	7	0	0	0	0	0	0
Unknown 2	4	1	0	0	0	0	0	0	0
TLC origin	15	15	15	16	19	20	20	3	2
Total	60	61	86	81	79	82	81	83	75

Conclusion

After administration of [phenyl-U-^{14}C]cyfluthrin at a rate of 5 mg/kg bw/day to laying hens, most of the residues were found in liver, kidney and gizzard, while residues in other tissues were low (0.1-0.4 mg/kg in muscles, fat) or even very low (≤0.05 mg/kg in eggs). Unextractables (after acid and enzymatic hydrolysis) accounted for 10-33 % TRR.

The main residue compounds were fat soluble cyfluthrin (ranging from 9 % in kidney to 75 % in fat), 4-OH-FPB_{acid} (not observed in fat; up to 21 % TRR in heart muscle) and FPB_{acid} (3 % TRR in fat and 26 % TRR in muscle).

The metabolic pathway observed for the phenyl-label is initiated by hydrolysis of the ester bond to lead to α-OH-FPB-ACN as unstable intermediate, which is assumed to form FPB_{acid} via FPB_{ald} (intermediate; not observed in chicken). FPB_{acid} undergoes hydroxylation at the 4`-position of the phenyl ring to form 4-OH-FPB_{acid}. The complete metabolic pathway for livestock animals is depicted in Figure B.7.2-5.

Severe limitations are observed in analytical and storage aspects that restrict the general applicability of the study results to additional information only, unless further information is provided to clarify the open points:
- No substantial analytical details are presented in the study report (no chromatograms, no autoradiograms)
- Low percentage of solid bound residues released by hydrolysis (Table B.7.2-20)
- Period of proven storage stability for animal matrices might be exceeded)) Table B.7.2.-21; sacrifice to date of study issue is 13 months; exact storage time not reported; no stability data for eggs)
- Storage conditions (-10 °C) not covered by storage stability studies (-23 °C).

Data point:	KCA 6.4.1 /02
Report:	[redacted] (1987): Biotransformation of Cyfluthrin in the chicken after oral adminstration of a high dose. Report No.: 15849, M-038063-01-1 TOX9401851
Guideline(s):	None stated. Not compliant to OECD 503.
Deviations:	Not relevant.
GLP:	No.
Acceptability:	Supporting information.

Materials and methods

The biotransformation of cyfluthrin in chicken (3 animals plus one control) was investigated after oral administration of unlabelled cyfluthrin at a high single dose of 3000 mg/kg bw (>300.000 N rate; isomer ratio I/II/III/IV = 25.1/19.5/32.9/22.5). No signs of toxicity were observed in the animals.

The excreta of birds was collected for 14 days after start of the study. Excreta were stored at -20 °C or immediately worked up after sampling.

Excreta were extracted with methanol for 7 hrs at 80 °C in a soxhlet apparatus. The extract was concentrated, the resulting aq extract partitioned into DCM three times. The aq phase was extracted at pH 6 and pH 2 with ethyl acetate. The organic phases were concentrated to near dryness and taken up

in methanol.

The structure of metabolites in the faeces was elucidated by mass and NMR spectra and co-chromatography with available standards. Isomeric changes of parent and metabolites were monitored.

Results

Identified metabolites
In addition to the parent compound (26-40 %), a total of more than 20 metabolites, whose structures could be elucidated, were found in the excreta collected in the 14-day period following the treatment.
FCR 3145, a corresponding dihydroxylated compound and 3-hydroxy-4-fluorobenzoic acid (a previously unknown metabolite in animal) were detected as main metabolites of the fluorophenyl fraction of the cyfluthrin molecule. All three metabolites occurred in both free and conjugated (glucuronide and sulphate) form.
No conjugates with amino acids were found. 1S-trans-permethric acid, the corresponding acid amide and the permethric acid derivatives oxidised at the methyl groups of the C2 of cyclopropane ring to the corresponding alcohol or acid were identified as main metabolites of permethric acid fraction.

Due to extremely high application rate, additional (intermediate) metabolites were identified (Table B.7.2-22), that are suitable to confirm the proposed metabolic pathway from the radiolabelled study in poultry (Chopade 1983; RIP9400869).

Table B.7.2-22: List of metabolites identified by means of mass and NMR spectrometry and/or co-chromatography with reference substances (rs) in hen after oral administration of unlabelled cyfluthrin at a rate of 3000 mg/kg bw (>300.000 N rate)

Metabolite nomenclature	Chemical name	Empirical formula
FCR 4150 (rs) M5	α-cyano-3-(4`-hydroxyphenoxy)-4-fluorobenzyl cis/trans-3-(2,2-dichlorvinyl)-2,2-dimethylcyclopropane-1-carboxylate)	$C_{22}H_{18}Cl_2FNO_4$
FCR 1271 (rs) M8	4-fluoro-α-hydroxy-3-phenoxybenzene acetonitrile	$C_{14}H_{10}FNO_2$
FCR 1260 (FPB aldehyde) (rs) M2	4-Fluoro-3-phenoxybenzaldehyde	$C_{13}H_9FO_2$
FCR 2899 (FPB acid; COE 538/78) (rs) M9	4-Fluoro-3-phenoxybenzoic acid	$C_{13}H_9FO_3$
FCR 4896 (rs) M19	(3-(4´-hydroxyphenoxy)-4-fluorobenzylalcohol)	$C_{13}H_{11}FO_3$
FCR 3137 (rs) M10	(3-(4´-hydroxyphenoxy)-4-fluorobenzaldehyde)	$C_{13}H_9FO_3$
FCR 3145 (4-OH-FPB acid) (rs) M16	3-(4'-Hydroxyphenoxy)-4-fluorobenzoic acid	$C_{13}H_9FO_4$
M17A	3-(3´-hydroxy-phenoxy)-4-fluorobenzoic acid	$C_{13}H_9FO_4$
M20 [a]		$C_{13}H_9FO_5$
M17C [a]		$C_{14}H_{11}FO_5$
M41 [a]		$C_{13}H_8FNaO_8S$
FCR 4209 [a] (rs) M14	3-Hydroxy-4-fluorobenzoic acid	$C_7H_5FO_3$
M unknown [a] (rs)		
M4 (rs)	Cis-permethric acid (DCVA)	$C_8H_{10}Cl_2O_2$
M6 (rs)	Trans-permethric acid (DCVA)	$C_8H_{10}Cl_2O_2$
FCR 5405 (rs) M17	Cis/trans-permethric acid amide	$C_8H_{11}Cl_2NO$
M7	Cis-OH, cis-permethric acid lactone	$C_8H_8Cl_2O_2$
M14C [a]		$C_8H_8Cl_2O_2$
FCR 4093 (rs) M7/1	Trans-3-2,2-dichlorovinyl)-cis-2-hydroxymethyl-trans-2-methyl-cyclopropane-1-carboxylic acid lactone	$C_8H_8Cl_2O_2$
M21B	Cis-OH, cis-methyl permethric acid	$C_8H_{10}Cl_2O_3$
M21A	Cis-OH, cis-methyl permethrate	$C_9H_{12}Cl_2O_3$
M18A	Trans-OH, trans-permethric acid	$C_8H_{10}Cl_2O_3$
M32	Methyl trans-OH, trans-or cis-permethrate	$C_9H_{12}Cl_2O_3$
M32A	Trans-COOH, trans- or cis permethric acid	$C_9H_{10}Cl_2O_4$

[a] partly or fully unreadable in the original report (empirical formula given, where possible)
rs: reference substance

Change of isomer ratio

No significant change in the isomer ratio was observed from cyfluthrin I+III→ II+IV (**Figure B.7.2-3**). Increased scattering of data from day 8 onwards can be attributed to the already almost complete excretion of applied cyfluthrin (>99.9 %).

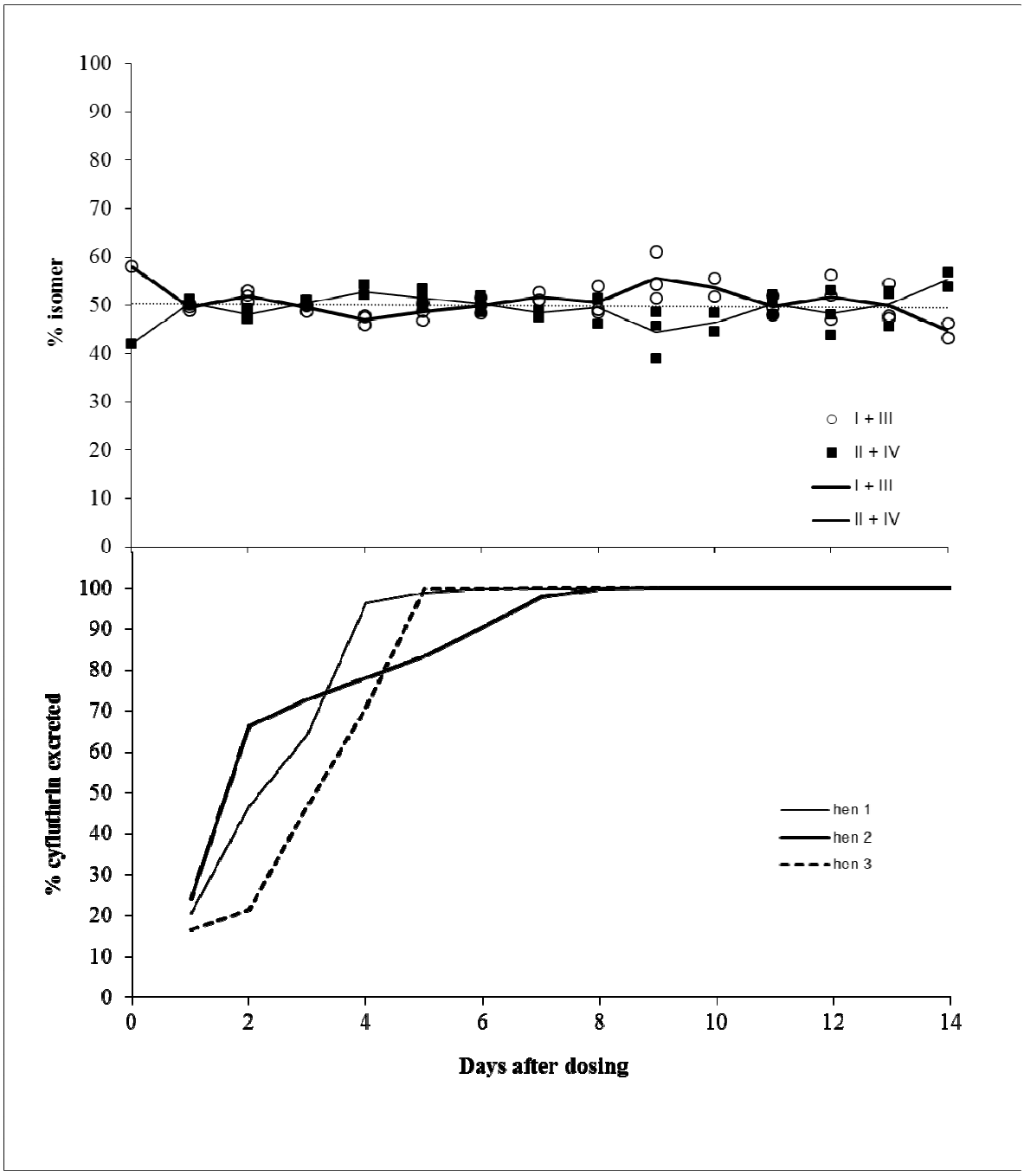


Figure B.7.2-3:Isomer ratio of cyfluthrin in hen after oral administration of 3000 mg/kg bw (>300.000 N rate)

Conclusion

The biotransformation observed in this study confirms the findings from the study Chopade (1983; RIP9400869). In this extreme high-dose study, some intermediates were identified, that were not observed in the radiolabel metabolism study at lower dosage. Although without GLP status, the study is of additional value in interpreting and extending the findings from other livestock metabolism studies.

No significant change in the isomer ratio from I+III (cyfluthrin type) → II+IV (beta-cyfluthrin type) is observed.

As some substantial information on metabolites is partly not readable in the report, the applicant is requested to update the metabolic pathway in animals comprising information from all livestock metabolism studies and rat.

B.7.2.2 Lactating ruminants

Data point:	KCA 6.2.3 /01
Report:	[redacted] (1983): Metabolism of Baythroid in a dairy cow (1st revision 15.10.1984: correcting value; 2nd revision 05.08.1985: Modification of liver residue identification) MR86043, M-052654-01-1 RIP9400870
Guideline(s):	None stated. Not compliant to OECD 503.
Deviations:	Not relevant.
GLP:	No.
Acceptability:	Tentatively acceptable pending confirmation of storage stability.

Materials and methods

The test material was prepared by dissolving 60.8 mg of [phenyl-U-^{14}C]cyfluthrin (radiochemical purity 98.5 %; specific activity 21.74 mCi/mmol; ratio of isomers not reported) and 186 mg unlabelled cyfluthrin (98 % chemical purity) in diethylether. The specific activity was therefore reduced to 5.83 mCi/mmol.

One dairy cow (484 kg bw) was treated orally with gelatin capsules containing the phenyl-UL-^{14}C-labelled cyfluthrin in a dose of 0.5 mg/kg body weight per day for 5 successive days (77N and 23N rate for meat and dairy ruminants, respectively; for dietary burden calculation see Table B.7.4-3). The doses were given after evening milking.

Milk was collected twice daily. All samples were radioassayed. Aliquots were extracted three times with acetone/chloroform (2:1). The combined extracts were concentrated to dryness, dissolved in hexane, and partitioned into acetonitrile. Both fractions were radioassayed. ACN fraction was concentrated, radioassayed and subjected to TLC and HPLC.

The cow was sacrificed on the sixths day within 24 hours after dosing. Samples of brain, heart, liver, kidney, fat (omental, subcutaneous, renal) and muscle (round, flanc, loin) were collected. Aliquots were homogenised and stored in a freezer. All samples were radioassayed.
Aliquots of samples (except fat) were extracted with acetone/chloroform (2:1). 2 ml of HCl were added to kidney/liver samples. The filtrate was evaporated and the residue subjected to hexane/ACN partitioning (as for milk). ACN fraction was concentrated, radioassayed and subjected to TLC and HPLC.

Aliquots of fat were homogenised in hexane, filtered, the filter cake repeatedly blended with ACN. The homogenate was filtered, and the filtrate partitioned with hexane. The hexane and combined ACN fractions were radioassayed. The ACN fraction was concentrated, radioassayed and subjected to TLC

The extracts were applied along with the following non-labelled reference standards:

- cyfluthrin (FCR 1272),
- COOH-cyfluthrin (FCR 2728),
- Me-cyfluthrin (FCR 2956),
- $CONH_2$-cyfluthrin (FCR 2978),
- FPB amid (FCR 2947),
- Me-FPB acid (COE 263/78),
- FPB acid (COE 538/78),
- FPB aldehyde (FCR 1260),
- FPB alcohol (FCR 1261),
- 4´-hydroxy FPB acid (FCR 3145),
- FPB (FCR 3030),
- α-hydroxy FPB acetonitrile (FCR 1271).

Confirmation of nature of residues in liver was confirmed by GC/MS analysis. Analyses were performed within 6 months after sacrifice (period between dosing and report finalisation; exact dates and storage temperature is not reported).

Results

The maximum detected residues in milk was 0.079 mg/kg, all other values were only reported graphically. A rough estimate on total residue levels is made by RMS (Table B.7.2-23). A plateau was reached after approximately 3 days of dosing. Analysis of the milk showed that 98 % of TRR was organosoluble and consisted on parent cyfluthrin only.

Table B.7.2-23: Radioactive residues in milk from a dairy cow dosed for 5 consecutive days with cyfluthrin at 0.5 mg/kg bw/day (23N rate)*

	TRR in milk (mg/kg)
12 hrs after 1st dose	*0.02* [a]
24 hrs after 1st dose	*0.04* [a]
12 hrs after 2nd dose	*0.05* [a]
24 hrs after 2nd dose	*0.06* [a]
12 hrs after 3rd dose	*0.06* [a]
24 hrs after 3rd dose	0.079
12 hrs after 4th dose	*0.06* [a]
24 hrs after 4th dose	*0.07* [a]
12 hrs after 5th dose	*0.05* [a]

[a] estimated from a graphical representation in the original report
*98 % of TRR in milk identified as parent

TRRs in tissues and individual residue levels are given in Table B.7.2-24. Total residues for tissues were found in the range of 0.021 (muscle, round) to 0.622 mg/kg (liver). In brain, 0.015 mg/kg were found. Extractability of residues is high (93-100 %). Two metabolites were major compounds in heart and kidney ($FPB_{alcohol}$ 29-43 %) and liver ($FPB_{aldehyde}$ 14 %).

However, based on proven instability of cyfluthrin residues in liver and kidney samples obtained from this metabolism study, it cannot be excluded that the identified metabolites are products of storage degradation within the first 6 months after sacrifice (Table B.7.1-10, p. 34). No conclusive statement is possible in absence of exact analysis dates.

Conclusion

After administration of [phenyl-U-^{14}C]cyfluthrin at a rate of 0.5 mg/kg bw/day (77N and 23N rate for meat and dairy ruminants), most of the residues were found in liver, fat and kidney, while residues in muscle (including heart) were low (0.021-0.04 mg/kg). Unextractables accounted for <10 % TRR.

The main residue compound was cyfluthrin.
$FPB_{alcohol}$ (FCR 1261) and $FPB_{aldehyde}$ (FCR 1260) were detected as major metabolites in kidney and liver. However, based on storage stability investigations with samples apparently obtained from this metabolism study ([redacted] 1983, ASB2009-1452; Table B.7.1-10, p. 34), it cannot be excluded that these metabolites are product of storage degradation.

Limitations are observed in analytical and storage stability aspects that restrict the general applicability of the study results to additional information only unless further information on storage stability is provided. Limitations are:

- Instability of residues during frozen storage cannot be excluded
- Attribution of HPLC peaks for liver and kidney is not traceable
- Non-GLP

Table B.7.2-24: Radioactivity determined in different tissues after treatment of a dairy cow with phenyl-UL-^{14}C-labelled cyfluthrin at 0.5 mg/kg bw/day (77N rate)

	Muscle						**Fat**						**Heart**		**Kidney**		**Liver**	
	Round		Shoulder		Loin		Renal		Subcutaneous		Omental							
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Cyfluthrin FCR 1272	99	0.022 [a]	98	0.021[a]	100	0.028 [a]	100	0.229 [a]	93	0.113 [a]	96	0.225 [a]	71	0.028 [a]	56	0.105 [a]	86	0.535 [a]
FPB aldehyde FCR 1260	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	14	0.087 [a]
FPB alcohol FCR 1261	-	-	-	-	-	-	-	-	-	-	-	-	29	0.011 [a]	43	0.081 [a]	-	-
Unextract-able [b]	1	<0.01 [a]	2	<0.01 [a]	-	-	-	-	7	<0.01 [a]	4	<0.01 [a]	-	-	1	<0.01 [a]	-	-
Total	100	0.022	100	0.021	100	0.028	100	0.229	100	0.122	100	0.234	100	0.040	100	0.188	100	0.622

[a] Calculated by RMS based on reported values for whole sample TRR (in mg/kg) and reported values for TRR (in %)
[b] Unextractables calculated by RMS (100% – extractables)

Data point:	KCA 6.5.3 /20
Report:	[redacted] (1993): Distribution of radioactive residue in milk following oral dosing of a dairy cow for 5 consecutive days with (Phenoxy-UL-^{14}C) cyfluthrin MR103221, M-060766-01-1 RIP9401069
Guideline(s):	None stated. Not compliant to OECD 503.
Deviations:	Not relevant.
GLP:	Yes.
Acceptability:	Acceptable.

Materials and methods

The test material was prepared by dissolving 0.16 g of [phenyl-U-^{14}C]cyfluthrin (radiochemical purity >99 %; specific activity 55.64 mCi/mmol; ratio of isomers not reported) and 1.28 g unlabelled cyfluthrin (95.2 % chemical purity) in ethyl acetate. The specific activity was therefore reduced to 6.054 mCi/mmole.

One dairy cow (511 kg bw) was treated orally with gelatin capsules containing the phenyl-UL-^{14}C-labelled cyfluthrin in a dose of 0.5 mg/kg body weight per day for 5 successive days (23N rate for dairy cows). The doses were given following afternoon milking.

Only one milk sample following the fith dose was collected. Whole milk was separated into cream and whey. Samples were radioassayed in triplicate. Butterfat was separated from whole milk with organic solvent extraction. The resulting hexane extract was radioassayed.
Aliquots of whole milk were extracted by hexane/acetonitrile and partitioned with acetonitrile. The ACN fraction was radioassayed, concentrated to dryness, taken up by hexane or acetone and subjected to TLC (normal and reverse-phase).

Results

Whole milk had residues of 0.05 mg/kg. The entire residue was identified as parent cyfluthrin (thereby demonstrating stability of cyfluthrin in milk over the entire storage period of at least 39 months (period between dosing and first extraction). Extraction efficiency amounted to 86-100 %, while recovery from the TLC plates was 89-99 % of applied radioactivity.

Following centrifugation of milk, 82 % of TRR was associated with cream (1.28 mg/kg), indicating a concentration factor of 26 (based on mg/kg). For butterfat, a concentration factor of 79 was determined (3.94 mg/kg).

Conclusion

The study quantitatively describes the concentration of cyfluthrin residues in milk fat (cream, butterfat) and supports the storage stability of cyfluthrin in milk over a period of at least 39 months. Results are fully in accordance to those of Shaw et al. (1983; RIP9400870; Table B.7.2-23) and de Bie et al. (2014, ASB2014-7899, Table B.7.2-26 and Table B.7.2-28).

Data point: KCA 6.2.3 /14

Report: [redacted] (2014): Metabolism and disposition of beta-cyfluthrin using [cyclopropane-1-^{14}C]beta-cyfluthrin in the lactating goat
Report 20236, M-481993-01-1, R-30158
ASB2014-7899

Guideline(s): OECD 503

Deviations: None.

GLP: Yes.

Acceptability: Acceptable

Materials and methods

Test material:	
Common name	Beta-cyfluthrin
Molar mass	434.29
Labelling	[cyclopropane-1-^{14}C]
Specific radioactivity	3.27 MBq/mg = 38.5 mCi/mmol
Radiochemical purity	> 98 % (HPLC, sum of isomers)
Dose level	Goat A: 0.11 mg/kg bw/day for 7 days Goat B: 1.0 mg/kg bw/day for 7 days

Test Animals:	
Species:	Lactating goat (*Capra hircus*)
Strain:	White Saanen Goat
Sex and numbers involved:	2 female animals
Age:	ca. 1.5 years
Body weight (period before dosing – prior to sacrifice):	Goat A: 53.4-54.2 kg Goat B: 59.3-57.6 kg

Two goats were orally dosed daily in the morning after milking for 7 consecutive days with 0.11 and 1.0 mg/kg bw/d (5N or 17N and 46N or 155N rate for dairy or beef ruminants, respectively).

Sampling and analysis
Milk was collected twice daily 6 and 22 h after each dose. Sub-samples were stored at 2-10ºC until analysis of radioactivity. The remaining milk was directly frozen (<-18ºC) for possible metabolite profiling. Aliquots of whole milk were separated in fat and aqueous phase.
Blood samples were collected approximately 1 h before the 2nd, 4th and 7th dose and 2, 4, 6 and 22 hours after the 7th dose. Plasma samples were taken for analysis of radioactivity.
Urine and faeces were collected twice daily during the study just after milking up to sacrifice. Aliquots of urine were taken for analysis of radioactivity. Faeces were pooled in 24 h intervals and homogenised before analysis. Aliquots of homogenised faeces stored at room temperature until combustion. Subsamples of the urine and faeces were stored at < -18ºC.

The goats were sacrificed within 22 hours after the final dose administration. Liver, kidneys, loin and flank muscle (separately), subcutaneous, omental and renal fat (separately), bile and contents of the complete GI tract were collected.
After sacrifice, the cages were rinsed and aliquots were taken for analysis. Tissues were homogenised using a blender prior to storage. All samples were stored at <-18 ºC. Analyses were terminated within 79 days after sacrifice. Between collection of organs/tissue and homogenisation, organs were placed in a refrigerator (2-10 °C).

Radioactivity was determined in all collected samples by LSC (dose formulations, urine, cage wash, bile, plasma, whole milk, milk fat aqueous milk phase, fat, muscle, liver, kidney, GI tract contents, faeces and blood.

Final extracts of milk, tissues and samples of urine were were profiled where possible on HPLC with UV-detector and coeluted with reference compounds.

Urine pools were prepared for each animal by pooling 1 % of each of the urine samples. The urine pools were counted for radioactivity before and after centrifugation to check for unsoluble radioactivity. The centrifuged samples were profiled on HPLC. Urine samples were spiked with the [^{14}C]-beta-cyflutrin and with non-labelled permethrin (DCVA) and cyflutrin.

To evaluate the presence of glucuronide or sulphate conjugates urine was incubated with either β-glucuronidase or sulphatase. After centrifugation, the supernatants were analysed by HPLC.

Faeces were pooled and homogenised with tetrahydrofuran (THF). The sample was centrifuged and the supernatant was collected. The resulting pellet was again extracted with THF, centrifuged and the supernatant was added to the first one. The THF was removed and the resulting pellet was resuspended in THF and DMSO. These extracts were analysed by HPLC. Faeces samples were spiked with the [^{14}C]-beta-cyflutrin and with non-labelled permethrin (DCVA).

Organs, tissues and milk of goat A were used for metabolite profiling and identification as residues in goat B were only 2-3 fold higher. Samples of kidney or liver were extracted with acetonitrile. The sample was centrifuged and the supernatant was collected. The resulting supernatant was extracted with n-hexane. The two layers (acetonitrile and hexane) were separated and the radioactivity in both layers was determined using LSC. The pellet was extracted with n-hexane and thereafter the pellet was treated with 1 M ammonia. Radioactivity in all phases was determined. As the extraction recovery was too low and because the extracted radioactivity in the acetonitrile layer could not be cleaned-up, it was not possible to inject the resulting extracts on the HPLC system.
Finally, a harsher acid extraction method was used to extract radioactivity from the liver and kidney tissue. Liver and kidney homogenate were hydrolysed for 20 minutes at 100 °C with 2.5M HCl. The sample was centrifuged at, the water phase was extracted at neutral conditions with acetonitrile and the remaining pellet following hydrolysis was extracted with acetonitrile.

Milk samples (goat A) collected from 22h after the 5th dose (M10) to 6h after the 7th dose (M13) were pooled. This pool was centrifuged and the fat separated from the aqueous fraction. Two samples of milk fat of goat A were extracted with acetonitrile. The sample was centrifuged and the supernatant collected. The resulting pellet was again extracted with acetonitrile and after centrifugation the supernatants were mixed. Radioactivity in the pellet was determined. The resulting supernatants of both samples were combined and extracted twice with n-hexane. The two layers (acetonitrile and hexane) were separated and the radioactivity in both layers was determined using LSC. The acetonitrile layer was evaporated and the resulting pellet was re-suspended in a mixture of acetonitrile and DMSO. The resulting sample was injected on the HPLC system.

Omental fat and renal fat of goat A were pooled. Subcutaneous fat was not included as the amount of radioactivity was below 0.01 mg/kg. The pooled fat was extracted with n-hexane. The n-hexane was extracted twice with acetonitrile. The two layers (acetonitrile and hexane) were separated and the radioactivity in both layers was determined using LSC. No extracts were further analysed on the HPLC system.

Metabolites in pooled urine and pooled faeces extract were identified using LC-MS. The samples were stored (-18 °C) until analysis. Non-labelled permethric acid (DCVA) and cyfluthrin were used as reference standards.

The most abundant metabolites of beta-cyfluthrin observed with LC-UV radioactivity detection in the

urine and faeces were identified using high-resolution liquid chromatography-photo diode array-mass spectrometry (LC-PDA-HRMS).

Results

Mass balance
The recovery of radioactivity is presented in Table B.7.2-25. In total 92.0 % (goat A) and 77.9 % (goat B) of the dosed amount of radioactivity was recovered within 22 h after the final dose. The relatively low recovery for goat B is most likely due to reduced absorption and the high dose and inhomogeneous distribution of radioactivity in the faeces and gastro intestinal tract of goat B.
A full mass balance was not obtained as only parts of the organs and tissues were sampled and analysed, not the complete animal.

Table B.7.2-25: Final distribution of residues in milk, muscle, fat, liver and kidney of lactating goats following oral administration of 7 daily doses of [cyclopropane-1-^{14}C]beta-cyfluthrin at a dose rate of 0.11 mg/kg bw/d or 1.0 mg/kg bw/d

Sample		Percent of total dose administered	
		Goat A (0.11 mg/kg bw/d)	Goat B (1.0 mg/kg bw/d)
Total urine		64.62	8.12
Total Faeces		19.85	62.84
Cage wash		0.56	0.32
GI-tract with contents		6.96	6.67
Milk (total)		0.201	0.037
Liver		0.065	0.023
Kidneys		0.021	0.003
Terminal blood		0.128	0.077
Muscle	loin (20 % BW)	0.081	0.015
	flank (25 % BW)	0.12	0.046
Fat	subcutaneous (5 % BW)	0.062	0.013
	omental (5 % BW)	0.105	0.018
	renal (5 % BW)	0.117	0.017
Bile		0.0013	0.0006
Total recovery (%)		**91.99**	**77.94**

Excretion of radioactivity
After the third dose, the urinary excretion reached a plateau of 65 % total radioactive dose for goat A. For goat B only 8 % was excreted in the urine, indicating that absorption was much lower. The faecal excretion reached plateaus of 20 % for goat A and 60-70 % for goat B (see Figure B.7.2-4). The gastro-intestinal tract contained ca 7 % of the administered radioactivity 22 h after the final dose. The excretion in milk accounted for approximately 0.20 % and 0.04 % in goat A and B, respectively. The major part of radioactivity was present in the fat phase of the milk (goat A: 30 times higher radioactivity in milk fat compared to water phase and 10 times higher compared to whole milk).

Blood and plasma kinetics
Both the low and high dose animal showed a plateau reached within 72 hours (Figure B.7.2-4). C_{max} values of 22.7 and 43.1 µg/kg in blood occurred at 6 h after the 7th dose in goat A and B, respectively, indicating that goat B had a much lower absorption, since the dose was 10 times higher. In plasma,

C_{max} values were slightly higher, 28.7 and 52.8 µg/kg in goat A and B, respectively. Total radioactivity in blood at sacrifice was low, 0.13 and 0.08 % in goat A and B, respectively.
Results of excretion and blood kinetics indicate saturation of the absorption at high dose.

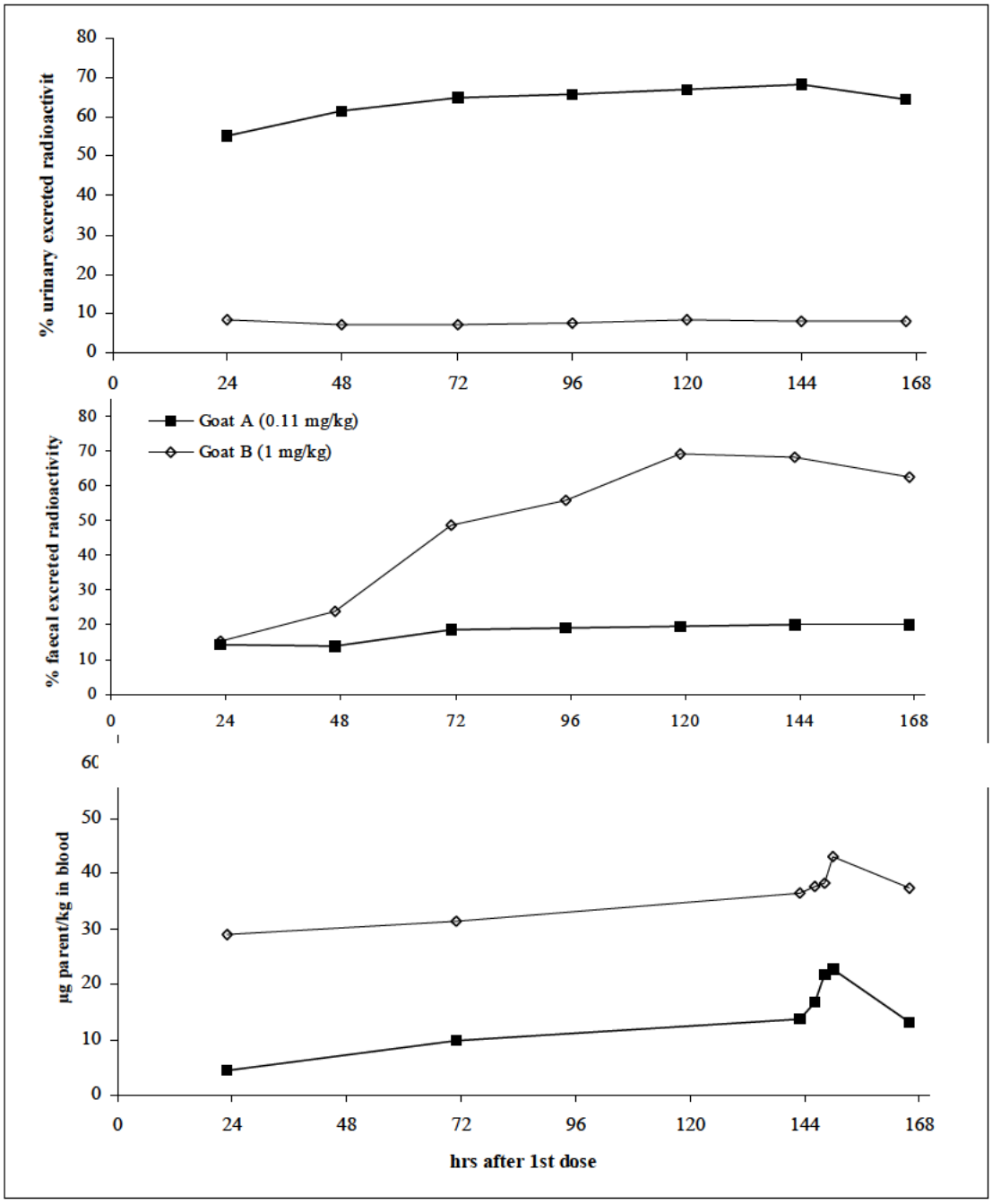


Figure B.7.2-4: Cumulative urinary and faecal excretion and blood levels of lactating goats after treatment of 7 daily doses of [cyclopropane-1-^{14}C]beta-cyfluthrin at a dose rate of 0.11 mg/kg or 1.0 mg/kg (pooled samples taken immediately before dosing)

Residues in milk
TRR in whole milk of goat A (dose rate 0.11 mg/kg bw/d) were found in the range of 0.005-0.012 mg/kg, for goat B (dose rate 1 mg/kg bw/d) in the range of 0.008-0.025 mg/kg. Plateau was already reached within 2 days after dosing. Pronounced fat solubility is confirmed. Residue levels in high dose animals are higher and adequately reflect the differences in blood residue levels (but not higher application rate due to the saturation of absorption; Figure B.7.2-4). The entire radioactivity is attributed to parent (identified in milk fat; >90 % of radioactivity in ACN fraction).

Table B.7.2-26: Distribution of radioactivity in milk after treatment of 7 daily doses of [cyclopropane-1-^{14}C]beta-cyfluthrin at a dose rate of 0.11 mg/kg (5N rate) or 1.0 mg/kg (46N rate)

	Goat A (0.11 mg/kg)			**Goat B (1.0 mg/kg)**		
	TRR (mg/kg)			TRR (mg/kg)		
Sample	Whole milk	Fat phase	Water phase	Whole milk	Fat phase	Water phase
6 h after 1st dose (M1)	0.007	0.073	0.003	0.008	0.042	0.004
22 h after 1st dose (M2)	0.005	0.065	0.001	0.021	0.280	0.008
6 h after 2nd dose (M3)	0.006	0.057	0.002	0.018	0.184	0.007
22 h after 2nd dose (M4)	0.008	0.101	0.002	0.011	0.128	0.004
6 h after 3rd dose (M5)	0.012	0.117	0.004	0.013	0.085	0.006
22 h after 3rd dose (M6)	0.007	0.086	0.002	0.019	0.201	0.009
6 h after 4th dose (M7)	0.009	0.071	0.003	0.017	0.146	0.007
22 h after 4th dose (M8)	0.008	0.100	0.002	0.019	0.209	0.008
6 h after 5th dose (M9)	0.009	0.076	0.003	0.020	0.168	0.010
22 h after 5th dose (M10)	0.007	0.107	0.002	0.020	0.262	0.007
6 h after 6th dose (M11)	0.010	0.099	0.003	0.025	0.238	0.008
22 h after 6th dose (M12)	0.008	0.116	0.002	0.015	0.163	0.006
6 h after 7th dose (M13)	0.010	0.088	0.003	0.019	0.169	0.008
22 h after 7th dose (M14)	0.006	0.062	0.002	0.018	0.155	0.005

Residues in organs and tissues
Radioactive residue levels in organs and tissues are summarised in Table B.7.2-27. TRRs in muscle of goat A (0.11 mg/kg bw) was below 0.01 mg/kg, in the other matrices between 0.01 and 0.054 mg/kg. TRRs in goat B (9 times higher dose rate) were approximately 2-3 times higher, i.e. non-linear increase as indicated by reduced absorption (Figure B.7.2-4).

Table B.7.2-27: Total radioactive residues in organs and tissues after repeated dosing of [cyclopropane-1-^{14}C]beta-cyfluthrin at a dose rate of 0.11 mg/kg or 1.0 mg/kg (17N or 155N rate)

Sample	**Goat A (0.11 mg/kg)**	**Goat B (1 mg/kg)**
	TRR (mg/kg)	TRR (mg/kg)
Kidneys	0.054	0.086
Liver	0.030	0.087
Fat (subc./omental/renal)	0.009 / 0.015 / 0.017	0.021 / 0.028 / 0.026
Muscle (loin/flank)	0.003 / 0.003	0.006 / 0.014

The sum of TRRs in liver, kidneys, terminal blood, muscle and fat was low and accounted for ca. 0.70 % and 0.21 % of the administered dose in goat A and B, respectively (Table B.7.2-25), indicating low absorption and/or fast depletion in organs and tissues. Like for milk, residue levels in high dose animals are higher at the ratio of blood residue levels (Figure B.7.2-4).

Metabolite profiling and identification
Extraction procedures were developed for characterisation of residues in urine, faeces, liver, kidney,

milk (fat phase), omental and renal fat. Radioactivity in muscles was not profiled (TRR <0.01 mg/kg). Organs, tissues and milk of goat A were used as the residues in goat B were in general only 2-3 times higher.
The final extracts were profiled on HPLC where possible (urine, faces, milk, fat) and co-eluted with reference compounds. For urine, faeces, milk (fat phase), omental and renal fat, the % recoveries in the extracts were above 90 %, but not for liver and kidney. The maximal total recovery of solvent extracted radioactivity was 75.2 % for liver and 36.2 % for kidney. For liver and kidney several harsh extraction methods were tried.
The most abundant metabolites of beta-cyfluthrin observed with LC-UV radioactivity detection in the urine and faeces were identified using LC-PDA-HRMS.
Some non-labelled unknown metabolites were screened for and subsequently identified using high resolution LC-ESI-HRMS in both the positive and negative ionisation mode. From these data the elemental composition of the metabolites could be determined and a proposal was made for the chemical structure of the unknown metabolites.
An overview of the distribution of total radioactive residue and metabolites in urine, faeces, milk fat and renal/omental fat (goat A) is presented in Table B.7.2-28.

Table B.7.2-28: Distribution of total radioactive residue (beta-cyfluthrin equivalents) and metabolites in urine, faeces, milk fat and renal/omental fat (goat A; 0.11 mg/kg bw/d)

Metabolite	Identity	% total dosed radioactivity*			
		Urine	Faeces	Milk (fat phase)	Renal/ Omental fat
M1	Unidentified	6.33			
M2	DCVA-OH	13.44			
M3	Glucuronic acids of permethric acid (DCVA)	3.13			
M4		19.43			
M5		3.69			
M6		12.30			
M7a	Permethric acid (DCVA)	4.87	2.92		
M7b		1.45	0.93		
M8	Unidentified		0.72		
M9	Cyfluthrin-amide (FCR2978 $CONH_2$)		2.39		
M10			1.02		
M11	Unidentified				0.04
M12	Unidentified				0.08
Parent	Beta-cyfluthrin		11.26	0.09	0.11
M13	Unidentified		0.62		
Sum identified compounds		77.0 %			

* Kidney/liver: too low recovery for identification

For kidneys (TRR 0.054 mg/kg) and liver (0.030 mg/kg, both at at a dose of 0.11 mg/kg bw/d), the extraction recovery was too low, and because the extracted radioactivity in the acetonitrile layer could not be cleaned-up, it was not possible to inject the resulting extracts on the HPLC system. After acid extraction of kidney and liver and fractioning into pellets, ACN and supernatants, the ACN fractions could not be injected into HPLC due to high viscosity. The amount of radioactivity in the supernatant following hydrolysis represents polar metabolites of beta-cyfluthrin, most likely permethric acid derived polar metabolites. The radioactivity in the acetonitrile fraction following extraction of the

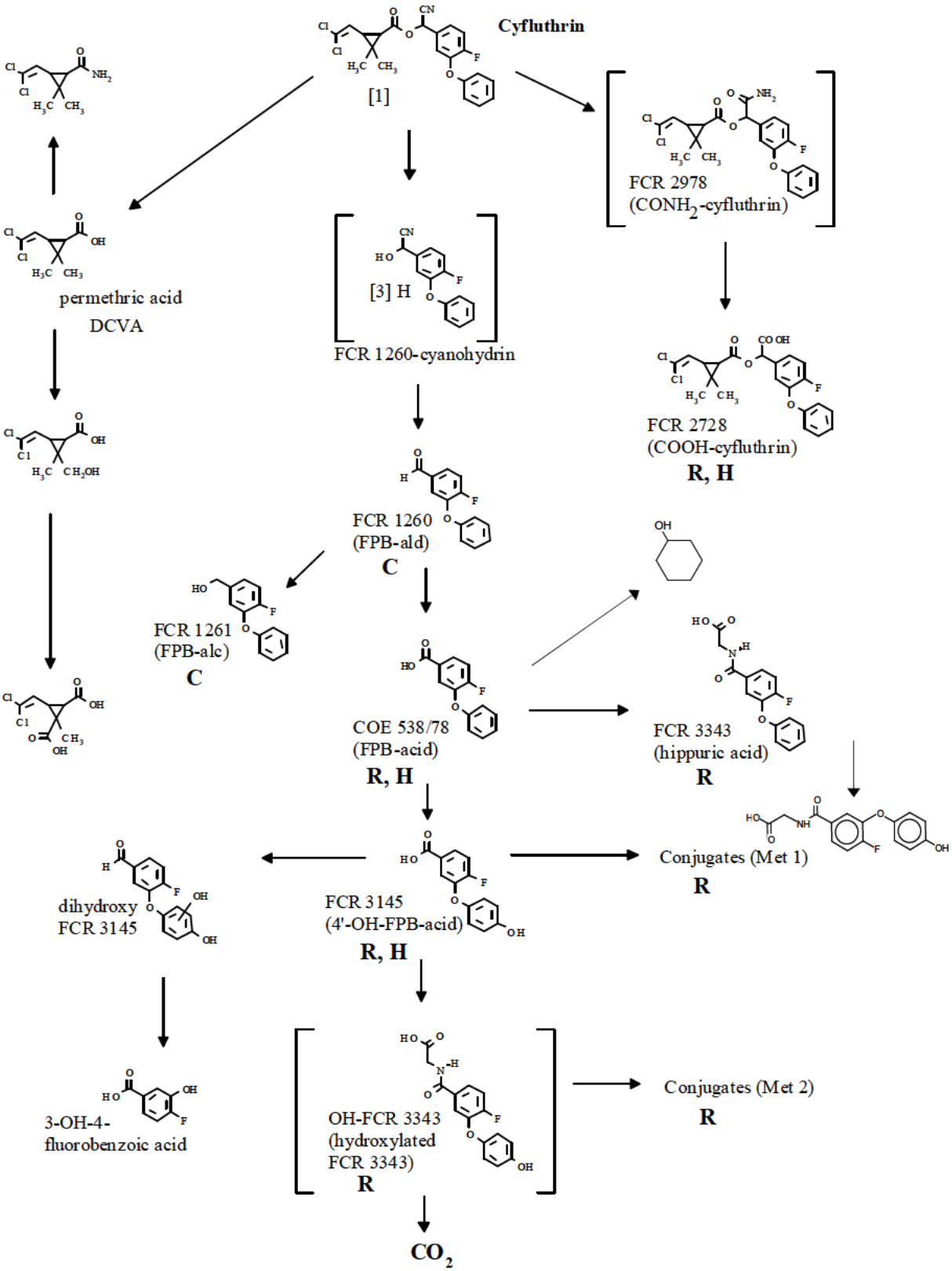
pellet most likely represent structures like cyfluthrin, cyflutrin-amide or permethric acid.

LC-MS analysis
Unknown metabolites of cyfluthrin in pooled urine and faeces extract of goat A and B were observed with LC-UV-Radioactivity detection. Besides the labeled unknown metabolites also additional metabolites which do not contain the labeled cyclopropane-ring were detected. Some non-labelled unknown metabolites were screened for and subsequently identified using high resolution LC-ESI-HRMS in both the positive and negative ionization mode.
The following metabolites are detected in the pooled urine Goat B sample: phenol sulphate and phenol glucuronide, OH-FCR 3343, FCR 3145, 4'-OH-FPBacid, FCR 3343 hippuric acid, COE 5338-78 FBP_{acid} and FCR 1271.

Conclusion

At a relevant daily dose with 0.11 mg as/kg bw for 7 consecutive days, the TRR in milk was 0.005-0.012 mg/kg and in edible tissues 0.030 mg/kg (liver), 0.054 mg/kg (kidneys), 0.003 mg/kg (muscle) and 0.009-0.017 mg (fat).
The residual radioactivity in milk reached a plateau within 2 days.
The extraction efficiency for urine, faeces, milk (fat phase), omental and renal fat were above 90 %, except for liver and kidney. The maximal total recovery of solvent extracted radioactivity was 75.2 % for liver and 36.2 % for kidney.
The amount of metabolites that could be identified and characterised in urine, faeces, milk fat, renal and omental fat was 77 % of the applied low dose. In addition, non-labelled metabolites of beta-cyfluthrin were identified in the urine and faeces of the low dose goat using LC-ESI-HRMS in both the positive and negative ionisation mode.
The [^{14}C]-labelled metabolites of beta-cyfluthrin excreted with faeces were permethric acid and cyfluthrin-amide (FCR 2978 $CONH_2$-cyfluthrin). The [^{14}C]-labelled metabolites of beta-cyfluthrin excreted with urine were permethric acid, permethric acid glucuronide conjugates and hydroxylated permethric acid.
Besides the labeled unknown metabolites also additional metabolites, which do not contain the labeled cyclopropane-ring, were detected in urine; phenol sulphate, phenol glucuronide, OH-FCR 3343, FCR 3145 4'-OH-FPB_{acid}, FCR 3343 hippuric acid, FBP_{acid} and FCR 1271.

Figure B.7.2-5: Metabolic pathway of cyfluthrin in livestock animals[6]



[6] Remarks: FCR 1260 cyanohydrin = FCR 1271 (unconjugated and gluc-conjugated); phenol (gluc- and sulphate-conjugated), DCVA (gluc-conjugated) and OH-FCR 3343 identified by LC-EIS-HRMS; additional metabolites from Eben et al. (1987; TOX9401851) not yet considered in pathway scheme

B.7.2.3 Pigs

No metabolism study available for pigs and none required, since the metabolite patterns in rodents (rats) and ruminants (goat, cow) is considered as similar.

B.7.2.4 Fish

Data point:	KCA 6.2.5/04
Report:	[redacted] (2014): [^{14}C]beta-Cyfluthrin: Metabolism Study in Rainbow Trout (Oncorhynchus mykiss) Report D78924, M-481603-01-1, R-33353 ASB2014-7897
Guideline(s):	Draft Working Document on Nature of Residues in Fish, Revision 3, 30. Jan. 2013, SANCO/11187/2013
Deviations:	None
GLP:	Yes
Acceptability:	Acceptable

Materials and methods

Common name	Beta-cyfluthrin
Label 1	[cyclopropane-1-^{14}C]beta-cyfluthrin
Specific radioactivity used for administration	3.27 MBq/mg = 88.44 µCi/mg
Radiochemical purity	98.9 % (HPLC, sum of isomers)
Dose level	11.7 mg/kg diet
Label 2	[fluorophenyl-UL-^{14}C]beta-cyfluthrin
Specific radioactivity used for administration	4360 kBq/mg = 117.9 µCi/mg)
Radiochemical purity	99.7 % (HPLC, sum of isomers)
Dose level	10.6 mg/kg diet
Species:	Common rainbow trout (*Oncorhynchus mykiss*)
Numbers involved:	5 fish per label group and 5 fish in control group
Body weight:	Label 1 group At the start of the test: 191.3-228.6 g (mean 215.3 g) At the day before dosing: 264.6-296.3 g (mean 277.1 g) At day 14 of dosing: 173.4-274.6 g (mean 243.0 g) Label 2 group At the start of the test: 217.3-267.6 g (mean 242.6 g) At the day before dosing: 219.7-267.8 g (mean 245.6 g) At day 14 of dosing: 201.3-250.4 g (mean 229.2 g)

Dosing
Two groups each with five fish were fed daily for 14 days with an appropriate fish diet. The feed was spiked with either [cyclopropane-1-^{14}C] beta-cyfluthrin or [fluorophenyl-UL-^{14}C] beta-cyfluthrin. Initially, one daily portion was fed. Because the fish did not consume the complete amount of the provided diet, starting with 9th feeding, the feed was provided in two portions to the fish, one portion in the morning, the second portion in the afternoon. The last feeding was at 312 hours (13 days) after the first feeding.
One control group of five fish was fed accordingly with feed containing no test item.

Sacrifice and dissection of organs and tissues
Six hours after the last feeding, the fish were sacrificed. The total intestinal tract was removed from the fish, but not further analysed. Muscle (including skin) and liver (without gall bladder) were collected. The tissues were shortly washed under flowing tab water to remove any attached blood. The individual samples were stored at -20 °C until homogenisation and TRR determination.
The gall bladder was collected at sacrifice from all fish and stored at approximately -20 °C for potential metabolite characterisation work.

Extraction
The homogenised *liver* tissue was extracted three times with acetone/water (80/20, v/v), followed by one extraction with methanol/ water (80/20, v/v), two extractions with acetone/water (80/20, v/v) under acidic conditions and a Soxhlet extraction with methanol.

All extracts except the Soxhlet extract were pooled and concentrated at approximately 40 °C. Water and acetonitrile were added so that the ratio acetonitrile/water was approximately 1. The extracts were partitioned twice with hexane. Thereafter, the acetonitrile was evaporated and the remaining aqueous phase was partitioned several times with dichloromethane or ethyl acetate under neutral and acidic conditions. The partitioned dichloromethane or ethyl acetate fractions were pooled (dichloromethane phase), concentrated and analysed by TLC. The remaining aqueous phase and the Soxhlet extract were not further analysed. The radioactivity in the hexane phase was concentrated and partitioned 3 times with acetonitrile. The acetonitrile fractions were pooled, concentrated and analysed by TLC (ACN phase). The Soxhlet extract was not further analysed.

The homogenised *muscle* tissue was extracted four times with acetone/water (80/20, v/v), followed by one extraction with methanol/water (80/20, v/v) and a Soxhlet extraction with methanol.

All extracts were pooled and concentrated at approximately 40 °C. Water and acetonitrile were added so that the ratio acetonitrile/water was approximately 1. The extracts were partitioned twice with hexane. Because most of the radioactivity could be partitioned into hexane, no further partitionings with e.g. dichloromethane were necessary. The remaining aqueous phase was not further analysed.
The radioactivity in the hexane phase was concentrated and partitioned with twice with acetonitrile. The acetonitrile fractions were pooled, concentrated and analysed by TLC and HPLC (organic phase).

Measurement and characterisation of radioactivity

Radioactivity in all specimens was determined by LSC. Samples containing organo-soluble radioactivity were analysed by TLC and HPLC as appropriate. Quantification and identification was made by comparison with reference items.

Results

There was no significant leaching of the test item from the diet into the water phase during the exposure period. On average after 10 min agitating, <1 % of radioactivity were measured as dissolved radioactivity in the water.

The radioactivity levels in for cyclopropyl- and fluorophenyl-label are presented in Table B.7.2-29.

Table B.7.2-29: Radioactivity levels in fish samples

Label	Sample	TRR (mg /kg)
cyclopropyl	Liver	0.083
	Muscle	0.073
fluorophenyl	Liver	0.078
	Muscle	0.053

The radioactivity from fish samples collected on day 14 of exposure for both labels was characterised by TLC (liver and muscle) and HPLC (muscle only).

Extraction of liver tissue and partitioning
Cyclopropyl-label
In total 81.5 % of total radioactive residue (TRR) or 0.068 mg/kg could be extracted. Only a small amount of non-extractable radioactivity remained (18.5 % TRR or 0.015 mg/kg).
30.6 % TRR (0.025 mg/kg) could be partitioned into hexane and 41.6 % (0.035 mg/kg) into CH_2Cl_2 or ethyl acetate. 30.5 % TRR (0.025 mg/kg) could be partitioned back from hexane into acetonitrile.

Fluorophenyl-label
In total 79.4 % of total radioactive residue (TRR) or 0.062 mg/kg could be extracted. Only a small amount of non-extractable radioactivity remained (20.6 % TRR or 0.016 mg/kg).
37.2 % TRR (0.029 mg/kg) could be partitioned into hexane and 35.1 % (0.027 mg/kg) into CH_2Cl_2 or ethyl acetate. 37.2 % TRR (0.029 mg/kg) could be partitioned back from hexane into acetonitrile.

The extractability of radioactivity from liver is summarised in Table B.7.2-30. The partitioning of extracted radioactivity from liver is summarised in Table B.7.2-31 and Table B.7.2-32.

Table B.7.2-30: Extractability of radioactivity from fish liver

Time	cyclopropyl		fluorophenyl	
	% TRR	mg/kg	% TRR	mg/kg
Extractable:				
Acetone/H_2O (80/20)	50.3	0.042	49.2	0.038
Acetone/H_2O (80/20)	19.7	0.016	20.5	0.016
Acetone/H_2O (80/20)	5.6	0.005	5.5	0.004
Methanol/H_2O (80/20)	2.0	0.002	1.5	0.001
Acetone/H_2O (80/20), acidic	1.4	0.001	1.0	0.001
Acetone/H_2O (80/20), acidic	0.2	<0.001	<0.1	<0.001
Soxhlet (MeOH)[a]	2.4	0.002	1.7	0.001
Subtotal extracted	81.5	0.068	79.4	0.062
Non-extractable	18.5	0.015	20.6	0.016
Total	100.0	0.083	100.0	0.078

[a] not further analysed

Table B.7.2-31: Partitioning of extracted radioactivity from fish liver

Time	cyclopropyl		fluorophenyl	
	% TRR	mg/kg	% TRR	mg/kg
Organic phase:				
Hexane	16.7	0.014	21.0	0.016
Hexane	14.0	0.012	16.2	0.013
Subtotal, hexane	30.6	0.025	37.2	0.029
CH_2Cl_2	12.9	0.001	13.4	0.010
CH_2Cl_2	8.9	0.007	7.8	0.006
Ethyl acetate	5.6	0.005	4.9	0.004
Ethyl acetate	7.1	0.006	1.8	0.001
CH_2Cl_2, acidic	6.8	0.006	5.3	0.004
CH_2Cl_2, acidic	0.3	<0.001	1.7	0.001
Subtotal CH_2Cl_2, and ethyl acetate	41.6	0.035	35.1	0.027
Subtotal	72.2	0.060	72.3	0.056
Aqueous phase [a]	6.8	0.006	5.5	0.005
Total	79.1	0.066	77.7	0.061

[a] not further analysed

Table B.7.2-32: Further partitioning of extracted radioactivity from fish liver from the hexane phase back into acetonitrile

Time	**cyclopropyl**		**fluorophenyl**	
	% TRR	mg/kg	% TRR	mg/kg
Organic phase:				
Acetonitrile	28.5	0.024	35.6	0.028
Acetonitrile	1.7	0.001	1.4	0.001
Acetonitrile	0.3	<0.001	0.2	<0.001
Subtotal, acetonitrile	30.5	0.025	37.2	0.029
Remaining hexane phase [a]	0.1	<0.001	<0.1	<0.001
Total	30.6	0.025	37.2	0.029

[a] not further analysed

Characterisation of radioactivity in the liver extract

Cyclopropyl-label

In the acetonitrile phase, at least 6 radioactive metabolite fractions were found. Radioactive fraction of beta-cyfluthrin was found in an amount of 15.7 % TRR or 0.013 mg/kg. All other radioactive fractions were observed in amounts ranging from <0.001 to 0.007 mg/kg.

In the dichloromethane phase, at least 8 radioactive metabolite fractions were found. Radioactive fraction of beta-cyfluthrin was found in an amount of 5.9 % TRR or 0.005 mg/kg. Fraction DCVA (Ref. F) was measured in an amount of 19.2 % TRR or 0.016 mg/kg. All other radioactive fractions were observed in amounts ranging from 0.001 to 0.004 mg/kg.

Fluorophenyl-label

In the acetonitrile phase, at least 8 radioactive metabolite fractions were found. Radioactive fraction of beta-cyfluthrin was found in an amount of 26.5 % TRR or 0.021 mg/kg. FCR 1260 (FPB-aldehyde)

was found in an amount of 2.0 % TRR or 0.002 mg/kg. All other radioactive fractions were observed in amounts ranging from <0.001 to 0.003 mg/kg.
In the dichloromethane phase, at least 8 radioactive metabolite fractions were found. Radioactive fraction of beta-cyfluthrin was found in an amount of 17.8 % TRR or 0.014 mg/kg. FCR 3145 (4´-OH-FPBacid) was measured in an amount of 4.7 % TRR or 0.004 mg/kg. All other radioactive fractions were observed in amounts ranging from 0.001 to 0.004 mg/kg.

A summary of the characterisation of extractable radioactivity of liver is presented in Table B.7.2-33.

Table B.7.2-33: Characterisation of extractable radioactivity of liver

Time	**Cyclopropyl**		**Fluorophenyl**	
	% TRR	mg/kg	% TRR	mg/kg
Acetonitrile phase:				
Beta-cyfluthrin (Parent)	15.7	0.013	26.5	0.021
FCR 1260 (FPB-aldehyde) 4-fluoro-3-phenoxy-benzaldehyd	---	---	2.0	0.002
Five unknown metabolite fractions	1.9 9.0 1.3 0.6 2.0	0.002 0.007 0.001 <0.001 0.002	---	---
Six unknown metabolite fractions	---	---	0.9 4.2 0.6 0.9 1.6 0.5	0.001 0.003 <0.001 0.001 0.001 <0.001
Remaining hexane phase	0.1	<0.001	<0.1	<0.001
Total hexane phase	30.1	0.025	37.2	0.029
Dichloromethane phase				
Beta-cyfluthrin (Parent)	5.9	0.005	17.8	0.014
DCVA (Ref. F)	19.2	0.016	---	---
FCR 3145 4´-OH-FPBacid	---	---	4.7	0.004
Six unknown metabolite fraction	5.2 3.1 3.7 1.6 0.8 2.2	0.004 0.003 0.003 0.001 0.001 0.002	---	---
Five unknown metabolite fractions	---	---	1.9 1.9 4.6 1.9 2.4	0.001 0.001 0.004 0.001 0.002
Total dichloromethane phase	41.6	0.035	35.1	0.027
Not analysed (Soxhlet extract)	2.4	0.002	1.7	0.001

Total aqueous phase	6.8	0.006	5.5	0.005
Total extracted	81.5	0.068	79.4	0.062
Non-extractable	18.5	0.015	20.6	0.016
Total	100.0	0.083	100.0	0.078

Extraction of muscle tissue and partitioning
Cyclopropyl-label
In total 99.1 % of total radioactive residue (TRR) or 0.072 mg/kg could be extracted. Only a small amount of non-extractable radioactivity remained (0.9 % TRR or 0.001 mg/kg).
90.4 % TRR (0.066 mg/kg) could be partitioned into hexane. Only a small amount of 8.7 % TRR (0.006 mg/kg) remained in the hexane phase

Fluorophenyl-label
In total 97.9 % of total radioactive residue (TRR) or 0.052 mg/kg could be extracted. Only a small amount of non-extractable radioactivity remained (2.1 % TRR or 0.001 mg/kg).
89.8 % TRR (0.048 mg/kg) could be partitioned into hexane. Only a small amount of 8.1 % TRR (0.004 mg/kg) remained in the hexane phase.

The extractability of radioactivity from muscle is summarised in Table B.7.2-34. The partitioning of extracted radioactivity from muscle is summarised in Table B.7.2-35 and Table B.7.2-36.

Table B.7.2-34: Extractability of radioactivity from muscle

Time	**cyclopropyl**		**fluorophenyl**	
	% TRR	mg/kg	% TRR	mg/kg
Extractable:				
Acetone/H_2O (80/20)	52.8	0.039	30.2	0.016
Acetone/H_2O (80/20)	30.6	0.022	41.9	0.022
Acetone/H_2O (80/20)	10.2	0.007	15.7	0.008
Acetone/H_2O (80/20)	3.6	0.003	6.2	0.003
Methanol/H_2O (80/20)	0.7	<0.001	1.3	0.001
Soxhlet (MeOH)[a]	1.1	0.001	2.6	0.001
Subtotal extracted	99.1	0.072	97.9	0.052
Non-extractable	0.9	0.001	2.1	0.001
Total	100.0	0.073	100.0	0.053

[a] not further analysed

Table B.7.2-35: Partitioning of extracted radioactivity from muscle into hexane

Time	**cyclopropyl**		**fluorophenyl**	
	% TRR	mg/kg	% TRR	mg/kg
Organic phase:				
Hexane	67.5	0.049	73.8	0.039
Hexane	20.0	0.015	13.7	0.007
Hexane	3.0	0.002	2.3	0.001
Subtotal, hexane	90.4	0.066	89.8	0.048

Aqueous phase [a]	8.7	0.006	8.1	0.004
Total	99.1	0.072	97.9	0.052

[a] not further analysed

Table B.7.2-36: Further partitioning of extracted radioactivity from muscle from the hexane phase back into acetonitrile

Time	**cyclopropyl**		**fluorophenyl**	
	% TRR	mg/kg	% TRR	mg/kg
Organic phase:				
Acetonitrile	81.7	0.060	85.6	0.045
Acetonitrile	3.0	0.002	3.4	0.002
Subtotal, acetonitrile	84.7	0.062	89.0	0.047
Remaining hexane phase [a]	5.7	0.004	0.8	<0.001
Total	90.4	0.066	89.8	0.048

[a] not further analysed

Characterisation of radioactivity in the muscle extract
Cyclopropyl-label
In the organic phase, at least 5 radioactive metabolite fractions were found. Radioactive fraction of beta-cyfluthrin was found in an amount of 82.0 % TRR or 0.060 mg/kg. COOH-cyfluthrin was detected in traces (<0.001 mg/kg). All other radioactive fractions were observed in amounts ranging from <0.001 to 0.001 mg/kg.

Fluorophenyl-label
In the organic phase, at least 5 radioactive metabolite fractions were found. Radioactive fraction of beta-cyfluthrin was found in an amount of 86.2 % TRR or 0.046 mg/kg. COOH-cyfluthrin was detected in traces (<0.001 mg/kg). All other radioactive fractions were observed in amounts ranging from <0.001 to 0.001 mg/kg.

A summary of the characterisation of extractable radioactivity of muscle is presented in Table B.7.2-37.

Table B.7.2-37: Characterisation of extractable radioactivity of muscle

Time	**cyclopropyl**		**fluorophenyl**	
	% TRR	mg/kg	% TRR	mg/kg
Acetonitrile phase:				
Beta-cyfluthrin (Parent)	82.0	0.060	86.2	0.046
COOH-cyfluthrin	0.4	<0.001	0.4	<0.001
Three unknown metabolite fractions	0.8 1.3 0.3	0.001 0.001 <0.001	---	---
Three unknown metabolite fractions	---	---	0.5 0.8 1.8	<0.001 <0.001 0.001
Remaining hexane phase	5.4	0.004	0.8	0.000
Total hexane phase	90.4	0.066	89.8	0.048

Total aqueous phase	8.7	0.006	8.1	0.004
Total extracted	99.1	0.072	97.9	0.052
Non-extractable	0.9	0.001	2.1	0.001
Total	100.0	0.073	100.0	0.053

Unknown radioactive fractions
None of the unknown fractions in the fish samples (liver and muscle) showed the same TLC behaviour as one of the reference items. All other unknown metabolites were more polar than the test item.

Conclusions

The fish were repeatedly administered for 14 days a diet with [cyclopropane-1-^{14}C]beta-cyfluthrin or [fluorophenyl-UL-^{14}C]beta-cyfluthrin at an actual concentration measured in the diet of 11.7 mg/kg diet for the cyclopropyl-label and 10.6 mg/kg diet for the fluorophenyl-label.
The fish were sacrificed at approximately 6 hours after the last (14th) administration and liver, muscle (including skin) were collected. Rather low levels of radioactivity were measured for liver (0.078 to 0.083 mg/kg) and muscle (0.053 to 0.073 mg/kg).
The radioactivity could be efficiently extracted from liver and muscle. The extracted amounts ranged from 79.4 % to 99.1 % of TRR. The extracted radioactivity could then be partitioned into organic solvents and the samples were analysed by TLC and HPLC.

The residues in muscle mainly consisted of unchanged parent compound. Also in liver parent compound was the main component of the extracted radioactivity.

Cyclopropyl specific compounds: In liver, besides parent DCVA was detected in an amount of 0.016 mg/kg. COOH-cyfluthrin was detected in traces in muscle. Unknown metabolites occurring in liver and muscle ranged from <0.001 to 0.007 mg/kg.

Fluorophenyl specific compounds: In liver, besides parent, FCR 3145 and FCR1260 were detect in small amounts of 0.004 and 0.002 mg/kg, respectively. COOH-cyfluthrin was detected in traces in muscle. Unknown metabolites occurring in liver and muscle ranged from <0.001 to 0.004 mg/kg.
On the basis of the results of this study it is concluded that the metabolism of beta-cyfluthrin in fish is well understood and the following metabolic pathway is proposed (Figure B.7.2-6).

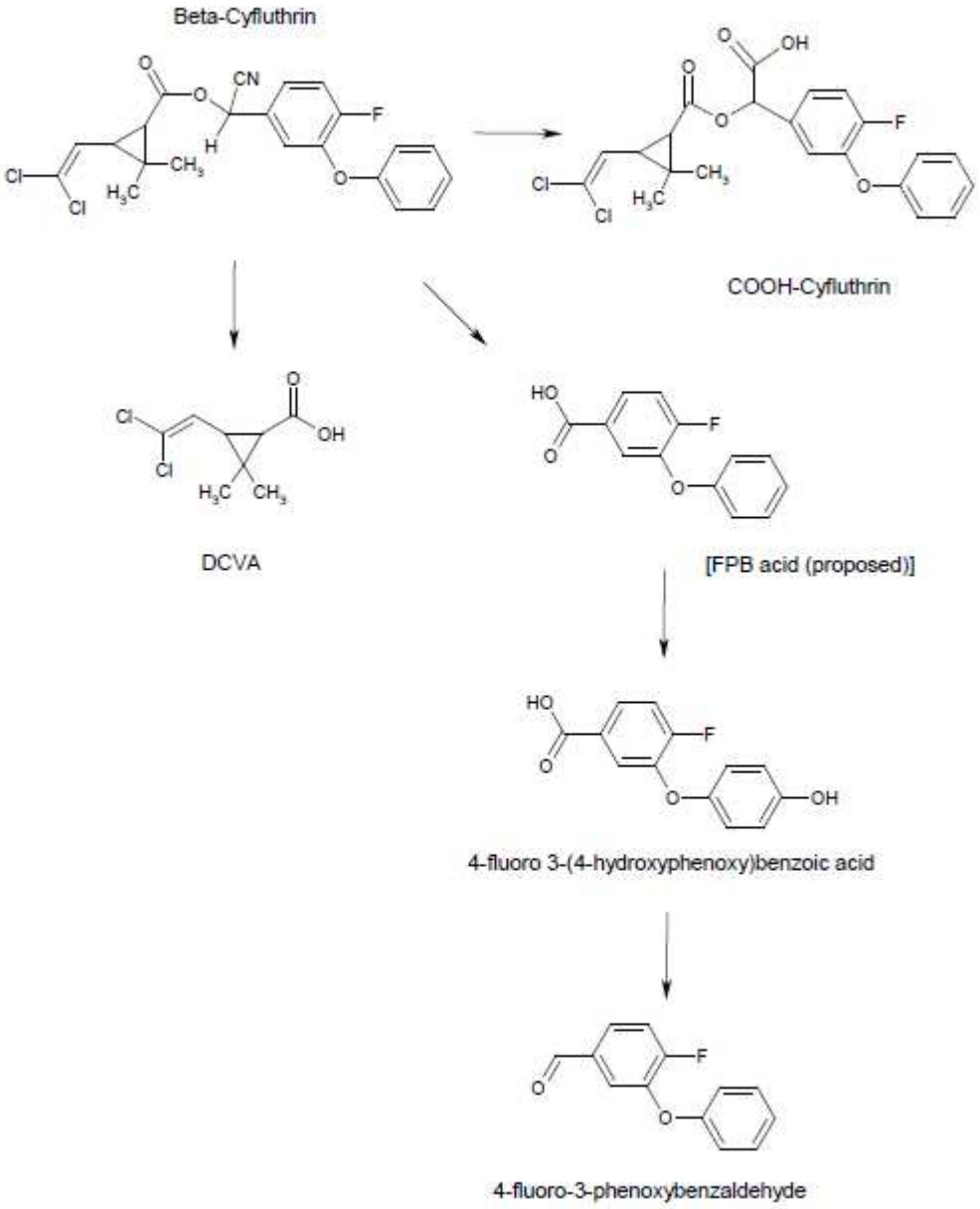


Figure B.7.2-6: Proposed metabolic pathway for beta-cyfluthrin in fish

B.7.3 Magnitude of residue trials in plants

EU MRLs for cyfluthrin (sum of isomers) were adopted and included in Annex II of Regulation (EC) No 396/2005, which adequately support claimed uses (Commission Regulation (EU) No 893/2010 of 10 October 2010).

Upon review of the database supporting the current uses, it was determined that while there were numerous residue studies with cyfluthrin and beta-cyfluthrin foliar applications in potato, tomato and wheat, many were older, non-GLP studies and did not always represent the current GAP. In order to provide an up-to-date set of studies, a representative set of trials was recently conducted with beta-cyfluthrin. In this submission only residue studies conducted with beta-cyfluthrin are presented to support the proposed foliar uses for beta-cyfluthrin.

B.7.3.1.1 Sugar beet

The critical GAPs for use of the representative formulation of beta-cyfluthrin on sugar beet are outlined in Table B.7.3-1.

Table B.7.3-1: Critical GAPs for use of beta-cyfluthrin on sugar beet

Region	**Outdoor/ Protected**	**Maximum Number of Applications**	**Method of application**	**Maximum**		**Minimum PHI (days)**
				Rate (g as/unit)	Rate (g as/ha)	
Northern/Central EU	Outdoor	1	seed treatment	8	10.4 *	n.a.
Southern EU	Outdoor	1	seed treatment	8	10.4 *	n.a.

n.a.: not applicable
* based on a max. seeding rate of 1.3 units/ha; 1 unit = 100,000 seeds

Data point: KCA 6.3.1/12

Report: Schöning, R., Reineke, A. (2011): Determination of the residues of beta-cyfluthrin in/on sugarbeet after seed treatment with Montur Forte FS 230 in the field in Germany and the Netherlands
Report 09-2044
M-404508-01-1
ASB2012-4627

Guideline(s): EC guidance working document 7029/VI/95 rev. 5

Deviations: None

GLP: Yes

Acceptability: Acceptable

Data point:	KCA 6.3.1/11
Report:	Meilland-Berthier, I. (2013): Determination of the residues of cyfluthrin in/on sugarbeet after seed treatment with Montur Forte FS 230 in Germany, northern France, United Kingdom, Spain, Italy, Greece and southern France Report 12-2029 M-463988-01-1 ASB2014-7883
Guideline(s):	EC guidance working document 7029/VI/95 rev. 5 OECD 509 Guideline for the testing of chemicals, Crop field trial US EPA OCSPP Guideline No. 860.1500
Deviations:	None
GLP:	Yes
Acceptability:	Acceptable

Materials and methods

Out of 10 supervised residue trials in sugar beet, 6 trials were conducted in N-EU (2009, 2012) and 4 trials in S-EU (2012). The seeds of sugar beet were treated with 8 g as/unit (100,000 seeds). These were sown with a rate of 1.2 - 1.3 units/ha equivalent to 9.6 - 10.4 g as/ha. Dislodgeable residues of beta-cyfluthrin were determined on treated seeds. Sugar beet samples (body and leaf with root collar) were collected 112-197 days after sowing. The storage period of deep-frozen samples ranged between 261 and 413 days for harvest samples (561 days for treated seeds).

In 2009 samples were analysed according to analytical method **00922**. Beta-cyfluthrin was extracted with acetone/water (2/1, v/v). After filtration, the extract is transferred into a separatory funnel and partitioned against dichloromethane (DCM). The organic phase is concentrated to dryness, redissolved in DCM and cleaned-up on a Florisil™ column cartridge. The eluate is evaporated to dryness and dissolved in a solution containing the internal standard in acetonitrile/water (1/1; v/v) with 5 mmol ammonium acetate/L. Extracts were subjected to LC-MS/MS and residues were quantified using internal stable labelled standards. The LOQ is 0.01 mg/kg for leaf with root collar and for body. For the determination of beta-cyfluthrin on treated seeds, seeds were shaken in acetonitrile/water (4/1, v/v) and cysteine hydrochloride solution. After filtration and dilution of the extract, internal standard was added and beta-cyfluthrin was quantified in the same conditions as the residue samples.

In 2012 samples were analysed according to analytical method 01379. Cyfluthrin was extracted from sugar beet samples with a mixture of acetone/water (2/1, v/v) using a blender. After filtration, the extract is transferred into a separatory funnel and partitioned against dichloromethane. The organic phase is concentrated to dryness, redissolved in dichloromethane and further cleaned-up on a Florisil™ column cartridge. The eluate is evaporated to dryness and dissolved in acetonitrile/water (50/50; v/v). The extracts were diluted with acetonitrile/water (1/2; v/v), adding the internal standards at this stage. Extracts were subjected to LC-MS/MS and residues were quantified using internal stable labelled standards. The limit of quantification (LOQ) is 0.01 mg/kg for leaf with root collar and for body. For the determination of beta-cyfluthrin on treated seeds, seeds were shaken in acetone/water (2/1, v/v). After dilution of the extract, internal standard was added and cyfluthrin was quantified in the same conditions as the residue samples.

Results

Procedural recoveries (see Table B.7.3-2 and Table B.7.3-3) were acceptable. Storage of samples (up to 12 months) is not covered by acceptable storage stability studies (see Table B.7.3-3). No residues

were found in untreated control samples.

Table B.7.3-2: Procedural recoveries for beta-cyfluthrin in sugar beet

Study No. Trial No. Year	Crop	Portion analysed	Compound		Fortification level	Recovery (%)		
				n	(mg/kg)	single value	mean	RSD
09-2044 09-2044-01 09-2044-02 2009	Sugar beet	Body	Beta-Cyfluthrin	3	0.01	80; 84; 79	81	3.3
				3	0.10	88; 92; 84	88	4.5
				6	overall		85	5.8
		Leaf with root collar	Beta-Cyfluthrin	3	0.01	94; 83; 104	94	11.2
				3	0.10	95; 93; 102	97	4.9
				6	overall		95	7.8

RSD = relative standard deviation

Table B.7.3-3: Procedural recoveries for cyfluthrin in sugar beet

Study No. Trial No. GLP Year	Crop	Portion analysed	Compound		Fortification level	Recovery (%)		
				n	(mg/kg)	single value	mean	RSD
12-2029 12-2029-01 12-2029-02 12-2029-03 12-2029-04 12-2029-05 12-2029-06 12-2029-07 12-2029-08 2012	Sugar beet	Body	Cyfluthrin	2	0.01	87, 97	92	-
				1	0.10	96	-	-
				3	overall		93	5.9
		Leaf with root collar	Cyfluthrin	2	0.01	81, 73	77	-
				1	0.10	77	-	-
				3	overall		77	5.2

RSD = relative standard deviation

Trial results are summarised in Table B.7.3-4 and Table B.7.3-5 (Northern Europe) as well as Table B.7.3-6 (Southern Europe).

No residues of beta-cyfluthrin and cyfluthrin above the LOQ (0.01 mg/kg) were found in any of the treated or untreated samples of sugar beet (root, leaf) at commercial harvest.

Conclusion

A guideline compliant residue data set of 10 trials for beta-cyfluthrin in sugar beets is available covering both N-EU and S-EU regions. No residues above the LOQ (0.01 mg/kg) were found in any of the treated or untreated samples of sugar beet body and sugar beet leaf with root collar sampled 112-197 days after sowing.
The analytical method is validated and procedural recoveries are acceptable.
Data sets for N-/S-EU can be combined due to the no-residue situation in roots and leaves. No discrepancy is observed to sugar beet metabolism studies.

Table B.7.3-4: Residues of beta-cyfluthrin in sugar beet matrices following seed treatment in outdoor trials in Northern Europe

RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)

Federal Institute for Risk Assessment, Berlin
Federal Republic of Germany

Content of as (g/kg or g/L) : 80 g/L
Formulation (e.g. WP) : FS (Flowable concentrate for seed treatment)
Commercial product (name) : Montur Forte FS 230
Applicant : Bayer CropScience

Active ingredient : beta-cyfluthrin
Crop / crop group : Sugar Beet
Crop Code : BEAVA

Submission date : 2013-09-02

Indoors / Outdoors : Outdoors (European North)
Other as in formulation
(content and common name) : 150 g/L imidacloprid
Residues calculated as : cyfluthrin isomer mixture

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment kg as/ha	Water L/ha	kg as/seed units	Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
	(a)	(b)				(c)		(a)		(d)	(e)
study 09-2044, trial 09-2044-01, seed treatment trial Germany (DE) 59457 Werl 2011-03-25	Beretta	1)2009-04-06 (sowing) 2) 3)2009-09-29 - 2009-12-20	0.0096		0.0080	n.a.	BBCH 00	treated seed leaf with top root body	2488 <0.010 <0.010	0 175 175	analytical method: 00922 (MR-190/04) (HPLC-MS/MS), LOQ(s): 0.01 mg/kg (leaf with top, root body), 1 mg/kg (treated seed), max. sample storage time in month(s): 19 seed treatment with 100 mL product/seed unit = 8 g/seed unit beta-cyfluthrin and 15 g/seed unit imidacloprid = 9.6 g/ha beta-cyfluthrin and 18 g/ha imidacloprid ASB2012-4627
study 09-2044, trial 09-2044-02, seed treatment trial Netherlands (NL) 1681 Zwaagdijk 2011-03-25	Beretta	1)2009-05-13 (sowing) 2) 3)2009-09-01 - 2009-09-15	0.0096		0.0080	n.a.	BBCH 00	treated seed leaf with top root body	2641 <0.010 <0.010	0[5)] 112 112	analytical method: 00922 (MR-190/04) (HPLC-MS/MS), LOQ(s): 0.01 mg/kg (leaf with top, root body), 1 mg/kg (treated seed), max. sample storage time in month(s): 18 seed treatment with 100 mL product/seed unit = 8 g/seed unit beta-cyfluthrin and 15 g/seed unit imidacloprid = 9.6 g/ha beta-cyfluthrin and 18 g/ha imidacloprid ASB2012-4627

Table B.7.3-5: Residues of cyfluthrin in sugar beet matrices following seed treatment in outdoor trials in Northern Europe

RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)

Federal Institute for Risk Assessment, Berlin
Federal Republic of Germany

Content of as (g/kg or g/L) : 80 g/L
Formulation (e.g. WP) : FS (Flowable concentrate for seed treatment)
Commercial product (name) : Montur Forte FS 230
Applicant : Feinchemie Schwebda GmbH

Active ingredient : beta-cyfluthrin
Crop / crop group : Sugar Beet
Crop Code : BEAVA

Submission date : 2014-08-08

Indoors / Outdoors : Outdoors (European North)
Other as in formulation
(content and common name) : 150 g/L imidacloprid
Residues calculated as : cyfluthrin isomer mixture

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment kg as/ha	Water L/ha	kg as/seed units	Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
	(a)	(b)				(c)		(a)		(d)	(e)
M-463988-01-1, 12-2029, RAAAN075, trial 12-2029-01, seed treatment trial Germany (DE) 51399 Burscheid 2013-09-03	Sabrina	1)2012-04-16 (sowing) 2) 3)2012-09-01 - 2012-11-30	0.0104		0.0080	n.a.	BBCH 00	leaf with top root body	<0.010 <0.010	147 147	seed treatment, analytical method: 01379, MR-13/052 (HPLC-MS/MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 16 TGW: 26.71 g, seed rate: 130000 seeds/ha, 8.24 g beta-cyfluthrin/unit (based on measurement of dislodgeable residues) ASB2014-7883
M-463988-01-1, 12-2029, RAAAN075, trial 12-2029-02, seed treatment trial Germany (DE) 59457 Werl 2013-09-03	Sabrina	1)2012-03-26 (sowing) 2) 3)2012-09-10 - 2012-12-20	0. 0104		0.0080	n.a.	BBCH 00	leaf with top root body	<0.010 <0.010	170 170	seed treatment analytical method: 01379, MR-13/052 (HPLC-MS/MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 11 TGW: 26.71 g, seed rate: 130000 seeds/ha, 8.48 g beta-cyfluthrin/unit (based on measurement of dislodgeable residues) ASB2014-7883

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment kg as/ha	Water L/ha	kg as/seed units	Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
	(a)	(b)				(c)		(a)		(d)	(e)
M-463988-01-1, 12-2029, RAAAN075, trial 12-2029-03, seed treatment trial France (FR) 95710 Chaussy 2013-09-03	Sabrina	1)2012-03-23 (sowing) 2) 3)2012-09-18 - 2012-09-21	0. 0104		0.0080	n.a.	BBCH 00	leaf with top root body	<0.010 <0.010	179 179	seed treatment analytical method: 01379, MR-13/052 (HPLC-MS/MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 11 TGW: 26.71 g, seed rate: 130000 seeds/ha, 8.24 g beta-cyfluthrin/unit (based on measurement of dislodgeable residues) ASB2014-7883
M-463988-01-1, 12-2029, RAAAN075, trial 12-2029-04, seed treatment trial United Kingdom (UK) CB22 5EU Little Shelford 2013-09-03	Sabrina	1)2012-04-02 (sowing) 2) 3)2012-10-01	0. 0104		0.0080	n.a.	BBCH 00	leaf with top root body	<0.010 <0.010	197 197	seed treatment, analytical method: 01379, MR-13/052 (HPLC-MS/MS),LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 10 TGW: 26.71 g, seed rate: 130000 seeds/ha, 8.40 g beta-cyfluthrin/unit (based on measurement of dislodgeable residues) ASB2014-7883

Table B.7.3-6: Residues of cyfluthrin in sugar beet matrices following seed treatment in outdoor trials in Southern Europe

RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)

Federal Institute for Risk Assessment, Berlin
Federal Republic of Germany

Content of as (g/kg or g/L) : 80 g/L
Formulation (e.g. WP) : FS (Flowable concentrate for seed treatment)
Commercial product (name) : Montur Forte FS 230
Applicant : Feinchemie Schwebda GmbH

Active ingredient : beta-cyfluthrin
Crop / crop group : Sugar Beet
Crop Code : BEAVA

Submission date : 2014-08-08

Indoors / Outdoors : Outdoors (European South)
Other as in formulation
(content and common name) : 150 g/L imidacloprid
Residues calculated as : cyfluthrin isomer mixture

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment			Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
			kg as/ha	Water L/ha	kg as/seed units						
	(a)	(b)				(c)		(a)		(d)	(e)
M-463988-01-1, 12-2029, RAAAN075, trial 12-2029-05, seed treatment trial Spain (ES) 46230 Alginet, La Moncarra 2013-09-03	Massima	1)2012-03-27 (sowing) 2) 3)2012-09-30 - 2012-10-30	0.0104		0.0080	n.a.	BBCH 00	leaf with top root body	<0.010 <0.010	157 157	seed treatment analytical method: 01379, MR-13/052 (HPLC-MS/MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 11 TGW: 26.71 g, seed rate: 130000 seeds/ha, 8.48 g beta-cyfluthrin/unit (based on measurement of dislodgeable residues) ASB2014-7883
M-463988-01-1, 12-2029, RAAAN075, trial 12-2029-06, seed treatment trial Italy (IT) 37050 Albaro 2013-09-03	Massima	1)2012-03-12 (sowing) 2) 3)2012-08-15 - 2012-08-30	0.0104		0.0080	n.a.	BBCH 00	leaf with top root body	<0.010 <0.010	151 151	seed treatment analytical method: 01379, MR-13/052 (HPLC-MS/MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 12 TGW: 26.71 g, seed rate: 130000 seeds/ha, 8.02 g beta-cyfluthrin/unit (based on measurement of dislodgeable residues) ASB2014-7883

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment kg as/ha	Water L/ha	kg as/seed units	Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
	(a)	(b)				(c)		(a)		(d)	(e)
M-463988-01-1, 12-2029, RAAAN075, trial 12-2029-07, seed treatment trial Greece (GR) 60200 Kalivia Varikon 2013-09-03	Massima	1)2012-04-03 (sowing) 2) 3)2012-09-08	0.0104		0.0080	n.a.	BBCH 00	leaf with top root body	<0.010 <0.010	153 153	seed treatment analytical method: 01379, MR-13/052 (HPLC-MS/MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 11 TGW: 28.99 g, seed rate: 130000 seeds/ha, 8.16 g beta-cyfluthrin/unit (based on measurement of dislodgeable residues) ASB2014-7883
M-463988-01-1, 12-2029, RAAAN075, trial 12-2029-08, seed treatment trial France (FR) 31200 Toulouse 2013-09-03	Massima	1)2012-03-29 (sowing) 2) 3)2012-03-29 - 2012-09-15	0.0104		0.0080	n.a.	BBCH 00	leaf with top root body	<0.010 <0.010	175 175	seed treatment analytical method: 01379, MR-13/052 (HPLC-MS/MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 11 TGW: 28.99 g, seed rate: 130000 seeds/ha, 8.4 g beta-cyfluthrin/unit (based on measurement of dislodgeable residues) ASB2014-7883

Remarks:
(a) According to CODEX Classification / Guide
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (Label pre-harvest interval, PHI, underline)
(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

B.7.3.2 Tomato

The critical GAP for use of beta-cyfluthrin on tomato is given in Table B.7.3-7.

Table B.7.3-7: Critical GAPs for use of beta-cyfluthrin on tomato

Region	Outdoor/ Protected	Maximum Number of Applications	Minimum Application Interval (days)	Maximum		Minimum PHI (days)
				Rate (g as/ha)	Water (L/ha)	
Northern/Central/Southern EU	Indoor	2	14	17.5	150-1000	3

Data point: KCA 6.3.2/12

Report: Schäufele, M. (2012): Magnitude of residues of beta-cyfluthrin in greenhouse tomato raw agricultural commodity after 2 applications of Bullock 25 EC or Bullock 25 CS – 8 decline trials – in northern and southern Europe (The Netherlands, Germany, Northern France, Greece, Spain and Italy) in 2011
Report Number: JDV0077
ASB2014-7711
M-481199-01-1; R-28672

Guideline(s): EU Directive 91/414/EEC as amended by Commission Directive 96/68/EC

Deviations: None

GLP: Yes

Acceptability: Acceptable

Materials and methods

Eight supervised indoor residue trials in tomato were conducted in 2011 (Germany, Netherlands, France, Spain, Greece, Italy). Tomatoes were treated according to GAP with two foliar applications at rates of 16-19 g as/ha and an interval of 13-15 days. Tomato fruits were collected at day 0, day 3-4 (target PHI) and day 6-7 after the last application. The samples were stored deep frozen for max. 202 days.

The samples (tomato fruit) were analysed for beta-cyfluthrin according to a validated multi residue method (MRM; LOQ 0.01 mg/kg; see Vol.3, B.5.1.2).

Results

Procedural recoveries were acceptable (Table B.7.3-8). Storage of samples (up to 7 months) is covered by acceptable storage stability studies (see Table B.7.3-8). No residues were found in untreated control samples.
Trial results are summarised in Table B.7.3-9, Residues in treated samples range from <0.01 to 0.02 mg/kg at target PHI or later.

Table B.7.3-8: Procedural recoveries for beta-cyfluthrin in tomatoes

Study No. Trial No. Year	Crop	Portion analysed	as/ metabolite		Fortification level	Recovery (%)		
				n	(mg/kg)	single value	mean	RSD
JDV0077 JDV0077-01 JDV0077-02 JDV0077-03 JDV0077-04 JDV0077-05 JDV0077-06 JDV0077-07 JDV0077-08 2011	Tomato	Fruit	Beta-cyfluthrin	3	0.01	75, 70, 94	80	16
				3	0.10	70, 74, 93	79	16
				6	overall	-	79	14

Conclusion

A fully guideline compliant residue data set of 8 trials for beta-cyfluthrin in indoor tomato is available. Residues ranged from <0.01-0.02 mg/kg. The analytical method is validated, procedural recoveries are acceptable and storage stability is covered.

Table B.7.3-9: Residues of beta-cyfluthrin in tomatoes matrices following application of various formulations in indoor trials

RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)

Federal Institute for Risk Assessment, Berlin
Federal Republic of Germany

Content of as (g/kg or g/L) : 25 g/L
Formulation (e.g. WP) : EC (Emulsifiable concentrate)
Commercial product (name) : Bulldock
Applicant : Feinchemie Schwebda GmbH

Active ingredient : beta-cyfluthrin
Crop / crop group : Tomato
Crop Code : LYPES

Submission date : 2014-08-08

Indoors / Outdoors : Indoors
Other as in formulation (content and common name) :
Residues calculated as : cyfluthrin isomer mixture

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment			Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
			kg as/ha	Water L/ha	kg as/hl						
	(a)	(b)				(c)		(a)		(d)	(e)
M-481199-01-1, R-28672, JDV0077-05, decline trial Spain (ES) 30876 Ramonete (Lorca) 2012-06-11	Alegro	1)2011-08-16 (sowing) 2)2011-09-10 - 2012-02-01 3)2011-11-24	0.018 0.019	630 640	0.0029 0.0030	2011-11-03[4)] 2011-11-17[4)]	BBCH 73	whole fruit	<0.010 <u>0.012</u> 0.010	0 4 7	4)spraying analytical method: JDV0079 (GC-MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 5 greenhouse, cultivated on rock wool ASB2014-7711
M-481199-01-1, R-28672, JDV0077-06, decline trial Greece (GR) 57008 Nea Magnisia 2012-06-11	Elpida	1)2011-08-01 (sowing) 2)2011-08-25 - 2011-11-15 3)2011-11-28	0.018 0.018	600 600	0.0030 0.0030	2011-11-08[4)] 2011-11-21[4)]	BBCH 77-85	whole fruit	<0.010 <u><0.010</u> <0.010	0 4 7	4)spraying analytical method: JDV0079 (GC-MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 5 greenhouse, cultivated on rock wool ASB2014-7711
M-481199-01-1, R-28672, JDV0077-07, decline trial Italy (IT) 18016 S. Bartolomeo al mare 2012-06-11	Arawak	1)2011-10-06 (sowing) 2)2011-11-04 - 2011-11-18 3)2011-12-19	0.018 0.018	500 510	0.0036 0.0035	2011-11-28[4)] 2011-12-12[4)]	BBCH 85	whole fruit	0.015 0.014 <u>0.016</u>	0 3 7	4)spraying analytical method: JDV0079 (GC-MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 4 greenhouse, cultivated on rock wool ASB2014-7711

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment			Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
			kg as/ha	Water L/ha	kg as/hl						
	(a)	(b)				(c)		(a)		(d)	(e)
M-481199-01-1, R-28672, JDV0077-08, decline trial Italy (IT) 20090 Caleppio di Settala 2012-06-11	Napika	1)2011-07-08 (sowing) 2)2011-08-01 - 2011-08-28 3)2011-10-05	0.018 0.017	420 390	0.0043 0.0044	2011-09-14[4)] 2011-09-29[4)]	BBCH 83	whole fruit	<0.010 <0.010 <0.010	0 4 6	4)spraying analytical method: JDV0079 (GC-MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 6 greenhouse, cultivated on rock wool ASB2014-7711
M-481199-01-1, R-28672, JDV0077-01, decline trial Netherlands (NL) 5856 CH Wellerlool 2012-06-11	Capricia RZ	1)2010-12-20 (sowing) 2)2011-01-10 - 2011-09-26 3)2011-09-26	0.018 0.018	610 630	0.0029 0.0029	2011-09-05[4)] 2011-09-19[4)]	BBCH 85-87	whole fruit	0.011 0.012 0.014	0 3 7	4)spraying analytical method: JDV0079 (GC-MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 7 greenhouse, cultivated on rock wool ASB2014-7711
M-481199-01-1, R-28672, JDV0077-02, decline trial Germany (DE) 47669 Wachtendonk 2012-06-11	Delisio	1)2011-01-17 (sowing) 2)2011-01-20 - 2011-09-26 3)2011-09-26	0.018 0.018	610 610	0.0029 0.0029	2011-09-05[4)] 2011-09-19[4)]	BBCH 85-87	whole fruit	0.015 0.011 0.011	0 3 7	4)spraying analytical method: JDV0079 (GC-MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 7 greenhouse, cultivated on rock wool ASB2014-7711
M-481199-01-1, R-28672, JDV0077-03, decline trial Germany (DE) 08412 Werdau 2012-06-11	Cocktail red	1)2011-05-20 (sowing) 2)2011-06-15 - 2011-08-26 3)2011-08-26	0.019 0.019	650 640	0.0029 0.0030	2011-08-05[4)] 2011-08-19[4)]	BBCH 84	whole fruit	<0.010 <0.010 <0.010	0 3 7	4)spraying analytical method: JDV0079 (GC-MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 8 greenhouse, cultivated on rock wool ASB2014-7711

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment			Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
			kg as/ha	Water L/ha	kg as/hl						
	(a)	(b)				(c)		(a)		(d)	(e)
M-481199-01-1, R-28672, JDV0077-04, decline trial France (FR) 62217 Beaurains 2012-06-11	Daikiri	1)2011-06-17 (sowing) 2)2011-07-15 - 2011-09-15 3)2011-09-19	0.019 0.018	640 610	0.0030 0.0029	2011-08-29[4)] 2011-09-12[4)]	BBCH 81	whole fruit	0.011 0.011 <0.010	0 3 7	4)spraying analytical method: JDV0079 (GC-MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 7 greenhouse, cultivated on rock wool ASB2014-7711

B.7.3.3 Potato

The critical GAPs for use of the representative formulation of beta-cyfluthrin on potato are outlined in Table B.7.3-10.

Table B.7.3-10: Critical GAPs for use of beta-cyfluthrin on potato

Region	Outdoor/ Protected	Maximum Number of Applications	Minimum Application Interval (days)	Maximum		Minimum PHI (days)
				Rate (g as/ha)	Water (L/ha)	
Northern/Central EU	Outdoor	2	14	7.5	150-500	3
Southern EU	Outdoor	2	14	12.5	300-1000	3

Data point: KCA 6.3.3/13

Report: Heinemann, O.; Seym, M. (1998): Determination of residues of Enduro 258 EC in/on potato following spray application in the field in Germany, Great Britain and France
Report No: RA-2147/96
ASB2014-6706
M-054896-01-1

Guideline(s): EU Directive 91/414/EEC as amended by Commission Directive 96/68/EC

Deviations: None

GLP: Yes

Acceptability: Acceptable

Data point: KCA 6.3.3/14

Report: Heinemann, O.; Seym, M. (1998): Determination of residues of Enduro 258 EC in/on potato following spray application in the field in France
Company: Bayer CropScience AG
Report No: RA-2148/96
ASB2014-7858
Edition No.: M-078830-01-1

Guideline(s): EU Directive 91/414/EEC as amended by Commission Directive 96/68/EC

Deviations: None

GLP: Yes

Acceptability: Acceptable

Data point:	KCA 6.3.3/11
Report:	Seym, M. (1998): Determination of residues of Bulldock 025 EC and Bulldock 025 SC on potato in Portugal and Spain RA-2004/95 ASB2014-6702 M-054896-01-1
Guideline(s):	EU Directive 91/414/EEC as amended by Commission Directive 96/68/EC
Deviations:	None
GLP:	Yes
Acceptability:	Acceptable

Data point:	KCA 6.3.3/12
Report:	Heinemann, O.; Schoening, R. (2002): Determination of residues of beta-cyfluthrin in/on potato after spray application of Bulldock 025SC in Greece RA-2125/01 RIP2003-272 M-059856-01-1
Guideline(s):	EU Directive 91/414/EEC as amended by Commission Directive 96/68/EC
Deviations:	None
GLP:	Yes
Acceptability:	Acceptable

Data point:	KCA 6.3.3/15
Report:	Lebrun, F. (2013): Magnitude of the residue of beta-cyfluthrin in potato (raw agricultural commodity) after two applications of Bulldock 25 EC - two decline curve trials and two harvest trials in Northern Europe) Northern France, United Kingdom and Germany) - 2012 12SGS078 ASB2014-6718 M-481204-01-1, R-30376
Guideline(s):	Regulation (EC) No 1107/2009
Deviations:	None
GLP:	Yes
Acceptability:	Acceptable

Materials and methods

In total, 15 supervised field residue trials were submitted to support the intended use of beta-cyfluthrin in potato: 11 trials in N-EU (1996, 2012) and 4 trials in S-EU (1995, 2001). Most trials do not follow the GAP treatment regime.

N-EU trials
In 4 trials, 3 applications at 8, 7 and 6 g as/ha were made instead of the required number of 2 x 7.5 g as/ha. Application intervals were between 7 and 9 days. Total applied amount is above 25 % of intended rate, while the last two applications are slightly below target rate (but within 25 %).
In three further trials (1996), applications were made at 2 x 5 g as/ha with intervals of 14 days. Application pattern is outside 25 % of intended rate.
In 4 trials (2012), beta-cyfluthrin was applied at 2 x 12.5 g as/ha, interval was between 14 and 18 days. Total applied amount is above 25 % of intended rate.

S-EU trials
In 3 trials (1995), applications were made at 3 x 13 g as/ha instead of 2 x 12.5 g as/ha. In 1 further trial (2001), applications were made at 2 x 10 g as/ha, interval was 15 days.

All samples were collected between 0 and 28 days after last application and stored frozen for max. 8 months. The target PHI is not always covered in trials.
Samples were analysed for beta-cyfluthrin according to validated methods (00255 and DFG S19; LOQ 0.01 mg/kg; see Vol. 3, B.5.1.2).

Results

Procedural recoveries were acceptable (Table B.7.3-11). Storage of samples (up to 8 months) is not covered by acceptable storage stability studies (see Table B.7.3-11). No residues were found in untreated control samples.
Trial results are summarised in Table B.7.3-12 (N-EU) and Table B.7.3-13 (S-EU). Residues in treated samples are all <0.01 mg/kg.

Table B.7.3-11: Procedural recoveries for beta-cyfluthrin in potato

Study No. Trial No. Year	Crop	Portion analysed	Compound		Fortification level	Recovery (%)		
				n	(mg/kg)	single value	mean	RSD
RA-2147/96 606618 606626 606634 606642 RA-2148/96 606650 607738 607746 1996	Potato	Potato, tuber	Beta-cyfluthrin	5	0.01	107, 108, 115, 116, 118	113	4.4
				8	0.10	99, 102, 109, 109, 111, 112, 113, 115	109	5.1
				13	overall	-	110	5.0
RA-2004/95 501794 501808 504254 1995	Potato	Potato, tuber	Beta-cyfluthrin	2	0.01	99, 99	99	-
				2	0.10	101, 104	103	-
				4	overall	-	101	2.4
RA-2125/01 0273/9 2001	Potato	Potato, tuber	Beta-cyfluthrin	2	0.01	100, 101	101	-
R-30376 12SGS078-FR01 12SGS078-UK02 12SGS078-UK03 12SGS078-GE03 2012	Potato	Potato, tuber	Beta-cyfluthrin	2	0.01	101, 80	91	-
				2	0.10	83,89	86	-
				4	overall	-	88	10.5

Conclusion

A guideline compliant residue data set of 15 trials for beta-cyfluthrin in S-EU and N-EU is available with application rates partly outside 25 % of target rate. Residues are all <0.01 mg/kg. In 7 trials (3xS-EU, 4xN-EU), samplings were made at the target date. The analytical method is validated, procedural recoveries are acceptable and storage stability is covered.
Trials with higher applications are included in acceptable trials. Trials with different samplings all support the findings by showing no residues directly after application as well as at the next sampling point.

Table B.7.3-12: Potato residue data for beta-cyfluthrin in N-EU

RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)

Federal Institute for Risk Assessment, Berlin
Federal Republic of Germany

Content of as (g/kg or g/L) : 8.7 g/L
Formulation (e.g. WP) : EC (Emulsifiable concentrate)
Commercial product (name) : Enduro 258 EC
Applicant : Feinchemie Schwebda GmbH

Active ingredient : beta-cyfluthrin
Crop / crop group : Potato
Crop Code : SOLTU

Submission date : 2014-08-08

Indoors / Outdoors : Outdoors (European North)
Other as in formulation
(content and common name) : 258 g/L oxydemeton-methyl
Residues calculated as : cyfluthrin isomer mixture

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment kg as/ha	Water L/ha	kg as/hl	Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
	(a)	(b)				(c)		(a)		(d)	(e)
M-078830-01-1, RA-2148/96, MO-02-012447, study 606650 France (FR) 27340 Martot 1998-02-20	Sirtema	1)1996-03-30 (planting) 2)1996-06-24 - 1996-07-17 3)1996-08-07	0.0052 0.0052	280 280	0.0019 0.0019	1996-07-03[4)] 1996-07-17[4)]	BBCH 69	tuber	<0.010 <0.010 <0.010	0 21 28	4) spraying analytical method: LC-GC Methode 00255 (RA-321/92) (GC-ECD), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 9 ASB2014-7858
M-078830-01-1, RA-2148/96, MO-02-012447, study 607738 France (FR) 27940 Venables 1998-02-20	Sirtema	1)1996-04-05 (planting) 2)1996-06-17 - 1996-07-17 3)1996-08-07	0.0052 0.0052	280 280	0.0019 0.0019	1996-07-03[4)] 1996-07-17[4)]	BBCH 69	tuber	<0.010 <0.010 <0.010	0 21 28	4) spraying analytical method: LC-GC Methode 00255 (RA-321/92) (GC-ECD), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 9 ASB2014-7858
M-078830-01-1, RA-2148/96, MO-02-012447, study 607746 France (FR) 78920 Ecquevilly 1998-02-20	Viola	1)1996-04-04 (planting) 2)1996-06-25 - 1996-07-17 3)1996-08-07	0.0052 0.0052	280 280	0.0019 0.0019	1996-07-03[4)] 1996-07-17[4)]	BBCH 69	tuber	<0.010 <0.010 <0.010	0 21 28	4) spraying analytical method: LC-GC Methode 00255 (RA-321/92) (GC-ECD), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 10 ASB2014-7858

RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)

Federal Institute for Risk Assessment, Berlin
Federal Republic of Germany

Content of as (g/kg or g/L) : 25 g/L
Formulation (e.g. WP) : EC (Emulsifiable concentrate)
Commercial product (name) : Bulldock
Applicant : ADAMA Deutschland GmbH

Active ingredient : beta-cyfluthrin
Crop / crop group : Potato
Crop Code : SOLTU

Submission date : 2014-06-19

Indoors / Outdoors : Outdoors (European North)
Other as in formulation (content and common name) :
Residues calculated as : cyfluthrin isomer mixture

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment kg as/ha	Water l/ha	kg as/hl	Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
	(a)	(b)				(c)		(a)		(d)	(e)
12SGS078, M-481204-01-1, R-30376, trial 12SGS078 FR01, decline trial France (FR) 08190 Poilcourt Sydney, Champagne-Ardenne 2013-08-21	Bintje	1)2012-05-16 (planting) 2)2012-06-13 - 2012-06-27 3)2012-08-20 - 2012-08-24	0.012 0.013	300 300	0.0041 0.0043	2012-07-30[4)] 2012-08-13[4)]	BBCH 48	tuber	<0.010 <0.010 <0.010	0 3 7	4) spraying analytical method: GA W0003 based on DFG S 19 (L 00.00-34) (GC-MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 9 ASB2014-6718
12SGS078, M-481204-01-1, R-30376, trial 12SGS078 UK02, decline trial United Kingdom (UK) IP10 0EU Nacton, Suffolk 2013-08-21	Carlingford	1)2012-07-25 (planting) 2)2012-09-20 - 2012-10-05 3)2012-11-01 - 2012-11-08	0.012 0.012	300 300	0.0040 0.0040	2012-10-19[4)] 2012-11-02[4)]	BBCH 49	tuber	<0.010 <0.010 <0.010	0 3 7	4) spraying analytical method: GA W0003 based on DFG S 19 (L 00.00-34) (GC-MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 6 ASB2014-6718

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment kg as/ha	Water l/ha	kg as/hl	Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
	(a)	(b)				(c)		(a)		(d)	(e)
12SGS078, M-481204-01-1, R-30376, trial 12SGS078 UK03, harvest trial United Kingdom (UK) L39 8BB Ormskirk, Lancashire 2013-08-21	Markie	1)2012-06-14 (planting) 2)2012-09-02 - 2012-09-14 3)2012-11-12 - 2012-11-16	0.012 0.013	290 300	0.0041 0.0043	2012-10-19[4)] 2012-11-06[4)]	BBCH 48	tuber	<0.010	3	4) spraying analytical method: GA W0003 based on DFG S 19 (L 00.00-34) (GC-MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 7 ASB2014-6718
12SGS078, M-481204-01-1, R-30376, trial 12SGS078 GE04, harvest trial Germany (DE) 49624 Löningen 2013-08-21	Fontane	1)2012-04-18 (planting) 2)2012-06-26 - 2012-07-17 3)2012-08-27 - 2012-09-10	0.013 0.012	310 290	0.0042 0.0041	2012-08-10[4)] 2012-08-24[4)]	BBCH 49	tuber	<0.010	3	4) spraying analytical method: GA W0003 based on DFG S 19 (L 00.00-34) (GC-MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 9 ASB2014-6718

RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)

Federal Institute for Risk Assessment, Berlin
Federal Republic of Germany

Content of as (g/kg or g/L) : 8.5 g/L
Formulation (e.g. WP) : EC (Emulsifiable concentrate)
Commercial product (name) : Enduro
Applicant : ADAMA Deutschland GmbH

Active ingredient : beta-cyfluthrin
Crop / crop group : Potato
Crop Code : SOLTU

Submission date : 2014-06-19

Indoors / Outdoors : Outdoors (European North)
Other as in formulation (content and common name) : 275.6 g/L oxydemeton-methyl
Residues calculated as : cyfluthrin isomer mixture

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment kg as/ha	Water L/ha	kg as/hl	Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
	(a)	(b)				(c)		(a)		(d)	(e)
RA-2147/96, trial 606618 Germany (DE) 51399 Burscheid, Versuchsgut Höfchen 1998-02-20	Hansa	1)1996-04-26 (planting) 2)1996-06-29 - 1996-07-19 3)1996-04-09	0.0085 0.0077 0.0068	300 300 300	0.0028 0.0026 0.0023	1996-07-29[4)] 1996-08-06[4)] 1996-08-14[4)]	BBCH 47	tuber	<0.010 <0.010 <0.010 <0.010 <0.010 <0.010	0[5)] 0 7 14 21 28	4) spraying 5) before last treatment analytical method: LC-GC Methode 00255 (RA-321/92) (GC-ECD), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 8 ASB2014-6706
RA-2147/96, trial 606626, decline trial Germany (DE) 40789 Monheim, Laacherhof 1998-02-20	Sieglinde	1)1996-04-25 (planting) 2)1996-06-19 - 1996-07-15 3)1996-08-16	0.0085 0.0077 0.0068	300 300 300	0.0028 0.0026 0.0023	1996-07-11[4)] 1996-07-19[4)] 1996-07-27[4)]	BBCH 48	tuber	<0.010 <0.010 <0.010 <0.010 <0.010 <0.010	0[5)] 0 6 13 20 27	4) spraying 5) before last treatment analytical method: LC-GC Methode 00255 (RA-321/92) (GC-ECD), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 10 ASB2014-6706
RA-2147/96, trial 606634, decline trial United Kingdom (UK) IP31 3SH Great Green, Thurston, Suffolk 1998-02-20	Maris Peer	1)1996-04-25 (planting) 2) 3)1996-08-21	0.0085 0.0077 0.0068	300 300 300	0.0028 0.0026 0.0023	1996-07-15[4)] 1996-07-24[4)] 1996-07-31[4)]	BBCH 46	tuber	<0.010 <0.010 <0.010	0 21 28	4) spraying analytical method: LC-GC Methode 00255 (RA-321/92) (GC-ECD), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 9 ASB2014-6706

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment kg as/ha	Water L/ha	kg as/hl	Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
	(a)	(b)				(c)		(a)		(d)	(e)
RA-2147/96, trial 606642, decline trial France (FR) 27340 Criquebeuf-sur-Seine 1998-02-20	Charlotte	1)1996-04-03 (planting) 2)1996-06-24 - 1996-07-12 3)1996-08-07	0.0085 0.0077 0.0068	300 300 300	0.0028 0.0026 0.0023	1996-07-01 **4)** 1996-07-09 **4)** 1996-07-17 **4)**	BBCH 43	tuber	<0.010 <0.010 <0.010	0 21 28	4) spraying analytical method: LC-GC Methode 00255 (RA-321/92) (GC-ECD), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 11 ASB2014-6706

Remarks: (a) According to CODEX Classification / Guide
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (Label pre-harvest interval, PHI, underline)
(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

Table B.7.3-13: Potato residue data for beta-cyfluthrin in S-EU

RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)

Federal Institute for Risk Assessment, Berlin
Federal Republic of Germany

Content of as (g/kg or g/L) : 25 g/L
Formulation (e.g. WP) : EC (Emulsifiable concentrate)
Commercial product (name) : Bulldock
Applicant : ADAMA Deutschland GmbH

Active ingredient : beta-cyfluthrin
Crop / crop group : Potato
Crop Code : SOLTU

Submission date : 2014-06-19

Indoors / Outdoors : Outdoors (European South)
Other as in formulation
(content and common name) :
Residues calculated as : cyfluthrin isomer mixture

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment kg as/ha	Water L/ha	kg as/hl	Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
	(a)	(b)				(c)		(a)		(d)	(e)
RA-2004/95, R504254, trial 501808, decline trial Spain (ES) 22000 Tamarite de Litera 1997-03-25	Jaerla	1)1995-03-07 (sowing) 2) 3)1995-07-01	0.013 0.013 0.013	800 800 800	0.0016 0.0016 0.0016	1995-05-30 4) 1995-06-14 4) 1995-06-28 4)	BBCH 48	tuber	<0.010 <0.010 <0.010	0 3 14	4) spraying analytical method: LC-GC Methode 00255 (RA-321/92) (GC-ECD), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 11 ASB2014-6702 RIP1999-314 (summary) ASB2009-3161 (amendment)
RA-2004/95, R504254, trial 501794, decline trial Portugal (PT) 2580 Alenquer 1997-03-25	Raja	1)1995-02-20 (planting) 2)1995-05-12 - 1995-05-25 3)1995-06-09	0.013 0.013 0.013	800 800 800	0.0016 0.0016 0.0016	1995-04-21 4) 1995-05-05 4) 1995-05-19 4)	BBCH 65	tuber	<0.010 <0.010 <0.010	0 3 14	4) spraying analytical method: LC-GC Methode 00255 (RA-321/92) (GC-ECD), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 12 ASB2014-6702 RIP1999-314 (summary) ASB2009-3161

Remarks: (a) According to CODEX Classification / Guide
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (Label pre-harvest interval, PHI, underline)
(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)

Federal Institute for Risk Assessment, Berlin
Federal Republic of Germany

Content of as (g/kg or g/L) : 25 g/L
Formulation (e.g. WP) : SC (Suspension concentrate (= flowable concentrate))
Commercial product (name) : Bulldock SC
Applicant : ADAMA Deutschland GmbH

Active ingredient : beta-cyfluthrin
Crop / crop group : Potato
Crop Code : SOLTU

Submission date : 2014-06-19

Indoors / Outdoors : Outdoors (European South)
Other as in formulation
(content and common name) :
Residues calculated as : cyfluthrin isomer mixture

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment kg as/ha	Water L/ha	kg as/hl	Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
	(a)	(b)				(c)		(a)		(d)	(e)
RA-2004/95, trial 504254, decline trial Portugal (PT) 2580 Alenquer 1997-03-25	Raja	1)1995-02-20 (planting) 2)1995-05-12 -1995-05-25 3)1995-06-09	0.013 0.013 0.013	800 800 800	0.0016 0.0016 0.0016	1995-04-21[4)] 1995-05-05[4)] 1995-05-19[4)]	BBCH 65	tuber	<0.010 <0.010 <0.010	0 3 14	4) spraying analytical method: LC-GC Methode 00255 (RA-321/92) (GC-ECD), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 12 ASB2014-6702 RIP1999-314 (summary) ASB2009-3161 (amendment)

RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)

Federal Institute for Risk Assessment, Berlin
Federal Republic of Germany

Content of as (g/kg or g/L) : 25 g/L
Formulation (e.g. WP) : SC (Suspension concentrate (= flowable concentrate))
Commercial product (name) : Bulldock SC
Applicant : Feinchemie Schwebda GmbH

Active ingredient : beta-cyfluthrin
Crop / crop group : Potato
Crop Code : SOLTU

Submission date : 2014-08-08

Indoors / Outdoors : Outdoors (European South)
Other as in formulation (content and common name) :
Residues calculated as : cyfluthrin isomer mixture

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment kg as/ha	Water L/ha	kg as/hl	Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
	(a)	(b)				(c)		(a)		(d)	(e)
RA-2125/01, study 0273-01, R2001 0273/9, decline trial Greece (GR) 34400 Psahna-Evia 2002-09-20	Spunta	1)2001-02-15 (planting) 2)2001-05-15 - 2001-05-31 3)2001-06-30	0.010 0.010	800 800	0.0013 0.0013	2001-05-23[4)] 2001-06-07[4)]	BBCH 47-49	tuber	<0.010 <0.010 <0.010 <0.010 <0.010	0[5)] 0 7 14 21	4) spraying 5) before last treatment analytical method: GC-Meth. Nr. 00255, RA-321/91 (GC-ECD), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 4 RIP2003-272

Remarks: (a) According to CODEX Classification / Guide
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (Label pre-harvest interval, PHI, underline)
(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

B.7.3.4 Wheat

The critical GAPs for use of the representative formulation of beta-cyfluthrin in wheat are outlined in Table B.7.3-14.

Table B.7.3-14: Critical GAPs for use of beta-cyfluthrin in wheat

Region	Outdoor/ Protected	Maximum Number of Applications	Minimum Application Interval (days)	Maximum		Minimum PHI (days)
				Rate (g as/ha)	Water (L/ha)	
Northern/Central EU	Outdoor	2	14	12.5	150-400	21
Southern EU	Outdoor	2	14	12.5	150-400	21

Data point: KCA 6.3.4/08

Report: Seym, M. (1993): Determination of residues of FCR 4545 125 SC in/on common oat, spring barley and spring wheat under actual use conditions in the Federal Republic of Germany
RA-2053/91
RIP9500587
M-052205-01-1

Guideline(s): Not reported

Deviations: None

GLP: Yes

Acceptability: Acceptable

Data point: KCA 6.3.4/10

Report: Seym, M. (1993): Determination of residues of FCR 4545 125 SC in/on spring barley, spring wheat and common oat under actual use conditions in Germany
RA-2073/92
M-052195-01-1
RIP9500588

Guideline(s): Not reported

Deviations: None

GLP: Yes

Acceptability: Acceptable

Data point:	KCA 6.3.4/28
Report:	Bousquet, C. (2013): Magnitude of the Residue of beta-cyfluthrin in winter wheat (Raw Agricultural Commodity) after two applications of Bulldock 25 EC - 4 harvest trials in Northern Europe (Northern France, United Kingdom and Germany) – 2012 12SGS096 ASB2014-6714 M-481205-01-1, R-30394
Guideline(s):	Directive 91/414/EEC, amended by Commission Directive 96/68/EC
Deviations:	None
GLP:	Yes
Acceptability:	Acceptable

Data point:	KCA 6.3.4/27
Report:	Heinemann, O.; Schoening, R. 2001 Determination of residues of beta-cyfluthrin on wheat following spray treatment of Bullock 025 EC in Italy, Spain and France - Amendment No. 1 from 2001-11-13 RA-2037/00 RIP2003-275 M-073236-02-1
Guideline(s):	Directive 91/414/EEC, amended by Commission Directive 96/68/EC
Deviations:	None
GLP:	Yes
Acceptability:	Acceptable

Materials and methods

N-EU
Eight GLP residue trials in wheat were conducted (1991, 1992, 2012). Wheat plants were treated according to GAP with 2 foliar applications at nominal rates of 12.5 g as/ha (mean deviation: -12.5 %) and an interval of 10-46 days. Grain and straw were collected at commercial harvest stages, not always compliant to GAP (PHI 19-48 d).The samples were stored deep frozen for max. 12 months.

S-EU
Four GLP residue trials in wheat were conducted in one year (2000). Wheat plants were treated according to GAP with 2 foliar applications at nominal rates of 12.5 g as/ha (mean deviation: +3.2 %) and an interval of 13-14 days. Grain and straw were collected compliant to GAP (PHI 21-22 d). The samples were stored deep frozen for max. 5 months.

The samples were analysed for beta-cyfluthrin according to validated methods (method 00255 and 00015; see Vol.3, B.5.1.2).

Results

Procedural recoveries were acceptable except for trial RA-2053/91, where the relative standard deviation exceeds acceptable limits. However, this is not considered to challenge the validity of the trial results relevant for risk assessment and monitoring (Table B.7.3-15).

Storage of samples (up to 12 months) is covered by acceptable storage stability studies (see

Table B.7.3-15). No residues were found in untreated control samples.

Trial results for N-EU are summarised in Table B.7.3-16. Residues in treated grain samples range from <0.01 to 0.016 mg/kg and <0.02 mg/kg at target PHI or later (commercial harvest stage). Where separation into grain and ear was not possible at the target PHI, later sampling was considered adequate to cover realistic growing conditions.Residues in straw were between 0.24 and 1.1 mg/kg.

Trial results for S-EU are summarised in Table B.7.3-17. Residues in grain were constantly <0.01 mg/kg; in straw, residues were in the range of 0.42-0.78 mg/kg. Due to significant residues in straw and the residue situation in N-EU, a no-residue situation can not be stated for wheat grain. The residue data set is therefore not considered complete for S-EU.

Conclusion

A guideline compliant residue data set of 8 trials for beta-cyfluthrin in wheat (N-EU) is available. For S-EU, residue data set with 4 trials is incomplete. A no-residue situation cannot be claimed based on residues in N-EU (lower GAP) and data for straw in both zones.
Residues were found up to 0.016 mg/kg or <0.02 mg/kg in N-EU trials, depending on the analytical method applied. The methods are validated and procedural recoveries acceptable.

Storage stability is covered by adequate studies. The data set is not complete in terms of number of S-EU trials and does not fully cover the regulatory needs.

Table B.7.3-15: Procedural recoveries for beta-cyfluthrin in wheat

Study No. Trial No. Year	Crop	Portion analysed	Compound		Fortification level	Recovery (%)		
				n	(mg/kg)	single value	mean	RSD
RA-2053/91 100986 100994 1991	Wheat	Green material	Beta-cyfluthrin	4	0.04	65, 71, 101, 102	85	23.0
				2	0.40	89, 100	95	-
				2	1.0	76, 79	78	-
				8	overall	-	85	17.1
		Grain	Beta-cyfluthrin	4	0.02	85, 97, 103, 111	99	11.1
				3	0.20	92, 98, 82	91	8.9
				2	1.0	96, 99	98	-
				9	overall	-	96	9.2
		Straw	Beta-cyfluthrin	4	0.05	85, 88, 84, 92	87	4.1
				1	0.50	102	102	-
				2	1.0	74, 86	80	10.6
				7	overall	-	87	9.7

Study No. Trial No. Year	Crop	Portion analysed	Compound		Fortification level	Recovery (%)		
				n	(mg/kg)	single value	mean	RSD
RA-2073/92 203122 2000	Wheat	Green material	Beta-cyfluthrin	2	0.04	104, 107	106	-
				1	0.4	103	103	-
				3	overall	-	105	2.1
		Grain	Beta-cyfluthrin	2	0.01	102, 103	103	-
				1	0.2	100	100	-
				3	overall	-	102	1.5
		Straw	Beta-cyfluthrin	4	0.05	75, 88	82	-
RA-2073/92 200255 2000	Wheat	Green material	Beta-cyfluthrin	2	0.04	84, 93	89	-
				2	0.2	92, 108	100	-
				4	overall	-	94	10.6
		Grain	Beta-cyfluthrin	2	0.02	100, 103	102	-
				1	0.20	95	95	-
				3	overall	-	99	4.1
		Straw	Beta-cyfluthrin	2	0.05	83, 84	84	-
				1	0.20	98	98	-
				3	overall	-	88	9.5
RA-2037/00 0031-00 0232-00 0233-00 0234-00 2000	Wheat	Rest of plant	Beta-cyfluthrin	2	0.04	92, 92	92	-
		Grain	Beta-cyfluthrin	2	0.01	90, 90	90	-
				4	0.1	96, 98, 101, 107	101	4.8
				6	overall	-	97	6.8
		Straw	Beta-cyfluthrin	2	0.04	87, 90	89	-
R-30394 12SGS096FR01 12SGS096FR02 12SGS096GE03 12SGS096UK04 2012	Wheat	Whole plant w/o ears	Beta-cyfluthrin	1	0.01	94	-	-
		Ears	Beta-cyfluthrin	1	0.01	86	-	-
		Grain	Beta-cyfluthrin	3	0.01	70, 80, 105	85	18.0
				3	overall	-	85	18.0
		Straw	Beta-cyfluthrin	3	0.1	70, 88, 95	84	12.9
				3	overall	-	84	12.9

Table B.7.3-16: Residue data for beta-cyfluthrin in wheat (N-EU)

RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)

Federal Institute for Risk Assessment, Berlin
Federal Republic of Germany

Content of as (g/kg or g/L) : 125 g/L
Formulation (e.g. WP) : SC (Suspension concentrate (= flowable concentrate))
Commercial product (name) : FCR 4545
Applicant : Bayer CropScience

Active ingredient : beta-cyfluthrin
Crop / crop group : Spring Soft Wheat
Crop Code : TRZAS

Submission date : 1994-05-27

Indoors / Outdoors : Outdoors (European North)
Other as in formulation
(content and common name) :
Residues calculated as : cyfluthrin isomer mixture

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment kg as/ha	Water L/ha	kg as/hl	Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
	(a)	(b)				(c)		(a)		(d)	(e)
RA-2053/91, 100986, 0098-91 Germany (DE) 6510 Worms Heppenheim 1993-04-30	Star	1)1991-03-27 (sowing) 2)1991-06-24 - 1991-07-08 3)1991-07-29	0.010 0.010	300 300	0.0033 0.0033	1991-06-19[4)] 1991-07-08[4)]	BBCH 69	forage ears of grain grain straw	0.32 0.32 0.59 0.090 <0.020 <0.020 0.47 <0.020	0 7 14 14 21 28 21 28	4) spraying analytical method: GC-Meth. Nr. 00015/M010 RA-318/92 (GC-ECD), LOQ(s): 0.02 mg/kg (grain), 0.04 mg/kg (forage), 0.05 mg/kg (straw), max. sample storage time in month(s): 12 seed treatment with 150ml/dt Baythroid 100 ES (149,8g beta-cyfluthrin/l) RIP9500526 RIP9500587
RA-2053/91, 100994, 0099-91 Germany (DE) 4019 Monheim 1993-04-30	Star	1)1991-03-18 (sowing) 2)1991-06-21 - 1991-06-28 3)1991-08-19	0.010 0.010	300 300	0.0033 0.0033	1991-07-04[4)] 1991-07-29[4)]	BBCH 69	forage grain straw	0.30 <0.020 <0.020 <0.020 0.84 0.82 0.67	0 7 14 21 28 7 14 21 28	4) spraying analytical method: GC-Meth. Nr. 00015/M010 RA-318/92 (GC-ECD), LOQ(s): 0.02 mg/kg (grain), 0.04 mg/kg (forage), 0.05 mg/kg (straw), max. sample storage time in month(s): 9 seed treatment with 150ml/dt Baythroid 100 ES (149,8g beta-cyfluthrin/l) RIP9500526 RIP9500587

RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)

Federal Institute for Risk Assessment, Berlin
Federal Republic of Germany

Content of as (g/kg or g/L) : 25 g/L
Formulation (e.g. WP) : EC (Emulsifiable concentrate)
Commercial product (name) : Bulldock
Applicant : ADAMA Deutschland GmbH

Active ingredient : beta-cyfluthrin
Crop / crop group : Winter Soft Wheat
Crop Code : TRZAW

Submission date : 2014-06-19

Indoors / Outdoors : Outdoors (European North)
Other as in formulation (content and common name) :
Residues calculated as : cyfluthrin isomer mixture

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment kg as/ha	Water l/ha	kg as/hl	Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
	(a)	(b)				(c)		(a)		(d)	(e)
12SGS096, R-30394, M-481205-01-1, trial 12SG096 FR01, harvest trial France (FR) 37370 St Paterne Racan 2013-06-24	Arezzo	1)2011-10-24 (sowing) 2)2012-05-29 - 2012-06-05 3)2012-07-25	0.012 0.012	240 240	0.0050 0.0049	2012-06-08[4)] 2012-06-18[4)]	BBCH 77	grain straw	0.013 0.012 *0.013** 0.24	29 29 29	4) spraying analytical method: GA W 0002 based on DFG S 19 (L 00.00-34) (GC-MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 8 validated level for straw in this study: 0.1 mg/kg *mean of duplicate analyses ASB2014-6714
12SGS096, R-30394, M-481205-01-1, trial 12SG096 FR02, harvest trial France (FR) 02190 Amifontaine, Picardie 2013-06-24	Glasgow	1)2011-10-05 (sowing) 2)2012-05-20 - 2012-06-01 3)2012-08-01	0.012 0.012	190 200	0.0062 0.0061	2012-06-14[4)] 2012-06-28[4)]	BBCH 83	rest of plant ears of grain grain straw	0.16 0.11 <0.010 <0.010 0.33 0.32 *0.33**	21 21 34 34 34 34	4) spraying analytical method: GA W 0002 based on DFG S 19 (L 00.00-34) (GC-MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 7 validated level for straw in this study: 0.1 mg/kg *mean of duplicate analyses ASB2014-6714

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment kg as/ha	Water l/ha	kg as/hl	Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
	(a)	(b)				(c)		(a)		(d)	(e)
12SGS096, R-30394, M-481205-01-1, trial 12SG096 GE03, harvest trial Germany (DE) 49685 Bühren 2013-06-24	Matrix	1)2011-10-28 (sowing) 2)2012-06-06 - 2012-06-20 3)2012-08-15 - 2012-08-16	0.012 0.012	190 200	0.0063 0.0060	2012-07-10[4)] 2012-07-24[4)]	BBCH 87	grain straw	<0.010 0.83	22 22	4) spraying analytical method: GA W 0002 based on DFG S 19 (L 00.00-34) (GC-MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 6 validated level for straw in this study: 0.1 mg/kg ASB2014-6714
12SGS096, R-30394, M-481205-01-1, trial 12SG096 UK04, harvest trial United Kingdom (UK) OX156EP Banbury, Oxfordshire 2013-06-24	JB Diego	1)2011-10-18 (sowing) 2) 3)2012-08-28	0.013 0.012	210 190	0.0062 0.0063	2012-07-27[4)] 2012-08-09[4)]	BBCH 85	grain straw	0.017 0.015 *0.016** 0.85	19 19 19	4) spraying analytical method: GA W 0002 based on DFG S 19 (L 00.00-34) (GC-MS), LOQ(s): 0.01 mg/kg max. sample storage time in month(s): 7 validated level for straw in this study: 0.1 mg/kg *mean of duplicate analyses ASB2014-6714

RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)

Federal Institute for Risk Assessment, Berlin
Federal Republic of Germany

Content of as (g/kg or g/l) : 125 g/L
Formulation (e.g. WP) : SC (Suspension concentrate (= flowable concentrate))
Commercial product (name) : FCR 4545
Applicant : Bayer CropScience

Active ingredient : beta-cyfluthrin
Crop / crop group : Spring Soft Wheat
Crop Code : TRZAS

Submission date : 1994-05-27

Indoors / Outdoors : Outdoors (European North)
Other as in formulation (content and common name) :
Residues calculated as : cyfluthrin isomer mixture

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment kg as/ha	Water L/ha	kg as/hl	Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
	(a)	(b)				(c)		(a)		(d)	(e)
RA-2073/92, 0025-92, 200255 Germany (DE) 51399 Burscheid 1993-10-15	Star	1)1992-03-05 (sowing) 2)1992-06-15 - 1992-06-19 3)1992-08-05	0.010 0.010	300 300	0.0033 0.0033	1992-05-18[4)] 1992-06-19[4)]	BBCH 69	forage ears of grain grain straw	0.17 0.080 <0.040 <0.020 0.18	0 21 21 48 48	4) spraying analytical method: GC-Meth. Nr. 00015/M010 RA-318/92 (GC-ECD), LOQ(s): 0.02 mg/kg (grain), 0.04 mg/kg (forage), 0.05 mg/kg (straw), max. sample storage time in month(s): 1 RIP9500530 RIP9500588
RA-2073/92, 203122 Germany (DE) 67551 Worms 1993-10-15	Star	1)1992-03-02 (sowing) 2)1992-06-03 - 1992-06-20 3)1992-07-20	0.010 0.010	300 300	0.0033 0.0033	1992-05-14[4)] 1992-06-29[4)]	BBCH 75	forage grain straw	0.62 <0.010 <0.010 1.1 0.57	0 21 28 21 28	4) spraying analytical method: GC-Meth. Nr. 00015/M010 RA-318/92 (GC-ECD), LOQ(s): 0.01 mg/kg (grain), 0.04 mg/kg (forage), 0.05 mg/kg (straw), max. sample storage time in month(s): 1 RIP9500530 RIP9500588

Table B.7.3-17: Residue data for beta-cyfluthrin in wheat (S-EU)

RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)

Federal Institute for Risk Assessment, Berlin
Federal Republic of Germany

Content of as (g/kg or g/L) : 25.8 g/L
Formulation (e.g. WP) : EC
Commercial product (name) : Bulldock 003977-00
Applicant : Bayer CropScience Deutschland GmbH

Active ingredient : beta-Cyfluthrin
Crop / crop group : Winter Wheat

Submission date : 2003-07-02

Indoors / outdoors : Outdoors (European South)
Other a. i. in formulation (common name and content) :
Residues calculated as : beta-Cyfluthrin

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment kg as/ha	Water L/ha	kg as/hl	Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
	(a)	(b)				(c)		(a)		(d)	(e)
RA-2037/00 0031-00 Spain 08220 Torrebonica 2001-09-13	Bonpaint	1)1999-12-17 (sowing) 2)2000-05-15 3)2000-06-30	0.0129 0.0129	300 300	0.0043 0.0043	2000-05-08 2000-05-22[4)]	BBCH 75-77	rest of plant ears of grain grain straw	0.46 0 28 <0.01 <0.01 0.43 0.40	0 0 22 44 22 44	4) spraying analytical method: GC-Meth. Nr. 00255, RA-321/91, LOQ(s): 0.01 mg/kg (grain), 0.04 mg/kg (rest of plant, ears of grain, straw), max. sample storage time in month(s): 5 RIP2003-275
RA-2037/00 0232-00 France 31790 St. Jory (Toulouse) 2001-09-13	Soissons	1)1999-11-10 (sowing) 2)2000-05-15 - 2000-05-25 3)2000-07-05	0.0129 0.0129	300 300	0.0043 0.0043	2000-05-31 2000-06-14[4)]	BBCH 85	rest of plant ears of grain grain straw	0.44 0 23 <0.01 0.01 0.71 0 50	0 0 21 28 21 28	4) spraying analytical method: GC-Meth. Nr. 00255, RA-321/91, LOQ(s): 0.01 mg/kg (grain), 0.04 mg/kg (rest of plant, ears of grain, straw), max. sample storage time in month(s): 4 RIP2003-275

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1)Sowing or planting 2)Flowering 3) Harvest	Application rate per treatment kg as/ha	Water L/ha	kg as/hl	Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
	(a)	(b)				(c)		(a)		(d)	(e)
RA-2037/00 0233-00 Italy 71100 Foggia 2001-09-13	Italo	1)1999-11-28 (sowing) 2)2000-04-20 - 2000-04-30 3)2000-06-15	0.0129 0.0129	300 300	0.0043 0.0043	2000-05-26 2000-06-09[4)]	BBCH 75	rest of plant ears of grain grain straw	0 92 0.42 <0.01 <0.01 0.49 0.78	0 0 21 28 21 28	4) spraying analytical method: GC-Meth. Nr. 00255, RA-321/91 LOQ(s): 0.01 mg/kg (grain), 0.04 mg/kg (rest of plant, ears of grain, straw), max. sample storage time in month(s): 5 RIP2003-275
RA-2037/00 0234-00 Spain 17473 Ventallo 2001-09-13	Sarina	1)1999-11-01 (sowing) 2)2000-04-29 - 2000-05-02 3)2000-06-15	0.0129 0.0129	300 300	0.0043 0.0043	2000-05-09 2000-05-23[4)]	BBCH 85	rest of plant ears of grain grain straw	0 32 0 25 <0.01 <0.01 0.40 0.42	0 0 22 29 22 29	4) spraying analytical method: GC-Meth. Nr. 00255, RA-321/91 LOQ(s): 0.01 mg/kg (grain), 0.04 mg/kg (rest of plant, ears of grain, straw), max. sample storage time in month(s): 5 RIP2003-275

B.7.4 Feeding studies

The overall exposure of livestock by treated feed is integral part of the assessment of active substances as is the limited view on the representative uses in the RAR. Therefore, two types of dietary burden calculations are presented to put the residue transfer from feed to livestock animal in the perspective of the overall and the exposure by intended uses of the applicants.

Dietary burden calculation (overall approach)
The potential intake of cyfluthrin and beta-cyfluthrin residues by livestock was evaluated in the EFSA Reasoned opinion on the modification of the existing MRLs for cyfluthrin in various commodities of plant and animal origin (EFSA Journal 2010;8(5):1618, ASB2012-3412). In its reasoned opinion, EFSA considered the residue input values from authorised and applied uses to calculate potential intakes of residues by livestock (Table B.7.4-1).

Table B.7.4-1: Input values for the dietary burden calculation (EFSA Journal 2010;8(5):1618)

Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: cyfluthrin, including other mixtures of constituent isomers (sum of isomers)				
Alfalfa	0.43	STMR (Germany, 2007)	0.65	HR (Germany, 2007)
Cabbage	0.11	STMR (Germany, 2007)	0.34	HR (Germany, 2007)
Sugar beet leaves	0.04	STMR (Germany, 2007)	0.04	HR (Germany, 2007)
Fodder beet leaves	0.04	STMR (Germany, 2007)	0.04	HR (Germany, 2007)
Alfalfa silage	0.43 (0.43*1)	STMR (Germany, 2007) *PF (EFSA, 2009)	0.65 (0.65*1)	HR (Germany, 2007) *PF (EFSA, 2009)
Maize silage	0.01 (0.01*1)	STMR (Germany, 2007) *PF (EFSA, 2009)	0.01 (0.01*1)	HR (Germany, 2007) *PF (EFSA, 2009)
Apples pomace (wet)	0.19 (0.07*2.7)	STMR*PF (Germany, 2007)	0.19 (0.12*2.7)	STMR*PF (Germany, 2007)
Alfalfa hay	1.72 (0.43*4)	STMR (Germany, 2007) *PF (EFSA, 2009)	2.6 (0.65*4)	HR (Germany, 2007) *PF (EFSA, 2009)
Potato	0.03	STMR (Germany, 2007)	0.04	HR (Germany, 2007)
Wheat grain	0.02	MRL	0.02	MRL
Barley grain	0.02	MRL	0.02	MRL
Rye grain	0.02	MRL	0.02	MRL
Oat grain	0.02	MRL	0.02	MRL
Maize grain	0.01	STMR (Germany, 2007)	0.01	HR (Germany, 2007)
Wheat bran	*0.16 (0.02*8)*	*MRL*PF (EFSA, 2009)*	*0.16 (0.02*8)*	*MRL*PF (EFSA, 2009)*
Rye bran	*0.16 (0.02*8)*	*MRL*PF (EFSA, 2009)*	*0.16 (0.02*8)*	*MRL*PF (EFSA, 2009)*
Wheat straw	0.94	STMR (Germany, 2007)	2.2	HR (Germany, 2007)
Barley straw	1.65	STMR (Germany, 2007)	10	HR (Germany, 2007)
Rye straw	0.94	STMR (Germany, 2007)	2.2	HR (Germany, 2007)
Oat straw	1.65	STMR (Germany, 2007)	10	HR (Germany, 2007)
Peas (dry)	0.01	STMR (Germany, 2007)	0.01	HR (Germany, 2007)

Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Beans (dry)	0.01	STMR (Germany, 2007)	0.01	HR (Germany, 2007)
Rape seed	0.05	MRL	0.05	MRL
Rape seed meal	0.05 (0.05*1)	MRL*PF (DE, 2009)	0.05 (0.05*1)	MRL*PF (DE, 2009)

The median and maximum dietary burdens were then calculated for the different types of livestock using the methodologies described in the EU Guidance Document (SANCO 7031/VI/95 rev. 4, 22/07/1996). No re-calculation using the OECD feeding table is performed in this RAR.
The reported median and maximum dietary burdens are summarised in Table B.7.4-2.

Table B.7.4-2: Results of the dietary burden calculation (EFSA Journal 2010;8(5):1618)

	Maximum dietary burden (mg/kg bw/d)	Median dietary burden (mg/kg bw/d)	Highest contributing commodity	Max dietary burden (mg/kg DM)	Trigger exceeded
Risk assessment residue definition: cyfluthrin, including other mixtures of constituent isomers (sum of isomers)					
Dairy ruminants	0.18	0.078	Alfalfa silage	4.93	Yes
Meat ruminants	0.32	0.092	Alfalfa silage	7.44	Yes
Poultry	0.013	0.007	Potatoes	0.21	Yes
Pigs	0.027	0.019	Alfalfa (fresh)	0.68	Yes

Dietary burden calculation (RAR approach)
In order to evaluate the representative uses in sugar beet, potato, wheat and tomato, a separate dietary burden calculation is performed focusing on these uses only. The input values in Table B.7.4-3 were used.

Table B.7.4-3: Input values for the dietary burden calculation (input values from RAR 2015)

Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: cyfluthrin, including other mixtures of constituent isomers (sum of isomers)				
Sugar beet leaves	0.01[a]		0.01 [a]	
Potato	0.01 [a]		0.01 [a]	
Wheat grain	0.01		0.01 [b]	
Wheat straw	0.72[c]		1.1	

[a] all values <LOQ
[b] median residue input level
[c] tentatively; combined data set for NEU (complete set) and SEU (incomplete set)

The median and maximum dietary burdens were then calculated for the different types of livestock using the OECD feeding table (as integrated in EFSA spreadsheet 2015). The calculated median and maximum dietary burdens are summarised in Table B.7.4-4.

Table B.7.4-4: Results of the OECD dietary burden calculation (input values from RAR 2015)

	Maximum dietary burden (mg/kg bw/d)	Median dietary burden (mg/kg bw/d)	Highest contributing commodity	Maximum dietary burden (mg/kg DM)	Trigger exceeded
Risk assessment residue definition: cyfluthrin, including other mixtures of constituent isomers (sum of isomers)					
Cattle					
Beef	0.006	0.004	Wheat straw	0.27	Yes
Dairy	0.010	0.007	Wheat straw	0.27	Yes
Sheep					
Ram/ewe	0.017	0.012	Wheat straw	0.52	Yes
Lamb	0.022	0.015	Wheat straw	0.51	Yes
Swine					
Breeding	0.001	0.001	Potato	0.03	No
Finishing	0.001	0.001	Potato	0.03	No
Poultry					
Broiler	0.001	0.001	Potato	0.01	No
Layer	0.009	0.006	Wheat straw	0.14	Yes
Turkey	0.001	0.001	Potato	0.02	No

An overview of N rates for all metabolism and feeding studies is presented in Table B.7.4-5. These N rates are used to assess the relevance of metabolites detected in the various livestock studies under conditions of intended uses. The metabolites' relevance for dietary risk assessment (not MRL setting) is checked by making use of adequate consumption data (apart of generic values, e.g. 0.01 mg/kg), and therefore they rely, with regard to meat ruminants, on data for beef cattle rather than sheep data, although the dietary burden for the latter exceeds that from cattle.

Table B.7.4-5: N rates of metabolism and feeding studies

Metabolism or feeding study [b]	Animal	Dose rate [mg/kg bw/d]			N rate [c,d]			
			RAR 2015 (OECD feeding table)			EFSA 2010 (EC feeding table)		
			Beef cattle [a]	Ewe	Poultry	Beef ruminants	Dairy ruminants	Poultry
KCA 6.2.3 /01	Cow	0.5	77	23		1.6	2.8	
KCA 6.5.3 /20	Cow	0.5	77	23		1.6	2.8	
KCA 6.2.3 /14	Goat	0.11	17	5		0.3	0.6	
	Goat	1	155	46		3.1	5.6	
KCA 6.2.2 /08	Hen	5			530			385
KCA 6.4.1 /02	Hen	3000			333333			230769
KCA 6.4.1/04	Hen	0.848			94			65
	Hen	2.26			251			174
	Hen	8.5			944			654
KCA 6.4.2/05	Cow	0.163	25	7		0.5	0.9	
	Cow	0.507	78	23		1.6	2.8	
	Cow	1.61	249	74		5.0	8.9	
KCA 6.4.2/08	Cow	0.45	70	21		1.4	2.5	
	Cow	1.5	232	69		4.7	8.3	
	Cow	4.5	696	206		14	25	

[a] critical intake of lamb/ram not considered for N rate calculation as no reliable food consumption data are currently available
[b] including supporting studies
[c] RAR 2015 refers to the dietary burden from the representative uses based on OECD feeding table (Table B.7.4-4)
[d] EFSA 2010 refers to the dietary burden published in EFSA Journal 2010;8(5):1618 based on EU feeding table (Table B.7.4-2)

B.7.4.1 Residue analytical methods for products of animal origin

Analytical methods used for the assessment of poultry and ruminant feeding studies are presented in Table B.7.4-6. Full assessment of these methods is provided in Vol.3, B.5.1.2.

Table B.7.4-6: Residue analytical methods used for feeding studies with cyfluthrin

			Analytical method							
Feeding study	**Report No.**		85883	90388	90392	85981	85982	85983	86217	84631
		BfR-No.	RIP94 00740	RIP94 00741	RIP94 00742	RIP94 01251	RIP94 01252	MET94 00017	RIP94 00874	RIP94 00878
	Cow									
	90383	RIP9400726	x		x					
	86039	RIP9400717	x			x				
	86218	RIP9400722							x	
	90387	RIP9400725	x	x						
	86040	RIP9400716	x							
	88970	RIP9400724	x							
	90386	RIP9400726	x		x					
	Hen									
	86046	RIP9400721							x	
	86033	RIP9400718	x					x		
	86658	RIP9400723							x	x
	86034	RIP9400719	x				x			

In general, two methods including their amendments were used for analysis of animal matrices. The conclusion of assessments state:

Method 1, code/numbers I476 / 85883 (method used in animal feeding studies)
In accordance to SANCO/3029/99 rev 4 the method cannot be considered as valid. Valid studies with identical extraction methods and cleanup are not presented. Therefore, any sound estimation of LOQ is not possible and reported residue concentrations <0.10 mg/kg should be considered as ≤ 0.10 mg/kg.

Justification:
The extent of recovery trials (number of replicates per level) is too low. The linearity of calibration and the selectivity (chromatograms of control samples) are not or inadequately demonstrated. All recovery data are obtained by single level calibration using a standard corresponding to 0.10 mg/kg. Many control samples have shown too high signal intensities at the retention time of cyfluthrin.
It could be shown by Murphy (1985, RIP9400724) that the extraction efficiency strongly depends on experimental parameters. The exchange of an Omni Mixer (applied in Morse Laboratories) by a Tekmar Tissumizer resulted in ≥ 800 % recovery of cyfluthrin from kidney and liver samples with incurred residues.

Method 2, code/number I488/86217 (method used in animal feeding studies)
In accordance to SANCO/3029/99 rev 4 the method cannot be considered as valid. Valid studies with identical extraction methods and cleanup are not presented. Therefore, any sound estimation of LOQ is not possible and reported residue concentrations <0.10 mg/kg should be considered as ≤ 0.10 mg/kg. The comment made by Seym (1995, ASB2009-1209; KCA 4.1.2/53) is not accepted.

Justification:
The extent of recovery trials (number of levels and replicates per level) is too low. The selectivity (chromatograms of control samples) is not or inadequately demonstrated. All recovery data are obtained by single level calibration using a standard corresponding to 0.10 mg/kg. The reliability of the methods suffers from the complexity of cleanup and derivatization, which makes losses of residues likely. Finally, the high sample concentration in final will reduces the selectivity of the method.
It could be shown by Murphy (1985, RIP9400724) that the extraction efficiency strongly depends on experimental parameters. The exchange of an Omni Mixer (applied in Morse Laboratories) by a Tekmar Tissumizer resulted in ≥ 800 % recovery of cyfluthrin from kidney and liver samples with incurred residues.

Conclusion
No validated LOQ is available for the feeding studies, but a surrogate LOQ of 0.1 mg/kg can be proposed (see Vol. 3, B.5.1.2). However, in the following assessment of livestock feeding studies, the LOQ of 0.01 mg/kg is reported as is done in the original reports. These values should be considered as indicative only, and they will not form the basis for subsequent risk assessments.

B.7.4.2 Poultry

Data point:	KCA 6.4.1/04
Report:	[redacted] (1983): A 28 day Baythroid poultry feeding study Report MR86046 M-060241-02-1 RIP9400721
Guideline(s):	None stated. Study design follows largely OECD 505.
Deviations:	-
GLP:	No
Acceptability:	Acceptable

Supporting study I
Analysis of tissue samples from report RIP9400721 for residues of cyfluthrin in tissues with residue analytical method from report RIP9400740 and modifications in MET9400017

Data point:	KCA 6.4.1/03
Report:	[redacted] (1983): Residues of Baythroid in chicken tissues. Raw data (parent in chicken tissues). Report 86033 M-062920-01-1 RIP9400718
Guideline(s):	None stated. Study design follows largely OECD 505.
Deviations:	-
GLP:	No
Acceptability:	Acceptable as part of RIP9400721

	Supporting study II Analysis of tissue samples from report RIP9400721 for residues of metabolites acid-cyfluthrin, FPBalc, FPBald and FPBacid in tissues with residue analytical method from report RIP9400740 and modifications in RIP9401252
Data point:	KCA 6.4.1/05
Report:	[redacted] (1984): A 28 day Baythroid poultry feeding study. Raw data (metabolites in chicken tissues) Report MR86658 M-068248-01-1 RIP9400723 Metabolite analyses; 31.01.-
Guideline(s):	None stated. Study design follows largely OECD 505.
Deviations:	-
GLP:	No
Acceptability:	Acceptable as part of RIP9400721
	Supporting study III Analysis of egg samples from report RIP9400721 for residues of cyfluthrin in eggs with residue analytical method from report RIP9400740 and modifications in RIP9401252
Data point:	KCA 6.4.1/06
Report:	[redacted] (1983): Residues of Baythroid in chicken eggs. Raw data (parent in eggs) Report 86034 M-136924-01-1 RIP9400719
Guideline(s):	None stated. Study design follows largely OECD 505.
Deviations:	-
GLP:	No
Acceptability:	Acceptable

Materials and methods

Forty laying hens were divided into 4 groups of 10 hens each. Cyfluthrin was applied via feed treatment. The administered dose in the groups was to 2, 5.6 and 20 mg/kg feed for 28 days, corresponding to 0, 0.848, 2.26 and 8.50 mg/kg bw/d (referring to pre-treatment body weight). N rates referring to laying hens are 90, 240 and 901.

Eggs were collected daily, separated from shells, homogenised and stored frozen until analyses within 3 weeks after final sampling (day 28 samples were analysed only).
Each group of hens was sacrificed 28 days after the first dose (hours elapsed between last dose and sacrifice not reported). For each group, samples of liver, muscle (composite of breast, leg and thigh), heart, gizzard (minus lining and contents), fat, kidney and skin were combined, homogenised, and stored frozen for 5 weeks (parent) or 6 months (metabolites) prior to analysis. Storage temperature is not reported.

Housing conditions in, feed uptake, significant egg production and slight body weight losses were recorded. High temperatures during performance of the study may have influenced body weights/egg production, however, this is not not considered to impact the quantitative transfer of cyfluthrin from

feed to animal.

Analyses of samples were performed using the methods reported in Table B.7.4-6. Samples of liver, gizzard, muscle and skin were also analysed for the cyfluthrin metabolites acid-cyfluthrin (FCR 2728), FPBalc (FCR 1261), FPBald (FCR 1260) and FPBacid (COE 538/78) by method 86217 (RIP9400874). Acid cyfluthrin was analysed by GC, while FPBalc and FPBald were oxidised to FPBacid and then analysed by HPLC

Results

Stability of the test material in feed after room and freezer storage was proven. No procedural recoveries are reported.

Residues of cyfluthrin and metabolites are summarised in Table B.7.4-7. No residues were detected in control samples.

Table B.7.4-7: Cyfluthrin and metabolite residues in tissues and eggs from chickens fed treated feed for 28 days [b]

Dose level [c]	Gizzard	Skin	Muscle	Fat	Liver	Egg [a]
[mg/kg bw/d]	[mg/kg]	[mg/kg]	[mg/kg]	[mg/kg]	[mg/kg bw/d]	[mg/kg]
Cyfluthrin						
0.848 (90N)	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
2.26 (240N)	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01
8.50 (901N)	<0.01 <0.01	0.01 0.01	<0.01 <0.01	0.05 0.05	<0.01 <0.01	<0.01 <0.01
Acid-cyfluthrin (FCR 2728)						
0.848 (90N)	n.a.	n.a.	n.a.	n.a.	<0.01	n.a.
2.26 (240N)	n.a.	n.a.	n.a.	n.a.	<0.01	n.a.
8.50 (901N)	<0.01	<0.01	<0.01	<0.01	<0.01	n.a.
FPBalc (FCR 1261), FPBald (FCR 1260) and FPBacid (COE 538/78) determined as FPBacid						
0.848 (90N)	n.a.	n.a.	n.a.	n.a.	<0.01	n.a.
2.26 (240N)	<0.01	<0.01	<0.01	<0.01	0.02	n.a.
8.50 (901N)	<0.01	<0.01	<0.01	<0.01	0.02	n.a.

[a] 28 day samples
[b] duplicates of composite tissue samples from 10 animals
[c] rounded values, based on laying hen OECD dietary burden for RAR input values (Table B.7.4-4)
n.a. not analysed due to residues <LOQ in all samples of the 2.26 mg/kg bw/d group

Conclusion

In this non-GLP feeding study, adequate dose levels of the residue of concern, cyfluthrin, was administered to laying hens (dose range of 0.848 to 8.50 mg/kg bw/d; 90-901N refering to maximum rate; see Table B.7.4-2). Using analytical methods not satisfying current quality criteria (see Vol. 3, B.5.1.2), significant residue levels for parent were only found in the high dose group for fat. Levels of combined residues of FPBacid and metabolites oxidised to FPBacid were 0.02 mg/kg in liver of the medium and high dose groups.

The following limitations are noted:
- Non-GLP
- The analytical method does not allow for quantitative estimates of residue levels below 0.1 mg/kg

(see assessment of analytical method in Vol.3, B.5.1.2), therefore, risk assessments and MRL proposals will not use reported values below this level
- No information on sample handling and storage contained in the reports (e.g. time between last dose and sacrifice; storage temperature)
- Limited analysis of samples for eggs (day 28 only)
- No storage stability data available for cyfluthrin in eggs (data requirement)
- Limited storage stability data for metabolites available (FPBald stability is proven in liver for 13 months under defined storage conditions; no further data available; no data requirement)
- Composite samples analysed (no individual results)
- No procedural recoveries reported
- No chromatograms included in the various reports

The study is, despite of the noted limitations, considered adequate to quantitatively assess the occurrence of beta-cyfluthrin residues in poultry matrices. The uncertainties are addressed by sufficiently conservative estimates for monitoring and risk assessment.

B.7.4.3 Ruminants

Data point:	KCA 6.4.2/05
Report:	[redacted] (1984): Baythroid (TM) 28 day bovine feeding study (revised 23.01.1984) Report MR86045 M-055028-02-1 RIP9400720
Guideline(s):	None stated. Study design follows largely OECD 505.
Deviations:	-
GLP:	No.
Acceptability:	Acceptable (with limitations)

Supporting study I
Raw data to report RIP9400720 using residue analytical method from report RIP9400740

Data point:	KCA 6.4.2/03
Report:	[redacted] (1983): Residue of Baythroid in bovine milk. Report 86040 M-062087-01-1 RIP9400716
Guideline(s):	None stated. Study design follows largely OECD 505.
Deviations:	-
GLP:	No.
Acceptability:	Acceptable as part of RIP9400720

Supporting study II
Raw data to report RIP9400720 using residue analytical method from report RIP9400740, amended by RIP9401251

Data point: KCA 6.4.2/04

Report: [redacted] (1983): Residues of Baythroid in cattle tissues.
MR86039
M-062229-01-1
RIP9400717

Guideline(s): None stated. Study design follows largely OECD 505.

Deviations: -

GLP: No.

Acceptability: Acceptable as part of RIP9400720

Supporting study III
Re-analysis of liver and kidney samples from report RIP9400720 with residue analytical method from report 85883 (RIP9400740)

Data point: KCA 6.4.2/09

Report: [redacted] (1985): Baythroid: Identity of major components in cow liver (1st revision 05.08.1985)
Report 88970
M-053779-01-1
RIP9400724

Guideline(s): None stated. Study design follows largely OECD 505.

Deviations: -

GLP: No.

Acceptability: Acceptable as part of RIP9400720

Supporting study IV
Analysis of liver and kidney samples from report RIP9400720 for residues of acid-cyfluthrin (FCR 2728) and FPBald/FPBalc/FPBacid (FCR1260/FCR1261/COE 538/78) with residue analytical method from report RIP9400874

Data point: KCA 6.4.2/10

Report: [redacted]. (1984): Bovine residue feeding study (28 day): Analysis of Baythroid metabolite residues
MR86218
RIP9400722

Guideline(s): None stated. Study design follows largely OECD 505.

Deviations: -

GLP: No.

Acceptability: Acceptable as part of RIP9400720

[redacted] (1984, RIP9400720)
Twelve Holstein dairy cows were divided in four groups and dosed with cyfluthrin at nominal levels of 5, 15 and 50 mg/kg in the diet (corresponding to mean levels of 0.163, 0.507 and 1.61 mg/kg bw/d plus control group, based on 29d mean body weights). The respective rates (referring to the

representative uses assessed within this RAR), are between 25-249N for meat and 7-74N for milk (Table B.7.4-2).
Cyfluthrin was administered via capsule orally once per day after the morning milking. 29 morning doses were administered to each animal, with sacrifice shortly after dosing on day 29.

Aliquots of evening milk and the following morning's milk were mixed and retained frozen for up to 43 days before extraction and analysis. Storage conditions are not reported. Samples of muscle (composite of flank, loin and round), fat (composite of renal, omental and subcutaneous), liver and kidney were collected at sacrifice and stored retained frozen for up to 35 days prior to analysis.

Samples were analysed for parent cyfluthrin with residue analytical method 1476 (RIP9400740) and for metabolites FCR 1260, FCR 1261 and COE 538/78 with method 1488 (RIP9400874).

Samples were extracted with acetone/chloroform (2:1) for all tissues except fat for which hexane was used. The organosoluble extract was partitioned with various solvents to remove lipids and polar and non-polar interferences. The final purification step was column chromatography of the sample on either a silica gel column or a Florisil Sep-Pak. Determination of cyfluthrin residues was by GC-ECD. Recoveries for milk fortified at 0.02 mg/kg were 90 to 125 % and for tissues fortified at 0.05 mg/kg 67 to 100 %.

Residue levels of cyfluthrin in milk and tissues are summarised in Table B.7.4-8 and Table B.7.4-9. A plateau is apparently formed within the study period (however, based on four samplings only). No residues were detected in untreated control samples.

Samples were analysed for parent within 2 months after sacrifice (issue date of 1st report).

Table B.7.4-8: Cyfluthrin residues in milk from dairy cows dosed with cyfluthrin daily for 29 days

Dose level [a]	Day 7	Day 14	Day 21	Day 28
[mg/kg bw/d]	[mg/kg]	[mg/kg]	[mg/kg]	[mg/kg]
0.163 (7N rate*)	n.a.	n.a.	n.a.	0.02 0.02 0.01
Mean	-	-	-	***0.02***
0.507 (23N rate*)	n.a.	n.a.	n.a.	0.03 0.03 0.08
Mean	-	-	-	***0.05***
1.61 (74N rate*)	0.16 0.19 0.08	0.25 0.26 0.16	0.21 0.21 0.12	0.17 0.16 0.10
Mean	***0.14***	***0.22***	***0.18***	***0.14***

[a] values based on dairy cattle OECD dietary burden for RAR input values (Table B.7.4-4)
n.a. not analysed
*Refering to intake from representative uses

Table B.7.4-9: Cyfluthrin residues in tissues from dairy cows dosed with cyfluthrin daily for 29 days

Dose level [a]	Fat	Muscle	Liver		Kidney	
[mg/kg bw/d]	[mg/kg]	[mg/kg]	[mg/kg]		[mg/kg]	
0.163 (25N rate*)	0.30 0.24 0.21	<0.01 <0.01 <0.01	n.a.		n.a.	
Mean	***0.25***	***<0.01***	-		-	
0.507 (78N rate*)	0.66 0.71 0.73	<0.01 <0.01 0.02	<0.01 <0.01 <0.01		<0.01 <0.01 <0.01	
Mean	***0.7***	***0.01***	***<0.01***		***<0.01***	
1.61 (249N rate*)	2.38 2.54 3.00	0.03 0.03 0.03	<0.01 <0.01 <0.01	0.14 [b] 0.13 [b] 0.13 [b]	0.01 <0.01 0.02	0.18 [b] 0.16 [b] 0.16 [b]
Mean	***2.6***	***0.03***	***<0.01***		***0.01***	

[a] values based on beef cattle OECD dietary burden for RAR input values (Table B.7.4-4)
[b] re-analysis of samples with stringent extraction method (Murphy 1985, RIP9400724); values used for MRL and dietary risk assessment
n.a. not analysed because residues at higher feeding level are <0.01 mg/kg
*Refering to intake from representative uses

Murphy (1985, RIP9400724)
A re-analysis of liver and kidney high dose samples from the study [redacted] (RIP9400720) was performed to address the apparent discrepancies between the feeding (<0.01 mg/kg in kidney/liver) and metabolism study (0.105/0.535 mg/kg in kidney/liver; both at 0.5 mg/kg bw dose level in dairy cow). The re-analysis of liver and kidney samples uses a stronger mechanical homogenization/extraction method (homogenisation with ultra-sonication and producing shearing force). Results are summarised in Table B.7.4-9.

Anon. (1984, RIP9400722)
Kidney and liver samples were subsequently analysed for acid-cyfluthrin as well as combined residues of FPBald, FPBacid and FPBalc (all oxidized to FPBacid) with analytical method 86217 (Shaw et al. 1984, RIP9400874). Residue levels are summarised in Table B.7.4-10. No residues were detected in untreated control samples.

Table B.7.4-10: Residues of acid cyfluthrin in liver and kidney and combined residues of FPBald, FPBacid and FPBalc (dairy cows dosed with cyfluthrin daily for 29 days)

Dose level	Liver	Kidney	Liver	Kidney
[mg/kg bw/d]	[mg/kg]	[mg/kg]	[mg/kg]	[mg/kg]
	acid-cyfluthrin (FCR 2728)		FPBald (FCR 1260), FPBalc (FCR 1261), FPBacid (COE538/78)[a]	
0.163 (25N rate *)	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01
Mean	***<0.01***	***<0.01***	***<0.01***	***<0.01***
0.507 (78N rate *)	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	<0.01 <0.01 0.01

Mean	***<0.01***	***<0.01***	***<0.01***	***0.01***
1.61 (249N rate *)	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	0.03 0.02 0.02	0.05 <0.01 0.02
Mean	***<0.01***	***<0.01***	***0.02***	***0.03***

[a] determined as FPBacid (COE 538/78)
*Refering to intake from representative uses

Conclusion

A non-GLP feeding study covering the dose range of 0.163 to 1.61 mg/kg bw/d was performed on dairy cows. Using analytical methods not satisfying current quality criteria (see Vol. 3, B.5.1.2), the residue levels for parent were significant in all dose groups for fat and milk following a linear correlation.
In samples of kidney, muscle and liver, residues above 0.01 mg/kg were only determined in the highest dose group, however, results are of limited reliability due to analytical deficiencies of the method 86217 (see Vol. 3, B.5.1.2)
Storage stability data show that within the analysis period of this study (2 months), incurred residues of parent were not quantitatively recovered in kidney samples (see Table B.7.1-10, p. 34). An underestimation of residue levels can therefore not be excluded. However, considering the fat solubility of cyfluthrin, this finding for kidney is not challenging the validity of the study.

The following limitations are noted:
- Non-GLP
- The analytical method does not allow for quantitative estimates of residue levels below 0.1 mg/kg (see assessment of analytical method in Vol.3, B.5.1.2), therefore, risk assessments and MRL proposals will not use reported values below this level (if based on this study)
- No information on sample handling and storage (period, temperature) contained in the reports
- No storage stability for kidney demonstrated (storage period exceeds period of proven stability under frozen conditions)
- Limited samplings of milk
- No procedural recoveries reported
- No chromatograms included in the various reports

The study is, irrespective of the limitations, considered adequate for the assessment of beta-cyfluthrin within the whole data package of several feeding and metabolism studies. The relevant transfer of parent into fat and milk and non-relevant transfer into other matrices can be assessed in a quantitative way. Limitations are considered as additional uncertainties requiring a conservative approach for risk assessment.

Data point: KCA 6.4.2/08

Report: [redacted] (1994): Cyfluthrin - A 28 day dairy cattle feeding study
Report 106628
M-054521-01-1
RIP9500449

Guideline(s): EPA Ref. 171-4(j), Magnitude of the residue – Meat/milk

Deviations: None stated.

GLP: Yes.

Acceptability: Acceptable (with limitations)

	Supporting study I Raw data to report RIP9500449 using residue analytical method from report RIP9400740, amended by RIP9401251
Data point:	KCA 6.4.2/06
Report:	[redacted] (1985): Residue cattle feeding study (28 days). Bovine Milk. Report 90386 M-054888-01-1 RIP9400726
Guideline(s):	None stated.
Deviations:	-
GLP:	No.
Acceptability:	Acceptable (as part of RIP9500449)

	Supporting study II Raw data to RIP9500449 report using residue analytical method from report RIP9400740, amended by RIP9401251
Data point:	KCA 6.4.2/07
Report:	[redacted] (1985): 28 day residue feeding study. Cattle Tissues. Report 90387 M-054668-01-1 RIP9400725
Guideline(s):	None stated.
Deviations:	-
GLP:	No.
Acceptability:	Acceptable (as part of RIP9500449)

A second feeding study in lactating cows was performed to expand the range of administered doses. The report was issued in 1995, however, all raw data were generated between May and August 1985.

Materials and methods

Four groups of dairy cows (3 animals for each of 3 dose levels, one control animal) were fed daily with capsules containing cyfluthrin at nominal levels of 0, 15, 50 and 150 mg/kg in feed for 28 days. Effective doses were 14.3, 47.5 and 149.4 mg/kg, equivalent to 0.45, 1.5 and 4.5 mg/kg bw/d. With regard to intake from the representative uses (potato, wheat, sugar beet), this equals 70-696N (meat) and 21-206N (milk).

Dose level and stability of active substance in the capsule was verified prior and at the end of the study. Handling of animals, dosing, sacrifice, sampling collection and storage was adequately reported.

Evening and morning milkings were mixed and combined for analysis. At sacrifice, composite fat (omental, renal, and subcutaneous), muscle (round, flank, and loin), liver and kidney tissues were collected.

Results

Recovery data

Concurrent recovery data are presented in Table B.7.4-11. It is noted that residues in controls were constantly detected up to 0.092 mg/kg. This is also observed for numerous recoveries obtained in the validation studies (Vol. 3, B.5.1.2) and compromises the determined residues at low levels.
Recoveries in fat and muscle partly exceed the level of acceptance, even when residues in controls were subtracted. The data do also not cover the full range of reported values for treated samples.

Table B.7.4-11: Concurrent recovery data for cyfluthrin in tissues and milk

Matrix	**Fortification level (mg/kg)**	**Recovery**		**Control mg/kg**	**Corrected recovery [a]**	
		mg/kg	%		mg/kg	%
Liver	0.1	0.087 0.085 0.080	87 85 80	0.002 0.007 0.000	0.085 0.078 0.080	85 78 80
Kidney	0.1	0.105 0.094 0.096	105 94 96	0.004 0.004 0.004	0.101 0.090 0.092	101 90 92
Fat	0.1	0.176 0.180	176 180	0.092 0.060	0.084 0.120	84 120
Muscle	0.1	0.145 0.092 0.098	145 92 98	0.009 0.004 0.004	0.136 0.088 0.094	136 88 94

[a] corrected for control (indicative only, as levels are too low for being quantitatively reliable)

Further “recoveries” are reported without explanations to support an LOQ of 0.01 mg/kg for muscle, liver, kidney and milk (Table B.7.4-12). A full set of validation data is not presented. This claimed LOQ is not covered by the validation studies of the analytical method (Vol.3, B.5.1.2).
It is not clear, how these recovery data were related to the analytical runs of the feeding study (study report issued 10 years after final sample analysis). In general, it is unclear where, when and how these recoveries were determined. From the (limited) raw data it appears, that they are not concurrent recoveries. No chromatographs of recoveries are presented.

Table B.7.4-12: Additional recovery data for cyfluthrin in tissues and milk [a]

Matrix	**Fortification level mg/kg**	**Recovery mg/kg**	**Control mg/kg**	**Corrected recovery [b]**	
				mg/kg	**%**
Muscle	Control 0.01 0.01 0.02 0.05	- 0.0099 0.0082 0.0178 0.0430	0.0009	 0.0090 0.0073 0.0169 0.0421	 90 73 85 84
Liver	Control 0.01 0.01 0.02 0.05	- 0.0085 0.0096 0.0174 0.0432	0.0030	 0.0055 0.0066 0.0144 0.0402	 55 66 72 80
Kidney	Control 0.01 0.01 0.02 0.05	- 0.0075 0.0080 0.0156 0.0448	0.0029	 0.0046 0.0051 0.0127 0.0419	 46 51 64 84
Milk	0.01 0.02 0.05 0.10	0.0092 0.0171 0.0408 0.0918	-		92 85 82 92

[a] recoveries are not clearly attributed to sample analysis; therefore only of informative value
[b] corrected for control by RMS (indicative only, as levels are too low for being quantitatively considered)

Storage stability
Milk samples were analysed 10 and 64 days after sampling. Tissue samples were analysed within 19 and 36 days after sacrifice and thus within the period of proven stability. However, the storage conditions differ from those in the storage stability studies: Tissue samples were stored at 0 to -10 °C, while no temperature is indicated for frozen milk samples storage.

Residues in milk
Milk and tissue samples were analysed for cyfluthrin according to the method described in report 85883 (RIP9400740). Residues are reported in Table B.7.4-13.
Cyfluthrin residue in milk from the different treatment groups ranged from 0.05 to 0.08 mg/kg (45N), 0.12 to 0.24 mg/kg (150N) and 0.45 to 0.70 mg/kg (450N). Plateau was apparently reached within the first week of dosing.

Table B.7.4-13: Cyfluthrin residues in milk from cows

Dose level (mg/kg bw/d)	**Residues of cyfluthrin (mg/kg)**			
	Day 7	Day 14	Day 21	Day 28
0.45 (21N*)	0.07 0.08 0.07	0.07 0.10 0.06	0.04 0.07 0.05	0.06 0.06 0.06
Mean	0.07	0.08	0.05	0.06
1.5 (69N*)	0.21 0.26 0.20	0.24 0.27 0.20	0.22 0.20 0.16	0.13 0.16 0.08
Mean	0.22	0.24	0.19	0.12
4.5 (206N*)	0.49 0.68 0.50	0.56 0.89 0.41	0.50** 0.96** 0.65**	0.44 0.49 0.43
Mean	0.56	0.62	0.70	0.45

*Refering to intake from representative uses
**day 21 values used for MRL and dietary risk assessment

Residues in tissues
Cyfluthrin residues in fat were high in all dose groups: 1.2 – 1.4 mg/kg (70N), 2.2 – 3.3 mg/kg (232N) and 4.0 – 9.9 mg/kg (696N). In other tissues, no residues >0.01 mg/kg were found in the lowest dose group, and individual residues in the medium and high dose groups did not exceed 0.07 mg/kg and 0.11 mg/kg for the different tissues, respectively.

Table B.7.4-14: Cyfluthrin residues in tissues from dairy cows dosed with cyfluthrin daily for 28 days

Dose level	**Fat**	**Muscle**	**Liver**	**Kidney**
[mg/kg bw/d]	[mg/kg]	[mg/kg]	[mg/kg]	[mg/kg]
0.45 (70N*)	1.2 1.4 0.98	0.01 <0.01 <0.01	<0.01 <0.01 <0.01	0.01 <0.01 <0.01
Mean	1.2	0.01	<0.01	0.01
1.5 (232N*)	3.3 2.2 2.6	0.07 0.02 0.03	<0.01 <0.01 <0.01	0.07 0.02 <0.01
Mean	2.7	0.04	<0.01	0.03

4.5 (696N*)	6.5 4.0 9.9	0.05 0.04 0.11	0.01 0.03 <0.01	0.05 0.02 0.07
Mean	6.8	0.07	0.02	0.05

*Refering to intake from representative uses; N rate rounded

Conclusion

This GLP feeding study covers the dose range of 0.45 to 4.5 mg/kg bw/d (70-696N rate for meat; 21-206N rate for milk), thus complementing the dose range of the other feeding study (Shaw et al. 1984, RIP9400720; 0.16-1.61 mg/kg bw/d). Using analytical methods not satisfying current quality criteria (see Vol.3, B.5.1.2), the residue levels for parent were significant in all dose groups for fat and milk, while measured residues in liver, kidney and muscle were low for all dose groups (mean levels ≤0.07 mg/kg).

Residues show a linear relationship to the treatment rates used in the study. The findings for milk and tissues are in good agreement to the parallel feeding study in cows (RIP9400720). For assessment of MRLs and dietary risk, the highest level (4.5 mg/kg bw/d) is used to supplement the results of study RIP9400720.

Storage stability data show that within the analysis period of this study (36 days for tissues; 64 days for milk), incurred residues of parent were adequately recovered.

The following limitations are noted:
- The analytical method does not allow for quantitative estimates of residue levels below 0.1 mg/kg (see assessment of analytical method in Vol.3, B.5.1.2), therefore, risk assessments and MRL proposals will not use reported values below this level; additional recovery data, however, support to a certain extent the sensitivity of the analytical method.
- Storage conditions of tissue and milk samples (0 to -10 °C) do not conform to the conditions of the storage stability study (-18 to -23 °C). For samples like kidney, where significant degradation of incurred residues was observed for storage periods exceeding 43 days (Table B.7.1-10, p.34), this represents a major uncertainty.
- No procedural recoveries reported at the claimed LOQ (only 0.1 mg/kg)
- Regular detects in control samples

The study is, irrespective of the severe limitations, considered adequate for the assessment of beta-cyfluthrin within the whole data package of feeding and metabolism studies. The relevant transfer of parent into fat and milk (based on proven concentration in cream and butterfat) and the non-relevant transfer into other matrices can be assessed in a quantitative way. Limitations are considered quantitatively regarding the LOQ and as additional uncertainties requiring conservative estimates for dietary risk assessment.

Additional data

A report on metabolite analyses (Minor and Gronberg 1985, study number 90288; combined FPBald, FPBalc and FPBacid levels) in a high dose feeding study (150 mg/kg diet) is mentioned in JMPR evaluation of cyfluthrin (2007). However, this study report is not available to RMS.

B.7.4.4 Pigs

No feeding study in pigs is available and none is required.

B.7.4.5 Fish

No feeding study in fish is available and none is required.

B.7.5 Effects of processing

B.7.5.1 Nature of the residue

Data point:	KCA 6.5.1/01
Report:	Adam, D. (2012): [^{14}C]-beta-cyfluthrin: Simulated processing - Hydrolysis at 90, 100 and 120 °C 20120062 M-479731-01-1 ASB2014-6710
Guideline(s):	OECD Guideline for the Testing of Chemicals 507, Nature of Pesticide Residues in Processed Commodities – High Temperature Hydrolysis US-EPA Residue Chemistry Test Guideline OPPTS 860.1520 Processed Food/Feed EU Guidelines for the generation of the data concerning residues as provided in Annex II, Part A Section 6 and Annex III, Part A, Section 8 of the Directive 91/414/EEC concerning the placing of the plant protection product on the market. Appendix E, Document 7035/VI/95 rev.5, July 1997 Processing Studies.
Deviations:	None.
GLP:	Yes.
Acceptability:	Acceptable

According to Reg. (EU) 283/2013, no simulated processing study is required due to the low water solubility of beta-cyfluthrin (<0.01 mg/L).

Materials and methods

Identification:	[fluorophenyl-UL-^{14}C]-beta-cyfluthrin
Ratio of Isomers:	I : II : III : IV = 0.2 : 36.5 : 1.4 : 61.9
Purity:	radiochemical purity: > 99% (sum of isomers), 98.5% (sum of isomers) as determined by IES prior to treatment
Specific activity:	4.36 MBq/mg (117.9 µCi/mg)

A stock solution of the [^{14}C]-beta-cyfluthrin test material was prepared in acetonitrile at a concentration of 1’296’400 DPM/50 mL, resulting in a concentration of 0.005 mg/50 mL.
The stock solution was mixed with aqueous buffer solutions of three different pH values (pH 4, 5 and 6). All buffer solutions were prepared with acetic acid and sodium acetate. Buffer solutions were sterilised by either filtration or autoclave. The concentration of beta-cyfluthrin in buffered solutions ranged from 0.99 to 1.00 µg/L.

pH 4 and 90 °C - pasteurisation

The test solutions were placed in an oil bath for 20 min at 90.0±1.0 °C and pH 4.0 in closed high pressure glass flasks (100-mL capacity).

pH 5 and 100 °C - baking, brewing, boiling

The test solutions were placed in an oil bath for 60 min at 100.0±1.0 °C and pH 5.0 in high pressure glass flasks (100-mL capacity).

pH 6 and 120 °C - sterilisation

The test solutions were placed in an autoclave for 20 min at 120.0±1.0 °C and pH 6.0 in closed high pressure stainless steel vessels (100 mL capacity).

Duplicate samples were analysed immediately for time zero where no heat was used. After heating duplicate samples were retrieved from the respective oil bath or autoclave. The pH value of the samples was measured in separate solutions, which were treated with the unlabelled test item and incubated under the same conditions as the test solutions, in order to avoid the substance sticking to the pH electrode.
After incubation, the samples were partitioned three times with ethyl acetate. The organic phases were combined, the volumes of the organic and aqueous phases determined and the radioactivity present in the individual phases measured by LSC.
The organic phase containing the test item was concentrated to dryness, the residue re-dissolved in acetonitrile/water 1:1 v/v measured by LSC to check for work-up recovery and subjected to HPLC analysis, to determine the amount of [^{14}C]-beta-cyfluthrin and eventual hydrolysis products.
The test solutions submitted to sterilisation conditions (20 min at 120.0±1.0 °C and pH 6.0) were subjected TLC analysis, additionally.

Results

The hydrolysis of beta-cyfluthrin test substance was examined at pH 4, pH 5 and pH 6 at 90 °C, 100 °C and 120 °C, respectively. The mass balance for the high temperature hydrolysis tests ranged from 95.3% to 106.5% applied radioactivity. The overall radioactivity before and after each test performance are given in Table B.7.5-1 .

Table B.7.5-1: Material balance of radiocarbon following hydrolysis of [^{14}C]-beta-cyfluthrin at high temperatures

Test	pH 4, 90 °C, 20 min	pH 5, 100 °C, 60 min	pH 6, 120 °C, 20 min
before test [% of applied dose]			
Rep A	95.7	101.0	111.0
Rep B	104.3	99.0	101.4
Mean	100.0	100.0	106.2
after test [% of applied dose]			
Rep A	109.9	99.2	98.7
Rep B	103.0	100.1	91.9
Mean	106.5	99.7	95.3

pH 4 and 90 °C - pasteurisation

[^{14}C]-beta-cyfluthrin was shown to be stable to hydrolysis at pH 4 and 90 °C, representing a mean amount of 106.5% (sum of isomers) after 20 minutes of incubation.

pH 5 and 100 °C - baking, brewing, boiling

[^{14}C]-beta-cyfluthrin represented 99.7% (sum of isomers) after 60 minutes of incubation in pH 5 at 100 °C.

pH 6 and 120 °C - sterilisation

At pH 6 at 120 °C, the test item degraded rapidly when compared to pH 4 and 5. The test item hydrolysed to 12.1 % AR after 20 min of incubation (Table B.7.5-2).

Up to eight radioactive fractions were detected after 20 min of incubation at 120 °C. Two were identified as 4-fluoro-3-phenoxybenzoic acid (FPB acid, M1) and 4-fluoro-3-phenoxybenzoic aldehyde (FPB aldehyde, M2) using co-chromatography with HPLC and TLC (FPB acid only). FPB acid (M1) represented 4.9 % AR and FPB aldehyde (M2) accounted for 33.6 %. An additional very polar fraction (M7) represented 21.9 % AR (single peak). Due to the limited amount of radioactivity present, it was not possible to identify the structure of M7.

A proposed metabolic pathway is presented in beta-cyfluthrin is stable to hydrolysis under pH 4/90 °C and pH 5/100 °C. Under pH 6/120 °C (sterilisation; relevant for tomato processing), beta-cyfluthrin is degraded rapidly.
Under study conditions, two fractions were identified as FPB acid, (named M1 in this study; 4.9 % AR) and FPB aldehyde (named M2 in this study; 33.6 % AR). An additional very polar fraction (M7) represented 21.9 % AR. It is stated that the limited amount of radioactivity precluded the identification of the structure of M7.
Under realistic conditions residues in commodities subjected to high temperature processing (e.g. canned tomatoes) might exceed levels, where formation of the unidentified degradation product M7 exceeds 0.01 mg/kg (relevant for non-representative uses only).
Further information on hydrolysis can be found in the JMPR evaluation of cyfluthrin/beta-cyfluthrin (JMPR 2007). Krohn (1983, Report M1590 not accessible to RMS) investigated the hydrolytic stability of cyfluthrin at pH 4, 7 and 9 (30-80 °C). The major hydrolysis products identified by HPLC were DCVA and FPBaldehyde. No further information on conditions of degradate formation in this study is available.
It is emphasised that the simulated hydrolysis study is not triggered. Therefore, no data requirement on further identification of M7 is proposed.

Table B.7.5-2: Balance and distribution pattern in pH 6 at 120 °C (organic phase after partitioning)

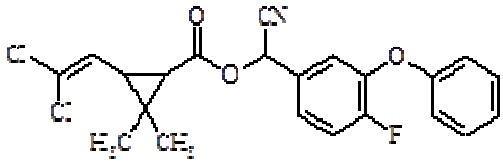
Analytes**	**Incubation time (pH 6, 120 °C)**			
	0 min		**20 min**	
	Replicate A/B	**Mean**	**Replicate A/B**	**Mean**
Beta-cyfluthrin	108.0 / 100.7	104.3	12.4 / 11.9	12.1
M1 (FPB acid)	*		5.3 /4.4	4.9
M2 (FPB aldehyde)	*		34.3 / 33.0	33.6
M4	*		4.4 / 4.3	4.3
M5	*		6.5 / 6.0	6.2
M6	*		7.4 / 2.4	4.9
M7	*		19.9 / 24.0	21.9
M8	*		* / 2.6	1.3
M9	*		7.3 / 2.5	4.9
Total characterised	108.0 / 100.7	**104.3**	97.5 / 91.1	**94.1**
Total (Table B.7.5-1)	111.0 / 101.4	**106.2**	98.7 / 95.3	**95.3**

* not detected or below detection limit
** notation of metabolites (M1-M9) is made according to the study report and is not identical to other studies

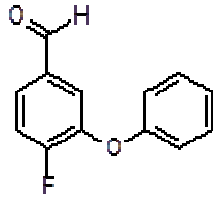
Conclusions

Beta-cyfluthrin is stable to hydrolysis under pH 4/90 °C and pH 5/100 °C. Under pH 6/120 °C (sterilisation; relevant for tomato processing), beta-cyfluthrin is degraded rapidly.
Under study conditions, two fractions were identified as FPB acid, (named M1 in this study; 4.9%

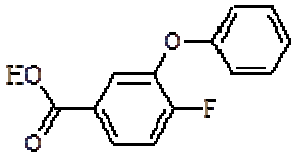
AR) and FPB aldehyde (named M2 in this study; 33.6 % AR). An additional very polar fraction (M7) represented 21.9 % AR. It is stated that the limited amount of radioactivity precluded the identification of the structure of M7.
Under realistic conditions residues in commodities subjected to high temperature processing (e.g. canned tomatoes) might exceed levels, where formation of the unidentified degradation product M7 exceeds 0.01 mg/kg (relevant for non-representative uses only).
Further information on hydrolysis can be found in the JMPR evaluation of cyfluthrin/beta-cyfluthrin (JMPR 2007). Krohn (1983, Report M1590 not accessible to RMS) investigated the hydrolytic stability of cyfluthrin at pH 4, 7 and 9 (30-80 °C). The major hydrolysis products identified by HPLC were DCVA and FPBaldehyde. No further information on conditions of degradate formation in this study is available.
It is emphasised that the simulated hydrolysis study is not triggered. Therefore, no data requirement on further identification of M7 is proposed.



Beta-cyfluthrin



FPB aldehyde (M2)



FPB acid (M1)

Figure B.7.5-1:Hydrolytic pathway for [^{14}C]-beta-cyfluthrin under simulated sterilisation process (pH 6, 120 °C)

No studies are submitted and none are required.

B.7.5.2 Magnitude of residues in processed commodities

If the level of residues in RAC is less than 0.1 mg/kg as for the representative uses of beta-cyfluthrin,

processing studies shall be carried out if the contribution of the commodity under consideration to the ADI is ≥10 % or if the estimated daily intake is ≥10 % of the ARfD for any European consumer group diet. This is not the case for the evaluated uses of beta-cyfluthrin, therefore, no further studies are required (see Table B.7.5-3). Although the trigger is below the LOQ for potatoes in the respective residue trials, a real no-residue situation is be assumed based on the proven non-systemic behaviour of beta-cyfluthrin.

Two quantitative processing studies are available.

Table B.7.5-3: Hypothetic residue levels for RACs of the representative GAPs leading to an exceedance of the triggers (≥10 % ADI or ARfD) for quantitative processing studies for beta-cyfluthrin

Commodity	Trigger value (mg/kg)	Based on ADI or ARfD
Potato	0.007	ARfD
Tomato	0.018	ARfD
Wheat	0.070	ARfD
Sugar beet	0.016	ARfD

Data point: KCA 6.5.3/22

Report: Schäufele, M. (2012): Bulldock 25 EC: Magnitude of residues of beta-cyfluthrin in greenhouse tomato raw agricultural commodity and processed fractions after 2 applications of Bulldock 25 EC - 2 trials - in northern Europe (Germany) in 2011
JDV0079, M-481079-01-1, R-28671
ASB2014-7712

Guideline(s): OECD Guideline 508

Deviations: None.

GLP: Yes.

Acceptability: Acceptable

Materials and methods

Two trials were conducted on tomato (greenhouse) during 2011 in Germany. Two spray applications of beta-cyfluthrin were performed at rates of 52-55 g as/ha (3N rate) with an interval of 14 days and a PHI of 7 days. In both trials samples of tomatoes were taken at BBCH 89.

Treated tomatoes were processed into canned tomatoes, raw juice and raw puree. Additionally samples of washed tomatoes (1st step of processing) and wet pomace (after pressing and sieving, during juice production) were taken.

Processing to canned tomatoes: Tomatoes were washed in tap water for three minutes. The ratio water to fruit was always 1:1. The water always covered the fruit. In order to peel the washed tomatoes they were blanched (1 min, 75-85 °C) and afterwards peeled. The peeled tomatoes were put into jars, covered with water to the rim and the jars were closed. The sterilisation (5-20 min, 118-125 °C) was done using an autoclave.

Processing to raw juice and puree: Washed tomatoes were crushed to tomato mash. The tomato mash was heated (30 min, 80-87 °C), pressed and sieved. Raw juice for puree was concentrated using a concentration plant (app. 60 °C, vacuum) until a dry matter content of 18-24 % was achieved.

The samples were analysed for beta-cyfluthrin according to a validated multi residue method (MRM;

see Vol. 3, B.5.1.2), with a limit of quantitation of 0.01 mg/kg for beta-cyfluthrin. This method was validated in course of this study.

Results

Procedural recoveries analysed alongside the treated sample analysis are summarised in Table B.7.5-4.

Table B.7.5-4: Procedural recoveries for beta-cyfluthrin in tomato

Study No. Trial No.	Crop	Portion analysed	Fortification level (mg/kg)	Recovery (mg/kg)	Recovery (%)
R-28671 JDV0079-01 JDV0079-02 ASB2014-7712 2012	Tomato	Fruit	0.01	Not reported	86
		Canned	0.01	Not reported	110
		Raw juice	0.1	Not reported	70
		Raw puree	0.1	Not reported	76
		Fruit	0.5	Not reported	85
		Fruit	0.5	Not reported	71

No residues of beta-cyfluthrin above the LOQ (0.01 mg/kg) were found in any of the untreated samples of tomato. Storage stability of samples (up to 8 months for processed items) is covered by adequate stability studies with commodities of high water content. Procedural recovery samples were extracted, stored and analysed alongside the study samples. Recovery in extracts over the storage period of 7 days is 94-110 %.

Results for treated samples are summarised in Table B.7.5-5. Resulting transfer factors are shown in Table B.7.5-6. Residues were reduced in washed tomato (pf 0.81), canned tomato (0.08), raw juice (0.28) and raw puree (0.64). Residues were concentrated in wet pomace by a factor of 3.14.

Table B.7.5-5: Residues of beta-cyfluthrin in tomato raw and processed matrices after application at 3N rate

Study No.			Application					Residues			
Trial No. Year	**Crop Variety**	**Country**	**FL**	**No.**	**g/ha (as)**	**g/hL (as)**	**GS**	**Portion analysed**	**DALA (days)**	**beta-cyfluthrin (mg/kg)**	**Analytical method**
R-28671 JDV0079-01 2012	Tomato	Germany, Europe, North	25 EC	2	52.1	13	85-87	fruit	7	0.056	MRM Fillion et al.
									7	0.046	
									mean	0.051	
								washed	7	0.042	
								canned	7	<0.01	
								wet pomace	7	0.159	
								raw juice	7	0.023	
								raw puree	7	0.042	

R-28671 JDV0079-02 Yes 2012	Tomato	Germany, Europe, North	25 EC	2	55	13	84	fruit	7	0.018	MRM Fillion et al.
									7	0.025	
									mean	0.022	
								washed	7	0.02	
									7	0.04	
								canned	7	<0.01	
								wet pomace	7	0.07	
								raw juice	7	<0.01	
								raw puree	7	<0.01	

FL = formulation GS = growth stage at last application DALA = days after last treatment

Table B.7.5-6: Beta-cyfluthrin transfer factors for processed tomato commodities

Matrix	Trial JDV0079-01	Trial JDV0079-02	Mean
Washed tomatoes	0.82	0.79	0.81
Canned tomatoes	0.05	0.12	0.08
Tomato wet pomace	3.1	3.2	3.14
Tomato raw juice	0.45	0.12	0.28
Tomato raw puree	0.82	0.47	0.64

Conclusion

The provided magnitude of processing study is acceptable in terms of study design, analytical method and storage stability of raw and processed samples to calculate processing factors for the relevant matrices. The number of procedural recovery determinations per matrix is low, but still acceptable. Raw data of analytical runs are lacking (only summaries provided).
Transfer factors in washed tomato (pf 0.81), canned tomato (0.08), raw juice (0.28), raw puree (0.64) and wet pomace (3.14) were calculated.

Data point: KCA 6.5.3/10

Report: Leslie, W. L. (1988): Baythroid - Magnitude of the residue on tomato processed products
98399, includes trial RTX-F2060-83P
M-136610-01-1
RIP9401061

Guideline(s): EPA Residue Chemistry Guidelines, Series 171-4, Magnitude of the residue crop processing products

Deviations: None

GLP: No

Acceptability: Not acceptable

Material and methods

A residue study on tomato was carried out in the US with six foliar applications of cyfluthrin (240 EC) at application rates of 0.05 kg as/ha each. Samples of whole tomatoes were taken at day 0.

The treated tomatoes were processed into juice, wet and dry pulp (i.e. pomace), ketchup and paste simulating commercial practice.

Tomatoes were cooked and then put through a grinder to separate out the skin and seeds. Some of the pulp and juice samples were further cooked to produce puree. A puree subsample was evaporated to ketchup consistency. A ketchup subsample was heated to paste consistency.

Analysis for cyfluthrin was performed with the method 85823, which is considered as valid with regard to the investigations performed in this study (see Vol.3, B.5.1.2). Procedural recoveries were determined alongside the treated sample analyses.

Results

Procedural recoveries (Table B.7.5-7) were acceptable for raw and processed samples. Storage of samples (up to 7 months) is covered by acceptable storage stability studies. No residues were found in untreated control samples except one in dry pomace (0.04 mg/kg).

Table B.7.5-7: (Procedural) recoveries for cyfluthrin in raw and processed tomatoes

Matrix	Compound	n	Fortification level	Recovery (mg/kg)	Recovery (%)		
			(mg/kg)	single values	single values	mean	RSD
Fruit (RAC)	Cyfluthrin	1	0.05	0.056	112	-	-
			0.1	0.084, 0.084, 0.085, 0.080, 0.090, 0.093	84, 84, 85, 80, 90, 83	84	3
			0.5	0.369, 0.361	74, 72	73	-
Juice	Cyfluthrin	1	0.05	0.055	110	-	-
		1	0.5	0.382	76	-	-
Ketchup	Cyfluthrin	1	0.05	0.046	92	-	-
		1	0.5	0.423	85	-	-
Puree	Cyfluthrin	1	0.05	0.035	70	-	-
		1	0.5	0.496	99	-	-
Paste	Cyfluthrin	1	0.05	0.052	104	-	-
		1	0.5	0.493	99	-	-
Wet pulp	Cyfluthrin	1	0.05	0.038	76	-	-
		1	0.5	0.369	74	-	-
Dry pulp	Cyfluthrin	1	0.05	0.086	84	-	-
		1	0.5	0.506	92	-	-

The tomato RAC contained resides of 0.06 mg/kg prior to processing. In Table B.7.5-8 the residue values of the processed commodities and the corresponding transfer factors are summarised.

Table B.7.5-8: Residue values and transfer factors of cyfluthrin in tomatoes

Sample material	Residues (mg/kg)	Processing factor
Tomato fruit (RAC)	0.06	-
Tomato juice	0.02	0.3
Tomato puree	0.04	0.7
Tomato ketchup	0.05	0.8

Tomato paste	0.11	1.8
Tomato wet pomace	0.39	6.5
Tomato dry pomace	1.3	22

Conclusion

During the processing of tomatoes, a concentration of cyfluthrin residues in paste and wet and dry pomace is observed with processing factors of 1.8, 6.5 and 22, respectively. Other commodities are characterised by decrease of concentrations.
Almost all relevant parameters of study design and performance are described in sufficient detail in the study and are considered scientifically valid.

The following deficiencies are noted:
- Processing duration, pH and temperatures are not recorded, however, it is assumed that the professional equipment and methods used in this study are covered by standard processing conditions.
- It is not clear, whether the reported recovery values were generated within the analysis run for the treated samples (procedural recoveries), or separately.
- Absence of GLP status.

B.7.6 Residues in rotational crops

The DT_{90} of beta-cyfluthrin in soil has been determined at a level of 359 days in field studies (see Vol.3, B.8). The relevant trigger of 10 % of the applied active substance 100 days after application is therefore exceeded and rotational crop studies required.

The scenario for evaluation is determined by the intended maximum application rate, the crop treated and the time of application. If required, the subsequent risk assessment has to take into account the type of potential succeeding crops.

For late outdoor applications like in wheat and potato, crop failure is unlikely. For these crops, the plant-back interval is determined by a realistic crop rotation period (30-60 d) after commercial harvest. The 1N rate is determined by the nominal application rate for the primary crop and the removal of residues with harvested products from the field. For wheat, it is assumed that most of the applied substance is removed with grain and straw (crop interception 70-90 %), while for potatoes, the treated foliage usually remains on the field and the full application rate needs to be taken into account.
For sugar beet seed treatment, the realistic crop rotation is also 30-60 days (crop failure), with full consideration of application rate.
For tomato indoor uses, complete removal of treated crops (crop interception 50-80 %) and crop rotation of 30-60 days has to be taken into account

Long-term accumulation of beta-cyfluthrin in soil is not considered relevant due to the high percentage of interception (see PEC_{soil} calculation in Vol. 3, B.8).

B.7.7 Residues in rotational crops

B.7.7.1 Metabolism in rotational crops

Data point:	KCA 6.6.2/01
Report:	Minor, R. G. and Ernst, V. J. (1983): Radioactive residues of Baythroid TM in rotational crops

	MR86050, M-067406-01-1 RIP9400841
Guideline(s):	None stated. Not compliant to OECD 502.
Deviations:	Not applicable
GLP:	No
Acceptability:	Additional information

Material and methods

On a soil container filled with 37.5 cm of sandy loam on top of 15 cm of sand, [phenyl-U-^{14}C] cyfluthrin (cis:trans 40:60; specific activity 21.71 mCi/mM, diluted with unlabelled parent to 7.25 mCi/mM) was applied to the surface at a rate of 988 g as/ha (28N rate). Following tilling the soil to a depth of 15 cm, rotational crops (kale, red beet and wheat) were planted at 36, 121 (both maintained indoors) and 285 days after application (outdoors).
Prior to planting and at each harvest, six soil cores of the tillering horizon were taken, mixed and the TRR determined.
Rotational crops were harvested at commercial maturity. The following samples were taken: Leaves of kale; foliage and roots of red beets; immature foliage (34 d after planting), stalks and heads (grain + chaff) of wheat.
Crops were homogenised and stored frozen less than 1 year (begin and end of study conduct; storage temperature not indicated).

Solid-phase extraction of soil samples in a Soxhlet apparatus was done with chloroform/methanol (7:3). After evaporation to dryness, the extract was redissolved in methanol, radioassayed and analysed by TLC.

Plant samples were homogenised and repeatedly extracted with methanol/water (4:1), filtered, radioassayed, evaporated to dryness, water added and radioassayed. The filter cake was refluxed with 6N HCl (1h), filtered and the extract radioassayed. Both extracts were partitioned against chloroform/acetone (1:2) and each subjected to TLC. The following non-radioactive standards were co-chromatographed along with the extracts:

- parent
- COOH-cyfluthrin (FCR 2728),
- Me-cyfluthrin (FCR 2956),
- $CONH_2$-cyfluthrin (FCR 2978)
- FPB amid (FCR 2947),
- Me-FPB acid (COE 263/78),
- FPB acid (COE 538/78),
- FPB aldehyde (FCR 1260),
- FPB alcohol (FCR 1261),
- 4´OH FPB acid (FCR 3145),
- FPB (FCR 3030).

Results

The decline of soil residues from the initial value of 0.72 mg/kg after application to 0.10 mg/kg at 359 days is shown in Figure B.7.7-1. The calculated level of residues in the top 15 cm (without loss of radioactivity) is 0.255 mg/kg. No mass balance is given in the study, however, quantitative metabolisation of cyfluthrin to CO_2 is reported in soil metabolism studies and could, besides uneven distribution of residues on the surface at day 0, explain the decrease of radioactive residues.
Analysis of the soil organic extracts of early samplings (day 0 to 106) showed parent as major residue compound (90-55 % of TRR). No analysis of soil samples from later samplings are reported.

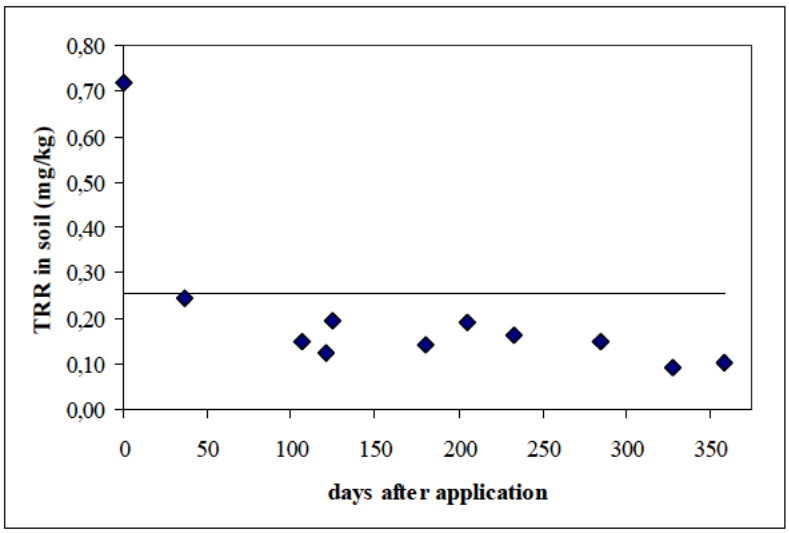


Figure B.7.7-1: Decrease of TRR levels in soil after surface application at a rate of 988 g as/ha (levels in 15 cm soil cores of the tillering horizon; calculated concentration of 0.255 mg as/kg in top 15 cm without loss of radioactivity)

Of the rotational crops planted at 36 days after soil application of ^{14}C-cyfluthrin, wheat contained the highest residues: 0.35 mg/kg (heads) and 0.16 mg/kg (stalks). Radioactive residues in mature crops decreased with each planting, thus reflecting the decreasing levels in the soil. Kale and beet samples harvested from planting 285 days after application of ^{14}C-cyfluthrin to soil contained radioactive residues of <0.01 mg/kg.

Table B.7.7-1: TRR in rotational crops after application of cyfluthrin onto bare soil at 996 g as/ha (28N rate)

Rotational crop	Plant-back interval		
	36 d	**121 d**	**285 d**
	TRR (mg/kg)	**TRR (mg/kg)**	**TRR (mg/kg)**
Kale	0.030	0.014	0.003
Wheat (immature)	n.r.	0.056	0.006
Wheat stalks	0.159	0.158	0.078
Wheat heads	0.348	0.189	0.020
Red beet foliage	0.025	0.027	0.004
Red beet roots	0.053	0.019	0.003

[a] days after planting
n.r. not reported

Further attempts to elucidate the nature of residue were made in wheat samples of the 36d PBI (stalks, heads). In heads and stalks only 11 % and 12 % of TRR was organosoluble, acid hydrolysis solubilised additional 3 % and 19 % of TRR. TLC revealed continuous undefined vertical smeared bands of radioactivity that could not be structurally related to known cyfluthrin metabolites. The nature of the radioactivity in the acid hydrolysed aqueous fraction (27 % in stalks and 54 % in heads) and solids (42 % in stalks and 32 % in heads) was not further characterised and was considered as natural plant constituents.

Conclusions

A quantitative transfer of radioactivity from cyfluthrin treated soil into rotational crops is demonstrated after application of 988 g as/ha (28N rate). TRRs in samples were highest in cereals (up to 0.348 mg/kg in heads). While parent cyfluthrin was detected in soil organic extracts of early samples (90 % of TRR at day 0 and 55 % at days 36 and 106), no cyfluthrin or its metabolites were identified in any rotational crop sample. Indications for incorporation of radioactivity into natural plant constituents are presented. It is not clear, in which structure the radioactivity is taken up by plants.

The study has the following limitations:
- Although results are conclusive and in accordance to information from soil metabolism (Vol.3, B.8) and to a new study on magnitude of residues in RC (Chevallier 2013; ASB2014-7884), analytical attempts to further identify the nature of residues are too limited to allow firm conclusions.
- Storage temperature not recorded.
- GLP status is lacking.

The study is not considered as a fully acceptable stand-alone-study due to the lack of GLP. However, the entire data package of RC metabolism and field studies (partly performed under GLP) is considered acceptable under conditions relevant for the assessment of representative uses within this RAR.

B.7.7.2 Magnitude of residues in rotational crops

Data point:	KCA 6.6.2/04
Report:	E. Chevallier (2013): Magnitude of the residue of beta-cyfluthrin in succeeding crops after applications of Bulldock 25 EC in two trials in Southern Europe (Southern France and Spain) – 2012 12SGS117, M-481208-01-1, R-30594 ASB2014-7884
Guideline(s):	None stated. Partly following OECD 504; primary crop field trials conducted according to EC Guidance 7029/VI/95 rev.5 and amendments
Deviations:	- Treatment regime (GAP treated primary crop plus one 0.5N rate soil treatment on day of planting rotational crops - Number of PBI intervals reduced (0 days) - Number of crops reduced (1 rotational crop on each site) - Number of trial sites reduced (2) - Samplings incomplete (carrot leaf not analysed) - Representative regions limited (S-EU)
GLP:	Yes
Acceptability:	Acceptable

Materials and methods

In 2012 two residue field trials were conducted on open-field lettuce in Southern France and Spain. Beta-cyfluthrin was applied twice by foliar spraying at the GAP rate of 12.5 g as/ha, with application intervals of 14 and 15 days.
Ten days after harvesting of the primary crop lettuce, one further application of beta-cyfluthrin was performed directly to bare soil on the treated plots at the target rate 12.5 g as/ha (0.5N rate regarding lettuce GAP). The application was done on the day of planting or seeding of succeeding crops (lettuce in Southern France and carrot in Spain). In both trials soil samples (0-10 and 10-20 cm soil depth) were collected just after the final soil application.

Lettuce whole plant was sampled at 11 DALA (BBCH 17) and at 41 DALA (BBCH 45). Soil core and lettuce heads were sampled at 60 DALA (BBCH 49). Carrot whole plant was sampled at 76 DALA (BBCH 41) and carrot root at 160 DALA (BBCH 45). Soil core and carrot root were sampled at 181 DALA (BBCH 49), the time of commercial harvest and stored at -18 °C up to 84 days (carrot), 225 days (lettuce), and 293 days (soil).
Untreated and treated lettuce samples were analysed for residues of beta-cyfluthrin with a fully validated analytical method. The method was additionally validated within this study for carrot and soil at 0.01 and 0.1 mg/kg (based on DFG S19; see Vol.3, B.5.1.2).

Results

Sample storage data for all crops are covered by acceptable storage stability studies (Table B.7.7-2) and no requirements are expressed for soil data. Stability in the extracts was confirmed by recoveries performed in parallel with the field sample analyses.
Procedural recoveries analysed alongside the sample analyses were acceptable.

Results of sample analyses are summarised in Table B.7.7-2: Residue data from rotational crop field trials on 2 sites in Southern Europe (applications to primary crop and pre-planting). No residues of beta-cyfluthrin were detected above the LOQ (0.01 mg/kg) in any soil sample and, consequently, in any untreated and treated samples of lettuce and carrot.

Table B.7.7-2: Residue data from rotational crop field trials on 2 sites in Southern Europe (applications to primary crop and pre-planting)

Trial	Commodity Variety	Application			Portion analysed	DALA / BBCH	Residues (mg/kg)
		kg as/ha	Water (L/ha)	kg (as/hL)			
Southern France (S-EU) 13870 Rognognas (Provence-Alpes-Côtes d'Azur) Decline curve trial 12SGS117FR01	Lettuce Bughatti	0.0128 0.0128 0.0122	667 667 293	0.0019 0.0019 0.004	Soil (0-10 cm)	0 DALA	<0.01
					Soil (10-20 cm)	0 DALA	<0.01
					Whole plants with roots	11 DALA/ BBCH 17	<0.01
					Whole plants with roots	41 DALA/ BBCH 45	<0.01
					Heads	60 DALA/ BBCH 49	<0.01
					Soil (0-10 cm)	60 DALA	<0.01
					Soil (10-20 cm)	60 DALA	<0.01
Spain (S-EU) 46470 Catarroja (Valencia) Decline curve trial 12SGS117SP02	Carrot Cabana RZ	0.0131 0.0130 0.0121	835 830 241	0.0016 0.0016 0.005	Soil (0-10 cm)	0 DALA	<0.01
					Soil (10-20 cm)	0 DALA	<0.01
					Whole plants with roots	76 DALA/ BBCH 41	<0.01
					Roots	160 DALA/ BBCH 45	<0.01
					Roots	181 DALA/ BBCH 49	<0.01
					Soil (0-10 cm)	181 DALA	<0.01
					Soil (10-20 cm)	181 DALA	<0.01

LOQ = 0.01 mg/kg; DALA = days after last treatment; BBCH = crop growth stage

Conclusions

After treatment according to a reasonable worst case residue situation in soil (covering the representative foliar and seed treatment application regimes), no residues of beta-cyfluthrin were detected above the LOQ of 0.01 mg/kg in any untreated or treated sample of soil, lettuce and carrot. The results are fully in accordance to theoretical levels of beta-cyfluthrin in soil after the chosen and GAP relevant application scheme. The study, which is based on a targeted rather than OECD study design and on fully validated analytical methods for all matrices, supports the conclusions of other studies (primary and rotational crop metabolism, field trials, environmental fate), that no residues of beta-cyfluthrin are expected in rotational crops after treatment according to GAP.

Data point:	KCA 6.6.2/02 KCA 6.6.2/03
Report:	Leslie, W. L. (1988): Baythroid R - residues in field rotational crops: field MR98429, M-067638-01-1 RIP9400845 Including Addendum 1 (containing storage stability data for cyfluthrin in soil, data on soil properties and weather information during study conduct) MR98429-1, M-067604-01-1 RIP9400848 Raw data in ASB2009-1324
Guideline(s):	None stated.
Deviations:	-
GLP:	No
Acceptability:	Additional information

Materials and methods

One field rotational crop study on cereals was conducted in the USA to determine the residue levels of cyfluthrin in winter wheat at approximately 30 and 120 days plant-back intervals. To address the findings of potential residue transfer to rotated cereals, wheat as the only test crop was sown in different types of soil (clay, loam and silty loam) after the last of a series of 10 applications of cyfluthrin at about 0.12 kg as/ha to bare soil. Samples were taken at the times of last treatment and planting (soil) and at forage stage (1 trial) and harvest (wheat) and stored at minimum -26 °C. Wheat samples (grain, straw) were stored for 22 months prior to analysis, soil samples up to 24 months.
For analysis of wheat samples, method 85823 was used (see Vol.3, B.5.1.2). Method validation for method 85823 for cereal grain was performed within this study at levels of 0.01, 0.02 and 0.05 mg/kg and is considered reliable.

For soil analyses, method 85886 was applied. Storage stability data on soil samples were determined within the study (Addendum) for a period of 12 months.

Results

No residues were found in the untreated control samples of soil and wheat. Procedural recoveries determined alongside the sample analyses are summarised in Table B.7.7-3. Storage stability of wheat samples is covered by adequate storage stability studies. For soil samples, storage stability is proven for only 12 instead of the whole storage period of 24 months, however there is no data requirement for storage stability of soil samples.

Table B.7.7-3: Procedural recoveries for cyfluthrin in rotational crop wheat and soil material

Study No. Year	Crop	Portion analysed		Fortification level	Recovery (mg/kg)	Recovery (%)		
			n	(mg/kg)	single value	single value	mean	RSD
Leslie 1988 RIP9400845	Wheat	Grain	3	0.05	0.055 0.038 0.048	110 76 96	94	18
	Wheat	Forage	2	0.05	0.041 0.043	82 86	84	-
	Wheat	Straw	3	0.05	0.053 0.043 0.041	106 86 82	91	14
	Soil		3	0.05	0.045 0.051 0.045	90 102 90	94	7

Residue levels in treated samples are reported in Table B.7.7-4. No detectable residues were found at the nominal 30 and 120 days plant-back interval in the immature and mature wheat crop components (forage, grain, straw). Soil samples (0-15 cm depth) taken at the time of sowing contained residues ≤0.03 mg/kg soil. At harvest residues in soil were always <0.01 mg/kg.

Table B.7.7-4: Residues of cyfluthrin in rotational crop wheat and soil after treatment of cyfluthrin at 10 x 28 g as/ha (8N rate)

Trial No.	Sample	Plant-back interval (days)	Plant-harvest interval (days)	Residues (mg/kg)
BD055-86R	Soil	0		0.06
	Soil	38 (planting)		0.03
	Soil	38 (harvest)		<0.01
	Forage	38	48	<0.01
	Grain	38	255	<0.01
	Straw	38	255	<0.01
BD054-86R	Soil	0		0.36
	Soil	135 (planting)		<0.01
	Soil	135 (harvest)		<0.01
	Grain	135	195	<0.01
	Straw	135	195	<0.01

BD056-86R	Soil	0		0.24
	Soil	105 (planting)		0.02
	Soil	105 (harvest)		<0.01
	Forage	105	45	<0.01
	Grain	105	241	<0.01
	Straw	120	241	<0.01

Conclusions

Although not performed according to GLP, the report contains information relevant for the assessment of residue transfer into rotational crop wheat (e.g. raw data on field tests including trial maintenance; method validation and procedural recovery data; dates of treatment, sampling and analysis; chromatograms, example calculations etc.). The analytical method was demonstrated to adequately quantify levels of cyfluthrin in soil and wheat. It could be shown, that after exaggerated treatment (8N rate) no significant transfer from soil to rotational crop wheat occurs. No information is available within this study on other crops, however, in combination with the GLP study Chevallier (2013; ASB2014-7884) and the RC metabolism study (Minor and Ernst 1983; RIP9400841), sufficient evidence is provided that no significant transfer occurs from soil to rotational crops after treatment according to GAP.

The following limitations are noted
– Non-GLP
– Only cereal crops and soil material tested
– Stability of residues in soil samples is not demonstrated for the storage time in the study.

B.7.8 Other studies

B.7.8.1 Effect on the residue level in pollen and bee products

No study available and none required for the representative uses of beta-cyfluthrin.

B.7.9 References relied on

No literature search is submitted with regard to the residue assessment of the representative uses of beta-cyfluthrin (ASB2014-7829; ASB2014-7833; ASB2014-7834). A literature search performed by the applicant addressing human health effects (ASB2014-7922) is assessed under Vol.3, B.6. The search criteria are not specific for residue assessment.

RMS has performed a literature search. Search strategy:

SCOPUS: (TITLE (*cyfluthrin) AND TITLE-ABS-KEY (*residu* OR soil* OR *metab*)) AND PUBYEAR > 2004; 36 hits
Web of Science: TITLE: (*cyfluthrin OR *6396753*) *AND* TOPIC: (residu* OR *soil* OR *metab*) Timespan: 2005-2016. Indexes: SCI-EXPANDED, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, CCR-EXPANDED, IC.
No hits were considered relevant for residue assessment.

In Table B.7.9-1, a list of those studies is presented that were submitted, but not assessed within Vol.3 B.7. Justifications are presented.

Table B.7.9-1: List of additional studies not considered relevant for the assessment of representative uses within Vol.3, B.7

Author and year	Annex point/Report No./BfR code	Justification
Wilkening et al. (1990)	KCA 6 /01, MO-01-020457 RIP1999-112	Guidance document
[redacted] 1983)	KCA 6.2 /01, PH 11872(F) RIP9400867	Rat study (refer to B.6)
[redacted] (1983)	KCA 6.2 /02, PH 11575(F), RIP9400866	Rat study (refer to B.6)
[redacted] (1983)	KCA 6.2 /03, PF-2059, RIP9400868	Rat study (refer to B.6)
[redacted] (1982)	KCA 6.2 /04, PF 1632 RIP9400862	Rat study (refer to B.6)
[redacted] (1981)	KCA 6.2 /05, 10130, RIP9400855	Rat study (refer to B.6)
Burgess (1989)	KCA 6.2 /06, 99848 ASB2014-12207	Daphnia study
Hassler (2014)	KCA 6.2 /07, M-482993-01-1 ASB2014-7719	Comparative in-vitro metabolism (rat/human) (refer to B.6)
Shaw et al. (1983)	KCA 6.2.2 /01, MO-03-011336, ASB2014-12191	Analytical method (refer to B.5)
Anon. (1983)	KCA 6.2.2 /02, 85982, ASB2014-12196	Analytical method (refer to B.5)
Anon. (1983)	KCA 6.2.2 /03, 85983, MET9400017	Analytical method (refer to B.5)
Shaw et al. (1985). J.; Lasley, M. B.	KCA 6.2.2 /04, I578, RIP9400880	Analytical method (refer to B.5)
Anon. (1984)	KCA 6.2.2 /05, 84631, RIP9400878	Analytical method (refer to B.5)
Shaw et al. (1985)	KCA 6.2.2 /06, I476, RIP9400740	Analytical method (refer to B.5)
Seym (1995)	KCA 6.2.2 /07, MR-303/95, ASB2009-1209	Analytical method (refer to B.5)
Anon. (1983)	KCA 6.2.3 /02, 85981, RIP9401251	Analytical method (refer to B.5)
Shaw et al. (1983)	KCA 6.2.3 /03, 85983 ASB2014-12191	Analytical method (refer to B.5)
Shaw et al. (1985)	KCA 6.2.3 /04, I578, RIP9400880	Analytical method (refer to B.5)
Anon. (1985)	KCA 6.2.3 /05, 87217, RIP9400875	Analytical method (refer to B.5)
Anon. (1984)	KCA 6.2.3 /06, 86220, RIP9400876	Analytical method (refer to B.5)
Anon. (1985)	KCA 6.2.3 /07, 87216, RIP9400877	Analytical method (refer to B.5)
Shaw et al. (1985)	KCA 6.2.3 /08, I476, RIP9400740	Analytical method (refer to B.5)

Author and year	Annex point/Report No./BfR code	Justification
Shaw et al. (1983)	KCA 6.2.3 /09, I488, RIP9400874	Analytical method (refer to B.5)
Gronberg and Pfankuche (1986)	KCA 6.2.3 /10, I657, RIP9400879	Analytical method (refer to B.5)
Maasfeld (1989)	KCA 6.2.3 /11, 00553, MET1999-99	Analytical method (refer to B.5)
Schoening (2001)	KCA 6.2.3 /12, 00553/E001, MET1999-99	Analytical method (refer to B.5)
Schoening (2001)	KCA 6.2.3 /13, 00553/E002, MET1999-993	Analytical method (refer to B.5)
[redacted] (1994)	KCA 6.2.5 /01, 106774, ASB2014-12209	Acute toxicity fish
[redacted] (1989)	KCA 6.2.5 /02, 99787, ASB2014-12211	Acute toxicity fish
[redacted] (1989)	KCA 6.2.5 /03, 99843, ASB2014-12213	Acute toxicity fish
Anon. (1995)	KCA 6.3 /01, MO-04-002798, RIP9501339	Statement of applicant on re-registration
Anon. (1989)	KCA 6.3.1 /01, 0488-88, RIP9500612	No GLP, non-compliant to GAP for representative uses
Anon. (1982)	KCA 6.3.1 /02, MO-04-002726, RIP9500613	No GLP, non-compliant to GAP for representative uses
Anon. (1989)	KCA 6.3.1 /03, MO-04-002714, RIP9500609	No GLP, non-compliant to GAP for representative uses
Anon. (1989)	KCA 6.3.1 /04, 0379-88, RIP9500606	No GLP, non-compliant to GAP for representative uses
Anon. (1990)	KCA 6.3.1 /05, MO-04-002716, RIP9500607	No GLP, non-compliant to GAP for representative uses
Schmidt (1992)	KCA 6.3.1 /06, PF-3744, ASB2009-148	Non-compliant to GAP for representative uses
Seym (1993)	KCA 6.3.1 /07, RA-2013/91, RIP9500608	Non-compliant to GAP for representative uses
Ohs (1993)	KCA 6.3.1 /08, RA-2054/91, RIP9500611	Non-compliant to GAP for representative uses
Bagnall (1984)	KCA 6.3.1 /09, MO-03-012233, RIP9400985	No GLP, non-compliant to GAP for representative uses
Bagnall (1986)	KCA 6.3.1 /10, TCR 288, RIP9400986	No GLP, non-compliant to GAP for representative uses
Seym (1994)	KCA 6.3.2 /01, RA-2039/92, RIP9500564	Non-compliant to GAP for representative uses
Anon. (1988)	KCA 6.3.2 /02, MO-03-012146, ASB2009-9278	No GLP, non-compliant to GAP for representative uses
Anon. (1982)	KCA 6.3.2 /03, MO-03-012134, RIP9400944	No GLP, non-compliant to GAP for representative uses
Anon. (1985)	KCA 6.3.2 /04, MO-03-012137, ASB2009-9228	No GLP, non-compliant to GAP for representative uses

Author and year	Annex point/Report No./BfR code	Justification
Anon. (1982)	KCA 6.3.2 /05, MO-03-012138, RIP9400946	No GLP, non-compliant to GAP for representative uses
Anon. (1984)	KCA 6.3.2 /06, 5621-83, RIP9400945	No GLP, non-compliant to GAP for representative uses
Anon. (1982)	KCA 6.3.2 /07, MO-03-012144, RIP9400947	No GLP, non-compliant to GAP for representative uses
Anon. (1985)	KCA 6.3.2 /08, MO-03-012145, RIP9400948	No GLP, non-compliant to GAP for representative uses
Seym (1997)	KCA 6.3.2 /09, RA-2005/95, ASB2014-6703	Non-compliant to GAP for representative uses
Seym and Schoening (1997)	KCA 6.3.2 /10, RA-2017/96, ASB2014-6707	Non-compliant to GAP for representative uses
Seym (1997)	KCA 6.3.2 /11, RA-2018/96, ASB2009-2704	Non-compliant to GAP for representative uses
Anon. (1989)	KCA 6.3.3 /01, MO-04-002633, RIP9500582	No GLP, non-compliant to GAP for representative uses
Anon. (1990)	KCA 6.3.3 /02, MO-04-002634, RIP9500583	No GLP, non-compliant to GAP for representative uses
Seym (1993)	KCA 6.3.3 /03, RA-2069/92, RIP9500584	Non-compliant to GAP for representative uses
Anon. (1987)	KCA 6.3.3 /04, MO-04-002617, RIP9401020	No GLP, non-compliant to GAP for representative uses
Anon. (1987)	KCA 6.3.3 /05, MO-04-002621, ASB2009-2238	No GLP, non-compliant to GAP for representative uses
Anon. (1988)	KCA 6.3.3 /06, MO-04-002623, RIP9401022	No GLP, non-compliant to GAP for representative uses
Anon. (1985)	KCA 6.3.3 /07, 8413-84, RIP9401024	No GLP, non-compliant to GAP for representative uses
Anon. (1986)	KCA 6.3.3 /08, 6800-85, RIP9401025	No GLP, non-compliant to GAP for representative uses
Anon. (1986)	KCA 6.3.3 /09, 59/86, RIP9401026	No GLP, non-compliant to GAP for representative uses
Anon. (1984)	KCA 6.3.3 /10, MO-04-002799, RIP9401027	No GLP, non-compliant to GAP for representative uses
Anon. (1988)	KCA 6.3.4 /01, 5721-87, ASB2009-2279	No GLP, non-compliant to GAP for representative uses
Anon. (1989)	KCA 6.3.4 /02, 0490-88, ASB2009-2280 RIP9500603	No GLP, non-compliant to GAP for representative uses
Anon. (1991)	KCA 6.3.4 /03, MO-04-002683, ASB2009-2281 RIP9500604	No GLP, non-compliant to GAP for representative uses
Anon. (1990)	KCA 6.3.4 /04, MO-04-002669, ASB2009-2282 RIP9500585	No GLP, non-compliant to GAP for representative uses
Anon. (1990)	KCA 6.3.4 /05, MO-04-002677, ASB2009-2283 RIP9500596	No GLP, non-compliant to GAP for representative uses

Author and year	Annex point/Report No./BfR code	Justification
Schmidt (1992)	KCA 6.3.4 /06, PF-3763, RIP9500586 ASB2009-2303	Non-compliant to GAP for representative uses
Schmidt (1992)	KCA 6.3.4 /07, PF-3743, RIP2003-120	Non-compliant to GAP for representative uses
Seym (1993)	KCA 6.3.4 /09, RA-2055/91, RIP9500590	Non-compliant to GAP for representative uses
Anon. (1993)	KCA 6.3.4 /11, MO-04-002642, RIP9401034	No GLP, non-compliant to GAP for representative uses
Anon. (1987)	KCA 6.3.4 /12, MO-04-002641, ASB2009-9262	No GLP, non-compliant to GAP for representative uses
Bagnall (1984)	KCA 6.3.4 /13, TCR 236, RIP9401036	No GLP, non-compliant to GAP for representative uses
Bagnall (1985)	KCA 6.3.4 /14, TCR 264, RIP9400897	No GLP, non-compliant to GAP for representative uses
Anon. (1984)	KCA 6.3.4 /15, MO-04-002643, RIP9401037	No GLP, non-compliant to GAP for representative uses
Anon. (1984)	KCA 6.3.4 /16, MO-04-002665, ASB2009-9296	No GLP, non-compliant to GAP for representative uses
Anon. (1988)	KCA 6.3.4 /17, MO-04-002711, ASB2009-2296	No GLP, non-compliant to GAP for representative uses
Anon. (1984)	KCA 6.3.4 /18, 5616-83, ASB2009-9230	No GLP, non-compliant to GAP for representative uses
Anon. (1984)	KCA 6.3.4 /19, 5617-83, ASB2009-9229	No GLP, non-compliant to GAP for representative uses
Anon. (1985)	KCA 6.3.4 /20, MO-04-002700, ASB2009-2299	No GLP, non-compliant to GAP for representative uses
Anon. (1985)	KCA 6.3.4 /21, MO-04-002705, ASB2009-2300	No GLP, non-compliant to GAP for representative uses
Anon. (1991)	KCA 6.3.4 /22, 0661-90, ASB2009-2298 RIP9401043	No GLP, non-compliant to GAP for representative uses
Seym, M. (1994)	KCA 6.3.4 /23, RA-2034/92, ASB2009-1486 RIP9401044	No GLP, non-compliant to GAP for representative uses
Anon. (1985)	KCA 6.3.4 /24, MO-04-002691, ASB2009-9285	No GLP, non-compliant to GAP for representative uses
Anon. (1986)	KCA 6.3.4 /25, 5637-85, ASB2009-2301	No GLP, non-compliant to GAP for representative uses
Anon. (1986)	KCA 6.3.4 /26, 6802-85, ASB2009-2302	No GLP, non-compliant to GAP for representative uses
Anon. (1988)	KCA 6.3.5 /01, MO-03-011998, RIP9500559	No GLP, non-compliant to GAP for representative uses
Anon. (1989)	KCA 6.3.5 /02, 0489-88, RIP9500560	No GLP, non-compliant to GAP for representative uses
Anon. (1989)	KCA 6.3.5 /03, MO-03-011988, RIP9500558	No GLP, non-compliant to GAP for representative uses

Author and year	Annex point/Report No./BfR code	Justification
Anon. (1984)	KCA 6.3.5 /04, MO-03-011983, ASB2009-9297	No GLP, non-compliant to GAP for representative uses
Anon. (1980)	KCA 6.3.5 /05, MO-03-011969, ASB2009-9246	No GLP, non-compliant to GAP for representative uses
Anon. (1981)	KCA 6.3.5 /06, MO-03-011972, RIP9400892	No GLP, non-compliant to GAP for representative uses
Anon. (1983)	KCA 6.3.5 /07, MO-03-011973, ASB2009-9288	No GLP, non-compliant to GAP for representative uses
Anon. (1986)	KCA 6.3.5 /08, MO-03-011976, RIP9400896	No GLP, non-compliant to GAP for representative uses
Bagnall (1985)	KCA 6.3.5 /09, MO-03-011977, RIP9400897	No GLP, non-compliant to GAP for representative uses
Anon. (1982)	KCA 6.3.5 /10, MO-03-011987, RIP9400902	No GLP, non-compliant to GAP for representative uses
Anon. (1981)	KCA 6.3.5 /11, 311/88054/U162, RIP9400905	No GLP, non-compliant to GAP for representative uses
Anon. (1983)	KCA 6.3.5 /12, 311/88379/W113, RIP9400906	No GLP, non-compliant to GAP for representative uses
Anon. (1982)	KCA 6.3.5 /13, 5647-81, RIP9400915	No GLP, non-compliant to GAP for representative uses
Anon. (1985)	KCA 6.3.5 /14, 5641-84, RIP9400913	No GLP, non-compliant to GAP for representative uses
Anon. (1984)	KCA 6.3.5 /15, MO-03-012042, ASB2009-9289	No GLP, non-compliant to GAP for representative uses
Anon. (1986)	KCA 6.3.5 /16, MO-03-012049, RIP9400911	No GLP, non-compliant to GAP for representative uses
Anon. (1986)	KCA 6.3.5 /17, MO-03-012052, RIP9400916	No GLP, non-compliant to GAP for representative uses
Anon. (1981)	KCA 6.3.5 /18, 311/88047/U155, RIP9400917	No GLP, non-compliant to GAP for representative uses
Anon. (1983)	KCA 6.3.5 /19, 311/88378/W112, RIP9400918	No GLP, non-compliant to GAP for representative uses
Anon. (1985)	KCA 6.3.5 /20, MO-03-012056, ASB2009-9247	No GLP, non-compliant to GAP for representative uses
Anon. (1985)	KCA 6.3.5 /21, MO-03-012058, RIP9400923	No GLP, non-compliant to GAP for representative uses
Anon. (1983)	KCA 6.3.5 /22, MO-03-012060, ASB2009-9263	No GLP, non-compliant to GAP for representative uses
Anon. (1986)	KCA 6.3.5 /23, MO-03-012062, RIP9400931	No GLP, non-compliant to GAP for representative uses
Anon. (1987)	KCA 6.3.5 /24, 311/88094/D31, RIP9400933	No GLP, non-compliant to GAP for representative uses
Anon. (1984)	KCA 6.3.5 /25, 5615-83, ASB2009-1876	No GLP, non-compliant to GAP for representative uses
Anon. (1984)	KCA 6.3.5 /26, MO-03-012075, ASB2009-9235	No GLP, non-compliant to GAP for representative uses

Author and year	Annex point/Report No./BfR code	Justification
Anon. (1991)	KCA 6.3.5 /27, MO-03-012085, RIP9400936	No GLP, non-compliant to GAP for representative uses
Anon. (1988)	KCA 6.3.5 /28, MO-03-012111, RIP9500561	No GLP, non-compliant to GAP for representative uses
Anon. (1989)	KCA 6.3.5 /29, 0491-88, RIP9500562	No GLP, non-compliant to GAP for representative uses
Anon. (1992)	KCA 6.3.5 /30, MO-03-012113, ASB2009-9245 RIP9500563	No GLP, non-compliant to GAP for representative uses
Anon. (1982)	KCA 6.3.5 /31, 5648-81, RIP9400940	No GLP, non-compliant to GAP for representative uses
Anon. (1984)	KCA 6.3.5 /32, MO-03-012081, ASB2009-9291	No GLP, non-compliant to GAP for representative uses
Anon. (1981)	KCA 6.3.5 /33, MO-03-012079, RIP9400937	No GLP, non-compliant to GAP for representative uses
Anon. (1981)	KCA 6.3.5 /34, 311/88009/U13, RIP9400941	No GLP, non-compliant to GAP for representative uses
Anon. (1988)	KCA 6.3.5 /35, 5623-87, RIP9400951	No GLP, non-compliant to GAP for representative uses
Anon. (1982)	KCA 6.3.5 /36, MO-03-012148, RIP9400954	No GLP, non-compliant to GAP for representative uses
Anon. (1985)	KCA 6.3.5 /37, MO-03-012149, RIP9400955	No GLP, non-compliant to GAP for representative uses
Seym (1993)	KCA 6.3.5 /38, RA-2035/92, ASB2009-3196	Non-compliant to GAP for representative uses
Seym (1994)	KCA 6.3.5 /39, RA-2017/93, ASB2009-3197	Non-compliant to GAP for representative uses
Anon. (1990)	KCA 6.3.5 /40, 0073-89, ASB2009-2034 RIP9400957	No GLP, non-compliant to GAP for representative uses
Anon. (1984)	KCA 6.3.5 /41, 5622-83, RIP9400956	No GLP, non-compliant to GAP for representative uses
Anon. (1985)	KCA 6.3.5 /42, MO-03-012170, RIP9400960	No GLP, non-compliant to GAP for representative uses
Seym (1993)	KCA 6.3.5 /43, RA-2071/92, RIP9500566	Non-compliant to GAP for representative uses
Anon. (1983)	KCA 6.3.5 /44, MO-03-012188, ASB2009-9232	No GLP, non-compliant to GAP for representative uses
Anon. (1985)	KCA 6.3.5 /45, MO-03-012172, ASB2009-9280	No GLP, non-compliant to GAP for representative uses
Anon. (1987)	KCA 6.3.5 /46, MO-03-012189, RIP9400965	No GLP, non-compliant to GAP for representative uses
Bagnall and Landen (1986)	KCA 6.3.5 /47, TCR 299, RIP9400967	No GLP, non-compliant to GAP for representative uses
Anon. (1984)	KCA 6.3.5 /48, 5619-83, RIP9400966	No GLP, non-compliant to GAP for representative uses
Anon. (1987)	KCA 6.3.5 /49, 5710-87, RIP9500567	No GLP, non-compliant to GAP for representative uses

Author and year	Annex point/Report No./BfR code	Justification
Anon. (1989)	KCA 6.3.5 /50, MO-03-012238, RIP9500568	No GLP, non-compliant to GAP for representative uses
Seym and Walz-Tylla (1993)	KCA 6.3.5 /51, RA-2074/92, RIP9500569	Non-compliant to GAP for representative uses
Anon. (1981)	KCA 6.3.5 /52, MO-03-012192, ASB2009-9248	No GLP, non-compliant to GAP for representative uses
Anon. (1985)	KCA 6.3.5 /53, MO-03-012199, RIP9400974	No GLP, non-compliant to GAP for representative uses
Anon. (1985),	KCA 6.3.5 /54, MO-03-012196, RIP9400973	No GLP, non-compliant to GAP for representative uses
Anon. (1983)	KCA 6.3.5 /55, MO-03-012219, ASB2009-9234	No GLP, non-compliant to GAP for representative uses
Anon. (1983)	KCA 6.3.5 /56, MO-03-012218, ASB2009-9293	No GLP, non-compliant to GAP for representative uses
Anon. (1985)	KCA 6.3.5 /57, MO-03-012223, RIP9400977	No GLP, non-compliant to GAP for representative uses
Anon. (1984)	KCA 6.3.5 /58, MO-03-012227, ASB2009-9244	No GLP, non-compliant to GAP for representative uses
Anon. (1987)	KCA 6.3.5 /59, MO-03-012229, RIP9400982	No GLP, non-compliant to GAP for representative uses
Anon. (1987)	KCA 6.3.5 /60, MO-03-012231, RIP9400983	No GLP, non-compliant to GAP for representative uses
Bagnall (1984)	KCA 6.3.5 /61, MO-03-012233, RIP9400985	No GLP, non-compliant to GAP for representative uses
Anon. (1992)	KCA 6.3.5 /62, MO-03-012246, RIP9500570	No GLP, non-compliant to GAP for representative uses
Seym (1993)	KCA 6.3.5 /63, RA-2072/92, RIP9500571	Non-compliant to GAP for representative uses
Anon. (1981)	KCA 6.3.5 /64, MO-03-012264, RIP9400987	No GLP, non-compliant to GAP for representative uses
Anon. (1982)	KCA 6.3.5 /65, MO-03-012268, RIP9400988	No GLP, non-compliant to GAP for representative uses
Anon. (1983)	KCA 6.3.5 /66, MO-03-012269, ASB2009-9249	No GLP, non-compliant to GAP for representative uses
Anon. (1986)	KCA 6.3.5 /67, MO-03-012273, RIP9400991	No GLP, non-compliant to GAP for representative uses
Anon. (1989)	KCA 6.3.5 /68, 0487-88, RIP9500572	No GLP, non-compliant to GAP for representative uses
Anon. (1989)	KCA 6.3.5 /69, 0485-88, RIP9500573	No GLP, non-compliant to GAP for representative uses
Anon. (1992)	KCA 6.3.5 /70, MO-03-012298, RIP9500574	No GLP, non-compliant to GAP for representative uses
Anon. (1992)	KCA 6.3.5 /71, MO-03-012293, RIP9500575	No GLP, non-compliant to GAP for representative uses
Anon. (1991)	KCA 6.3.5 /72, 0066-90, RIP9500576	No GLP, non-compliant to GAP for representative uses

Author and year	Annex point/Report No./BfR code	Justification
Anon. (1985)	KCA 6.3.5 /73, MO-03-012276, RIP9400992	No GLP, non-compliant to GAP for representative uses
Anon. (1988)	KCA 6.3.5 /74, MO-03-012277, RIP9400993	No GLP, non-compliant to GAP for representative uses
Bagnall (1984)	KCA 6.3.5 /75, TCR 253, RIP9400985	No GLP, non-compliant to GAP for representative uses
Bagnall (1985)	KCA 6.3.5 /76, TCR 285, RIP9400898	No GLP, non-compliant to GAP for representative uses
Bagnall and Landen (1989)	KCA 6.3.5 /77, TCR 345, RIP9400997	No GLP, non-compliant to GAP for representative uses
Anon. (1989)	KCA 6.3.5 /78, 0189-88, RIP9400998	No GLP, non-compliant to GAP for representative uses
Anon. (1985)	KCA 6.3.5 /79, MO-04-002635, ASB2009-9251	No GLP, non-compliant to GAP for representative uses
Heinemann and Seym (1996)	KCA 6.3.5 /80, RA-2025/94, RIP1999-425	Non-compliant to GAP for representative uses
Heinemann and Seym (1996)	KCA 6.3.5 /81, RA-2000/95, RIP1999-422	Non-compliant to GAP for representative uses
Anon. (1990)	KCA 6.3.5 /82, 42451-A, RIP9500580	No GLP, non-compliant to GAP for representative uses
Seym (1982)	KCA 6.3.5 /83, A25059, RIP9400730	No GLP, non-compliant to GAP for representative uses
Seym (1988)	KCA 6.3.5 /84, 98398, RIP9401018	No GLP, non-compliant to GAP for representative uses
Seym (1997)	KCA 6.3.5 /85, RA-2007/95, ASB2014-6704	Non-compliant to GAP for representative uses
Seym (1997)	KCA 6.3.5 /86, RA-2006/95, ASB2014-6701	Non-compliant to GAP for representative uses
Seym (1997)	KCA 6.3.5 /87, RA-2008/95, ASB2014-6705	Non-compliant to GAP for representative uses
Seym (1997)	KCA 6.3.5 /88, RA-2016/96, ASB2009-2706	Non-compliant to GAP for representative uses
Casida et al. (1979)	KCA 6.4 /01, M1892, RIP9400849	Literature data >10 years
Miyamoto et al. (1981)	KCA 6.4 /02, M2240, RIP9400854	Literature data >10 years
[redacted] (1983)	KCA 6.4 /03, PH 11872 (F), RIP9400867	Rat study (refer to B.6)
[redacted] (1983)	KCA 6.4 /04, PH 11575(F), RIP9400866	Rat study (refer to B.6)
[redacted] (1983)	KCA 6.4 /05, PF-2059, RIP9400868	Rat study (refer to B.6)
[redacted] (1983)	KCA 6.4 /06, PF 1632, RIP9400862	Rat study (refer to B.6)
[redacted] (1981)	KCA 6.4 /07, 10130, RIP9400855	Rat study (refer to B.6)

Author and year	Annex point/Report No./BfR code	Justification
Shaw et al. (1985)	KCA 6.4.2 /01, I476, RIP9400740	Analytical method (refer to B.5)
Wiedmann and Jablonski (1990)	KCA 6.5.3 /01, 100203, RIP9401057	Processing study not relevant for assessment of representative uses
Anon. (1995)	KCA 6.5.3 /02, MO-04-002798, RIP9501339	Statement of applicant on re-registration
Heinemann and Seym (1990)	KCA 6.5.3 /03, RA-3000/95, ASB2009-2263	Processing study not relevant for assessment of representative uses
Anon. (1988)	KCA 6.5.3 /04, MO-03-012111, RIP9500561	Processing study not relevant for assessment of representative uses
Anon. (1989)	KCA 6.5.3 /05, 0491-88, RIP9500562	Processing study not relevant for assessment of representative uses
Anon. (1992)	KCA 6.5.3 /06, MO-04-002757, RIP9500563	Processing study not relevant for assessment of representative uses
Anon. (1981)	KCA 6.5.3 /07, MO-03-012079, ASB2009-2018	Processing study not relevant for assessment of representative uses
Anon. (1985)	KCA 6.5.3 /08, 87246, RIP9401060	Processing study not relevant for assessment of representative uses
Anon. (1985)	KCA 6.5.3 /09, 87247, RIP9401059	Processing study not relevant for assessment of representative uses
Seym and Walz-Tylla (1993)	KCA 6.5.3 /11, RA-2074/92, RIP9500569	Processing study not relevant for assessment of representative uses
Anon. (1987)	KCA 6.5.3 /12, MO-04-002760, RIP9400972	Processing study not relevant for assessment of representative uses
Anon. (1989)	KCA 6.5.3 /13, MO-03-012328, RIP9500578	Processing study not relevant for assessment of representative uses
Seym and Walz-Tylla (1993)	KCA 6.5.3 /14, RA-2070/92, RIP9500579	Processing study not relevant for assessment of representative uses
Anon. (1984)	KCA 6.5.3 /15, MO-04-002763, RIP9401064	Processing study not relevant for assessment of representative uses
Anon. (1983)	KCA 6.5.3 /16, 84368, RIP9401063	Processing study not relevant for assessment of representative uses
Burger and Lenz (1992)	KCA 6.5.3 /17, 103835, RIP9501340	Processing study not relevant for assessment of representative uses
Anon. (1988)	KCA 6.5.3 /18, MO-04-002765, RIP9401031	Processing study not relevant for assessment of representative uses
Woodard (1989)	KCA 6.5.3 /19, 98509, ASB2009-1453	Processing study not relevant for assessment of representative uses
Burger and Lenz (1992)	KCA 6.5.3 /21, 103825, RIP9401066	Processing study not relevant for assessment of representative uses
Moraitis (1994)	KCA 6.7.1 /01, M-000956-01-2 RIP9401071	Council directive 94/29/EC
Moraitis (1994)	KCA 6.7.1 /02, M-000957-01-2 RIP9401072	Council Directive 94/30/EC

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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.1 /01	Minor, R. G.; Freeseman, P. L.	1989	Freezer storage stability of cyfluthrin in apples, cotton, potatoes and soybeans Mobay Chemical Corporation, Stilwell, KS, USA Bayer CropScience, Report No.: 99631, Edition Number: M-049792-01-1 EPA MRID No.: 42433002 Date: 1989-09-15 GLP/GEP: no, unpublished **...also filed: KCA 4.1.2 /40** ASB k.A. BVL-2610734 RIP9401053	N	N		Bayer CropScience
KCA 6.1 /02	Minor, R.G.; Freeseman, P. L.	1992	Freezer storage stability of cyfluthrin in corn green forage, head lettuce, and wheat green forage Bayer Corporation, Kansas City, MO, USA Bayer CropScience, Report No.: 102608, Edition Number: M-022101-02-1 Date: 1992-05-12 **...Amended: 1995-09-08** GLP/GEP: yes, unpublished **...also filed: KCA 4.1.2 /41** ASB 2009-1208 BVL-2610735 RIP9401054	N	N		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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.1 /03	Wiedmann, J. L.; Amato, S. L.; Koch, D. A.	1992	Storage stability of cyfluthrin in crops and processing fractions Miles Inc., Agriculture Division, Kansas City, MO, USA Bayer CropScience, Report No.: 103821, Edition Number: M-136649-01-1 EPA MRID No.: 42710402 Date: 1992-12-18 GLP/GEP: yes, unpublished **...also filed: KCA 4.1.2 /42** ASB k.A. BVL-2610736	N	N		Bayer CropScience
KCA 6.1 /04	Shaw, H. R.	1983	The effect of frozen storage at 0 to -10 degree F on baythroid in bovine tissues and milk Mobay Chemical Corporation, Stilwell, KS, USA Bayer CropScience, Report No.: 86041, Edition Number: M-060765-01-1 Date: 1983-09-20 GLP/GEP: no, unpublished ASB2009-1452 BVL-2619801	Y	N		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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.1 /05	[redacted]	1987	Storage stability of Baythroid in bovine liver [redacted] Bayer CropScience, Report No.: 94303, Report includes Trial Nos.: 84-R-170 Edition Number: M-136845-01-1 Method Report No.: 94303 EPA MRID No.: 43533703 Date: 1987-02-04 GLP/GEP: yes, unpublished ASB k.A. BVL-2610737 RIP9401049	Y	N		Bayer CropScience
KCA 6.1 /06	[redacted]	1987	Storage stability of FPB aldehyde (Baythroid metabolite) in bovine liver [redacted] Bayer CropScience, Report No.: 94304, Edition Number: M-069575-01-1 Date: 1987-02-04 GLP/GEP: yes, unpublished ASB k.A. BVL-2610738 RIP9401050	Y	N		Bayer CropScience

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KCA 6.1 /07	Wiedmann, J. L.; Amato, S. L.; Koch, D. A.	1994	Storage stability of cyfluthrin in crops and processed products Miles Inc., Agriculture Division, Kansas City, MO, USA Bayer CropScience, Report No.: 103821-1, Edition Number: M-051312-01-1 EPA MRID No.: 43510903 Date: 1994-04-25 GLP/GEP: yes, unpublished ASB k.A. BVL-2610739 RIP9401056	N	N		Bayer CropScience
KCA 6.1 /08	Wiedmann, J. L.; Amato, S. L.; Koch, D. A.	1994	Storage stability of cyfluthrin in crops and processed products Miles Inc., Agriculture Division, Kansas City, MO, USA Bayer CropScience, Report No.: 103821-2, Report includes Trial Nos.: 103821 103821-1 103821-3 Edition Number: M-051307-01-1 EPA MRID No.: 43510902 Date: 1994-07-27 GLP/GEP: yes, unpublished ASB2009-1322 BVL-2619811	N	N		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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.1 /09	Lenz, C. A.; Lemke, V. J.	1996	Addendum 3 - Storage stability of cyfluthrin in crops and processed products Bayer Corporation, Kansas City, MO, USA Bayer CropScience, Report No.: 103821-3, Report includes Trial Nos.: 103821 103821-1 103821-2 Edition Number: M-051281-01-1 EPA MRID No.: 45655803 Date: 1996-01-04 GLP/GEP: yes, unpublished ASB2009-1323 BVL-2619817	N	N		Bayer CropScience
KCA 6.1 /10	Minor, R. G.; Freeseman, P. L.	1995	Freezer storage stability of cyfluthrin in corn green forage, head lettuce, and wheat green forage Bayer Corporation, Kansas City, MO, USA Report No.: MO-04-003764, 102608-1 Edition Number: M-061762-01-1 Date: 1995-09-08 GLP/GEP: yes, unpublished ASB2009-1208 BVL-2610735 RIP9401054	N	N		

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KCA 6.1 /11	Grace, T. J.	1989	Freezer storage stability of cyfluthrin in hops Mobay Chemical Corporation, Stilwell, KS, USA Bayer CropScience, Report No.: 99203, Report includes Trial Nos.: 5617--86 5618-86 5619-86 Edition Number: M-049817-01-1 EPA MRID No.: 41150401 Date: 1989-06-28 GLP/GEP: no, unpublished ASB k.A. BVL-2619823 RIP9401052	N	N		Bayer CropScience
KCA 6.1 /12	Delk, J. L.	1988	Baythroid - Storage stability of residues in various frozen crops Mobay Chemical Corporation, Stilwell, KS, USA Bayer CropScience, Report No.: 98334, Edition Number: M-049821-01-1 EPA MRID No.: 41001608 Date: 1988-12-20 GLP/GEP: no, unpublished ASB k.A. BVL-2610740 RIP9401051	N	N		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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.1 /13	Anon.	1983	Effect of frozen storage at 0 to -10 degrees Fahrenheit on residues Mobay Chemical Corporation, Kansas City, MO, USA Report No.: MO-04-009081, Edition Number: M-088204-01-1 Date: 1983-09-23 GLP/GEP: no, unpublished **...also filed: KCA 7.1.2 /01** ASB2009-1324 BVL-2619828	N	N		Bayer CropScience
KCA 6.2.1 /01	Wagner, K.; Neitzel, H.	1986	Studies on metabolism of cyfluthrin (FCR 1272) in tomatoes Bayer AG, Leverkusen, Germany Bayer CropScience, Report No.: PF2578, Edition Number: M-063323-01-2 EPA MRID No.: 41001601 Date: 1986-03-07 GLP/GEP: no, unpublished ASB k.A. BVL-2610741 RIP9400821	N	N		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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.2.1 /02	Minor, R. G.; Freseman, P. L.	1985	Metabolism of (^{14}C) R Baythroid in apples Mobay Chemical Corporation, Kansas City, MO, USA Bayer CropScience, Report No.: 88833, Edition Number: M-063640-01-1 Date: 1985-08-06 GLP/GEP: no, unpublished ASB k.A. BVL-2610742 RIP9400838	N	N		Bayer CropScience
KCA 6.2.1 /03	Minor, R. G.; Ernst, V. J.	1983	Metabolism of Baythroid TM in potatoes Mobay Chemical Corporation, Stilwell, KS, USA Bayer CropScience, Report No.: MR86053, Edition Number: M-062850-01-1 Date: 1983-11-22 GLP/GEP: no, unpublished ASB2009-277 BVL-2610743 RIP9400836	N	N		Bayer CropScience
KCA 6.2.1 /04	Minor, R. G.; Ernst, V. J.	1983	Metabolism of Baythroid TM of soybeans Mobay Chemical Corporation, Kansas City, MO, USA Bayer CropScience, Report No.: MR86049, Edition Number: M-063915-01-1 Date: 1983-09-14 GLP/GEP: no, unpublished ASB k.A. BVL-2610744 RIP9400827	N	N		Bayer CropScience

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KCA 6.2.1 /05	Minor, R. G.; Ernst, V. J.	1983	Mertabolism of Baythroid TM in cotton Mobay Chemical Corporation, Kansas City, MO, USA Bayer CropScience, Report No.: MR86048, Edition Number: M-064360-01-1 Date: 1983-09-15 GLP/GEP: no, unpublished ASB k.A. BVL-2610745 RIP9400835	N	N		Bayer CropScience
KCA 6.2.1 /06	Minor, R. G.; Freseman, P. L.; Ernst, V. J.	1985	Metabolism of Baythroid in wheat Mobay Chemical Corporation, Kansas City, MO, USA Bayer CropScience, Report No.: MR88832, Edition Number: M-136985-01-1 EPA MRID No.: 41001602 Date: 1985-09-12 GLP/GEP: no, unpublished ASB k.A. BVL-2610746 RIP9400840	N	N		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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.2.1 /07	Preiss, U.	1985	Metabolism of Baythroid in cultured plant cells Bayerische Landesanstalt fuer Ernaehrung, Muenchen, Germany Bayer CropScience, Report No.: IM 1444, Edition Number: M-064802-01-2 Date: 1985-01-23 GLP/GEP: no, unpublished ASB k.A. BVL-2610747 RIP9400837	N	N		Bayer CropScience
KCA 6.6.2/02	Leslie, W. L.	1988	Baythroid R - residues in field rotational crops: field Cambridge Analytical Associates, Inc., Boston, MA, USA Bayer CropScience, Report No.: MR98429, Edition Number: M-067638-01-1 Method Report No.: MR98429 Date: 1988-11-28 GLP/GEP: yes, unpublished **...also filed: KCA 6.6.2 /02** **...also filed: KCA 7.1.1.1 /02** ASB k.A. BVL-2610961 RIP9400845	N	N		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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.6.2/03	Leslie, W. L.	1989	Baythroid R - residues in field rotational Cereal crops - addendum no. 1 Mobay Chemical Corporation, Stilwell, KS, USA Bayer CropScience, Report No.: MR98429-1, Edition Number: M-067604-01-1 Method Report No.: MR98429-1 EPA MRID No.: 40942701, 41190202 Date: 1989-07-12 GLP/GEP: yes, unpublished **...also filed: KCA 6.6.2 /03** **...also filed: KCA 7.1.1.1 /03** ASB k.A. BVL-2616664 RIP9400848	N	N		Bayer CropScience
KCA 6.2.1 /10	Bongartz, R.; Miebach, D.	2013	Metabolism of [cyclopropane-1-^{14}C]beta-cyfluthrin in sugar beets after seed treatment Bayer CropScience, Report No.: EnSa-13-0307, Edition Number: M-468898-01-1 Date: 2013-11-04 GLP/GEP: yes, unpublished ASB2014-7887 BVL-2632955	N	Y	plant metabolism after seed treatment	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**	**Verte-brate study Y/N**	**Data protection claimed Y/N**	**Justification if data protection is claimed**	**Owner**
KCA 6.2.1 /11	Bongartz, R.; Miebach, D.	2013	Metabolism of [fluorophenyl-UL-14C]beta-cyfluthrin in sugar beets after seed treatment Bayer CropScience, Report No.: EnSa-13-0308, Edition Number: M-468900-01-1 Date: 2013-11-04 GLP/GEP: yes, unpublished ASB2014-7886 BVL-2632956	N	Y	plant metabolism after seed treatment	Bayer CropScience
KCA 6.2.1 /12	Bonarius, T.	2004	Isomerisation of beta-cyfluthrin re-evaluation of residue trials Dr. Knoell Consult GmbH, Mannheim, Germany BCS-Irvita, Report No.: M-241664-01-2, Edition Number: M-241664-01-2 Date: 2004-06-01 GLP/GEP: n.a., unpublished ASB2014-7873 BVL-2632957	N	Y	data not submitted on EU Level	BCS-Irvita

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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.2.2 /08	[redacted]	1983	The distribution and metabolism of Baythroid in laying hens [redacted] Bayer CropScience, Report No.: MR-86044, Edition Number: M-054113-01-1 Date: 1983-09-20 GLP/GEP: no, unpublished **...also filed: KCA 4.1.2 /57** **...also filed: KCA 4.2 /12** **...also filed: KCA 5.1.1 /07** **...also filed: KCA 6.4.1 /01** ASB k.A. BVL-2610770 RIP9400869	Y	N		Bayer CropScience
KCA 6.2.3 /01	[redacted]	1983	Metabolism of Baythtroid in a dairy cow [redacted] Bayer CropScience, Report No.: MR86043, Edition Number: M-052654-01-1 Date: 1983-09-27 GLP/GEP: yes, unpublished **...also filed: KCA 4.1.2 /56** **...also filed: KCA 4.2 /11** **...also filed: KCA 5.1 /05** **...also filed: KCA 5.1.1 /06** **...also filed: KCA 6.4.2 /02** ASB k.A. BVL-2609930 RIP9400870	Y	Y		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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.2.3 /14	[redacted].	2014	Metabolism and disposition of beta-cyfluthrin using [cyclopropane-1-^{14}C]beta-cyfluthrin in the lactating goat [redacted] BCS-Irvita, Report No.: V20236, Edition Number: M-481993-01-1 Date: 2014-04-02 GLP/GEP: yes, unpublished ASB2014-7899 BVL-2632958	Y	Y	to investigate metabolism in the cyclpropyl moiety of the molecule	BCS-Irvita
KCA 6.2.5 /04	[redacted]	2014	[^{14}C]beta-cyfluthrin: Metabolism study in rainbow trout (Oncorhynchus mykiss) [redacted] BCS-Irvita, Report No.: D78924, Edition Number: M-481603-01-1 Date: 2014-03-03 GLP/GEP: yes, unpublished ASB2014-7897 BVL-2632959	Y	Y	new data requirement under Reg. 1107/2009	BCS-Irvita

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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.3.1 /11	Meilland-Berthier, I.	2013	Determination of the residues of cyfluthrin in/on sugarbeet after seed treatment with Montur Forte FS 230 in Germany, northern France, United Kingdom, Spain, Italy, Greece and southern France Bayer CropScience, Lyon, France Bayer CropScience, Report No.: 12-2029, Report includes Trial Nos.: 12-2029-01 12-2029-02 12-2029-03 12-2029-04 12-2029-05 12-2029-06 12-2029-07 12-2029-08 Edition Number: M-463988-01-1 Date: 2013-09-03 GLP/GEP: yes, unpublished ASB2014-7883 BVL-2632961	N	Y	data requirement under Reg. 1107/2009; new method has been developed and validated	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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.3.1 /12	Schoening, R.; Reineke, A.	2011	Determination of the residues of beta-cyfluthrin and imidacloprid in/on sugar beet after seed treatment of Montur Forte FS 230 in the field in Germany and the Netherlands Bayer CropScience, Report No.: 09-2044, Report includes Trial Nos.: 09-2044-01 09-2044-02 Edition Number: M-404508-01-1 Date: 2011-03-25 GLP/GEP: yes, unpublished **...also filed: KCA 4.1.2 /81** ASB2012-4627 BVL-2632962	N	Y	data requirement under Reg. 1107/2009	Bayer CropScience
KCA 6.3.2 /12	Schaeufle, M.	2012	Bulldock 25 EC and Bulldock 25 CS - Magnitude of residues of beta-cyfluthrin in greenhouse tomatoe raw agricultural commodity after 2 applications of Bulldock 25 EC or Bulldock 25 CS - 8 decline trials - in northern and southern Europe (the Nederlands, Germany, Northern France, Greece, Spain and Italy) in 2011 Huntington Life Sciences; Eye research centre, Suffolk, United Kingdom Irvita Plant Protection, Report No.: JDV0077, Edition Number: M-481199-01-1 Date: 2012-06-11 GLP/GEP: yes, unpublished **...also filed: KCA 4.1.2 /83** ASB2014-7711 BVL-2632963	N	Y	data not submitted on EU Level	Irvita Plant Protection

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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.3.3 /11	Seym, M.	1997	Determination of residues of Bulldock 025 EC and Bulldock 025 SC on potato in Portugal and Spain Bayer AG, Leverkusen, Germany Bayer CropScience, Report No.: RA-2004/95, Report includes Trial Nos.: 0179-95 0180-95 0425-95 501794 501808 504254 Edition Number: M-052579-01-1 Date: 1997-03-25 GLP/GEP: yes, unpublished ASB2009-3161, ASB2014-6702 BVL-2619976 (RIP1999-314)	N	N		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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.3.3 /12	Heinemann, O.; Schoening, R.	2002	Determination of residues of beta-cyfluthrin in/on potato after spray application of Bulldock 025 SC in Greece Bayer AG, Bayer CropScience, Monheim, Germany Report No.: RA-2125/01, Report includes Trial Nos.: 0273-01 R 2001 0273/9 Edition Number: M-059856-01-1 Date: 2002-09-20 GLP/GEP: yes, unpublished ASB k.A. BVL-2632964 RIP2003-272	N	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**	**Verte-brate study Y/N**	**Data protection claimed Y/N**	**Justification if data protection is claimed**	**Owner**
KCA 6.3.3 /13	Heinemann, O.; Seym, M.	1998	Determination of residues of Enduro 258 EC in/on potato following spray application in the field in Germany, Great Britain and France Bayer AG, Leverkusen, Germany Bayer CropScience, Report No.: RA-2147/96, Report includes Trial Nos.: 0661-96 0662-96 0663-96 0664-96 606618 606626 606634 606642 Edition Number: M-054896-01-1 Date: 1998-02-20 GLP/GEP: yes, unpublished ASB2014-6706 BVL-2632965	N	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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.3.3 /14	Heinemann, O.; Seym, M.	1998	Determination of residues of Enduro 258 EC in/on potato following spray application in the field in France Bayer AG, Leverkusen, Germany Report No.: RA-2148/96, Report includes Trial Nos.: 0665-96 0773-96 0774-96 606650 607738 607746 Edition Number: M-078830-01-1 Date: 1998-02-20 GLP/GEP: yes, unpublished ASB2014 BVL2632966	N	Y	data not submitted on EU Level	Bayer CropScience
KCA 6.3.3 /15	Lebrun, F.	2013	Magnitude of the residue of beta-cyfluthrin in potatoe (raw agricultural commodity) after two applications of Bulldock 25 EC - two decline curve trials and two trials in northern Europe (northern France, United Kingdom and Germany) - 2012 SGS AGRI MIN, Bruguieres, France Irvita Plant Protection, Report No.: 12SGS078, Edition Number: M-481204-01-1 Date: 2013-08-21 GLP/GEP: yes, unpublished ASB2014-6718 BVL-2632967	N	Y	data not submitted on EU Level	Irvita Plant Protection

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KCA 6.3.4 /08	Seym, M.	1993	Determination of residues of FCR 4545 125 SC in/on common oat, spring barley and spring wheat under actual use conditions in the Federal Republic of Germany Bayer AG, Leverkusen, Germany Bayer CropScience, Report No.: RA-2053/91, Report includes Trial Nos.: 0093-91 0094-91 0095-91 0097-91 0098-91 0099-91 100935 100943 100951 100978 100986 100994 Edition Number: M-052205-01-1 Date: 1993-04-30 GLP/GEP: yes, unpublished ASB k.A. BVL-2610908 RIP9500526, RIP9500587	N	N		Bayer CropScience

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KCA 6.3.4 /10	Seym, M.	1993	Determination of residues of FCR 4545 125 SC in/on spring barley, spring wheat and common oat under actual use conditions in Germany Bayer AG, Leverkusen, Germany Bayer CropScience, Report No.: RA-2073/92, Report includes Trial Nos.: 0024-92 0025-92 0311-92 0312-92 200247 200255 203114 203122 Edition Number: M-052195-01-1 Date: 1993-10-15 GLP/GEP: yes, unpublished ASB k.A. BVL-2610910 RIP9500530, RIP9500588	N	N		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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.3.4 /27	Heinemann, O.; Schoening, R.	2001	Determination of residues of beta-cyfluthrin on wheat following spray treatment of Bulldock 025 EC in Italy, Spain and France Bayer AG, Leverkusen, Germany Bayer CropScience, Report No.: RA-2037/00, Report includes Trial Nos.: 0031-00 0232-00 0233-00 0234-00 R 2000 0031/6 R 2000 0232/7 R 2000 0233/5 R 2000 0234/3 Edition Number: M-073236-02-1 Date: 2001-09-13 **...Amended: 2001-11-13** GLP/GEP: yes, unpublished ASB k.A. BVL-2632968 RIP2003-275	N	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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.3.4 /28	Bousquet, C.	2013	Magnitude of the residue of beta-cyfluthrin in winter wheat (raw agricultural commodity) after two applications of Bulldock 25 EC - 4 harvest trials in Northern Europe (Northern France, United Kingdom and Germany) - 2012 SGS AGRI MIN, Bruguieres, France Irvita Plant Protection, Report No.: 12SGS096, Edition Number: M-481205-01-1 Date: 2013-06-24 GLP/GEP: yes, unpublished ASB2014-6714 BVL-2632969	N	Y	data not submitted on EU Level	Irvita Plant Protection
KCA 6.2.2	[redacted]	1983	The distribution and metabolism of Baythroid in laying hens [redacted] Bayer CropScience, Report No.: MR-86044, Edition Number: M-054113-01-1 Date: 1983-09-20 GLP/GEP: no, unpublished **...also filed: KCA 4.1.2 /57** **...also filed: KCA 4.2 /12** **...also filed: KCA 5.1.1 /07** **...also filed: KCA 6.2.2 /08** ASB k.A. BVL-2610770 (see 6.2.2/08)	Y	N		Bayer CropScience

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KCA 5.1	[redacted]	1987	Biotransformation of Cyfluthrin in the chicken after oral adminstration of a high dose [redacted] Bayer CropScience, Report No.: 15849, Edition Number: M-038063-01-1 Date: 1987-06-24 GLP/GEP: no, unpublished **...also filed: KCA 4.2 /13** **...also filed: KCA 5.1.1 /08** ASB k.A. BVL-2609901 TOX9401851	Y	N		Bayer CropScience
KCA 6.4.1 /03	[redacted]	1983	FCR1272; feeding study; chicken; USA [redacted] Bayer CropScience, Report No.: 86033, Edition Number: M-062920-01-1 Date: 1983-09-12 GLP/GEP: no, unpublished ASB k.A. BVL-2610948 RIP9400718	Y	N		Bayer CropScience

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KCA 6.4.1 /04	[redacted]	1983	A 28 day Baythroid TM poultry feeding study [redacted] Report No.: MR86046, Edition Number: M-060241-02-1 Date: 1983-09-14 **...Amended: 1984-07-05** GLP/GEP: no, unpublished ASB k.A. BVL-2610949 RIP9400721	Y	N		Bayer CropScience
KCA 6.4.1 /05	[redacted]	1984	Baythroid metabolites in chicken tissues (muscle, fat, skin, liver, and gizzard) [redacted] Bayer CropScience, Report No.: MR86658, Edition Number: M-068248-01-1 Date: 1984-05-30 GLP/GEP: no, unpublished ASB k.A. BVL-2616601 RIP9400723	Y	N		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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.4.1 /06	[redacted]	1983	FCR 1272; feeding study; chicken; USA [redacted] Bayer CropScience, Report No.: 86034, Edition Number: M-136924-01-1 Date: 1983-09-12 GLP/GEP: no, unpublished ASB k.A. BVL-2616606 RIP9400719	Y	N		Bayer CropScience
KCA 6.4.2 /02	[redacted]	1983	Metabolism of Baythtroid in a dairy cow [redacted] Bayer CropScience, Report No.: MR86043, Edition Number: M-052654-01-1 Date: 1983-09-27 GLP/GEP: yes, unpublished **...also filed: KCA 4.1.2 /56** **...also filed: KCA 4.2 /11** **...also filed: KCA 5.1 /05** **...also filed: KCA 5.1.1 /06** **...also filed: KCA 6.2.3 /01** ASB k.A. BVL-2623805 RIP9400870	Y	N		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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.4.2 /03	[redacted]	1983	Raw data : bovine residue feeding study (28 day) - Baythroid [redacted] Bayer CropScience, Report No.: 86040, Edition Number: M-062087-01-1 Date: 1983-09-07 GLP/GEP: no, unpublished ASB k.A. BVL-2636631 RIP9400716	Y	N		Bayer CropScience
KCA 6.4.2 /04	[redacted]	1983	FCR 1272; feeding study; cow; USA [redacted] Bayer CropScience, Report No.: 86039, Edition Number: M-062229-01-1 Date: 1983-09-07 GLP/GEP: no, unpublished ASB k.A. BVL-2610950 RIP9400717	Y	N		Bayer CropScience

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KCA 6.4.2 /05	[redacted]	1983	Baythroid 28 day feeding study [redacted] Bayer CropScience, Report No.: MR-86045, Edition Number: M-055028-02-1 Date: 1983-09-14 **...Amended: 1984-01-23** GLP/GEP: no, unpublished ASB k.A. BVL-2610951 RIP9400720	Y	N		Bayer CropScience
KCA 6.4.2 /06	[redacted]	1985	FCR 1272; feeding study; cow; USA [redacted] Bayer CropScience, Report No.: 90386, Edition Number: M-054888-01-1 Date: 1985-09-25 GLP/GEP: no, unpublished ASB k.A. BVL-2610952 RIP9400726	Y	N		Bayer CropScience
KCA 6.4.2 /07	[redacted]	1985	FCR 1272; feeding study; cow; USA [redacted] Bayer CropScience, Report No.: 90387, Edition Number: M-054668-01-1 Date: 1985-09-19 GLP/GEP: no, unpublished ASB k.A. BVL-2610953 RIP9400725	Y	N		Bayer CropScience

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KCA 6.4.2 /08	[redacted]	1994	Cyfluthrin - A 28 - day dairy cattle feeding study [redacted] Bayer CropScience, Report No.: 106628, Edition Number: M-054521-01-1 EPA MRID No.: 43533702 Date: 1994-12-13 GLP/GEP: yes, unpublished ASB k.A. BVL-2610954 RIP9500449	Y	N		Bayer CropScience
KCA 6.4.2 /09	[redacted]	1985	Baythroid - Identity of major components in cow liver [redacted] Bayer CropScience, Report No.: MR-88970, Edition Number: M-053779-01-1 EPA MRID No.: 00152971 Date: 1985-03-05 GLP/GEP: no, unpublished ASB k.A. BVL-2610774 RIP9400724	Y	N		Bayer CropScience

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KCA 6.4.2 /10	[redacted]	1984	FCR 1272 metabolite : COE 538/78; cow; USA [redacted] Bayer CropScience, Report No.: 86218, Edition Number: M-068788-01-1 Date: 1984-01-03 GLP/GEP: no, unpublished ASB k.A. BVL-2616655 RIP9400722	Y	N		Bayer CropScience
KCA 6.5.1 /01	Adam, D.	2012	[^{14}C] beta-cyfluthrin: Simulated processing - Hydrolysis at 90, 100 and 120 degree Innovative Environmental Services (IES) Ltd., Witterswil, Switzerland BCS-Irvita, Report No.: 20120062, Edition Number: M-479731-01-1 Date: 2012-12-06 GLP/GEP: yes, unpublished ASB2014-6710 BVL-2632970	N	Y	New data requirement under Reg. 1107/2009	BCS-Irvita

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KCA 6.5.3 /10	Leslie, W. L.	1988	Baythroid - Magnitude of the residue on tomato processed products Mobay Chemical Corporation, Kansas City, MO, USA Bayer CropScience, Report No.: 98399, Report includes Trial Nos.: RTX-F2060-83P Edition Number: M-136610-01-1 EPA MRID No.: 41001615 Date: 1988-11-16 GLP/GEP: no, unpublished ASB k.A. BVL-2610956 RIP9401061	N	N		Bayer CropScience
KCA 6.5.3 /20	[redacted]	1993	Distribution of radioactive residue in milk following oral dosing of a dairy cow for 5 consecutive days with (Phenoxy-ul-^{14}C) cyfluthrin [redacted] Bayer CropScience, Report No.: MR103221, Edition Number: M-060766-01-1 EPA MRID No.: 42925001 Date: 1993-01-27 GLP/GEP: yes, unpublished ASB k.A. BVL-2610776 RIP9401069	Y	N		Bayer CropScience

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KCA 6.5.3 /22	Schaeufle, M.	2012	Bulldock 25 EC - Magnitude of residues of beta-cyfluthrin in greenhouse tomato raw agricultural commodity and processed fractions after 2 applications of Bulldock 25 EC - 2 trials - In northern europe (Germany) in 2011 Huntington Life Sciences; Eye research centre, Suffolk, United Kingdom Irvita Plant Protection, Report No.: M-481079-01-1, Edition Number: M-481079-01-1 Date: 2012-06-22 GLP/GEP: no, unpublished **...also filed: KCA 4.1.2 /87** ASB2014-7712 BVL-2632971	N	Y	data not submitted on EU Level	Irvita Plant Protection
KCA 6.6.2 /01	Minor, R. G.; Ernst, V. J.	1983	Radioactive residues of Baythroid TM in rotational crops Mobay Chemical Corporation, Kansas City, MO, USA Bayer CropScience, Report No.: MR86050, Edition Number: M-067406-01-1 Method Report No.: MR86050 EPA MRID No.: 00131496, 00137541 Date: 1983-09-15 GLP/GEP: no, unpublished **...also filed: KCA 7.1.1.1 /01** ASB k.A. BVL-2610960 RIP9400841	N	N		Bayer CropScience

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KCA 6.6.2 /02	Leslie, W. L.	1988	Baythroid R - residues in field rotational crops: field Cambridge Analytical Associates, Inc., Boston, MA, USA Bayer CropScience, Report No.: MR98429, Edition Number: M-067638-01-1 Method Report No.: MR98429 Date: 1988-11-28 GLP/GEP: yes, unpublished **...also filed: KCA 6.2.1 /08** **...also filed: KCA 7.1.1.1 /02** ASB k.A. BVL-2610961 RIP9400845	N	N		Bayer CropScience
KCA 6.6.2 /03	Leslie, W. L.	1989	Baythroid R - residues in field rotational Cereal crops - addendum no. 1 Mobay Chemical Corporation, Stilwell, KS, USA Bayer CropScience, Report No.: MR98429-1, Edition Number: M-067604-01-1 Method Report No.: MR98429-1 EPA MRID No.: 40942701, 41190202 Date: 1989-07-12 GLP/GEP: yes, unpublished **...also filed: KCA 6.2.1 /09** **...also filed: KCA 7.1.1.1 /03** ASB k.A. BVL-2616664 RIP9400848	N	N		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	Verte-brate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.6.2 /04	Chavelier, E.	2013	Magnitude of the residue of beta-cyfluthrin in succeding crops after application of Bullock 25 EC in two trials in southern Europe (southern France and Spain) - 2012 Huntington Life Sciences; Eye research centre, Suffolk, United Kingdom Irvita Plant Protection, Report No.: 12SGS117, Edition Number: M-481208-01-1 Date: 2013-10-17 GLP/GEP: yes, unpublished ASB2014-7884 BVL-2632972	N	Y	data not submitted on EU Level	Irvita Plant Protection
KCA 6.3	Schöning, R., Nüßlein, F.	2010	Determination of residues of Cyfluthrin on barley after two spray applications of Baythroid 050 EC in France, Italy and Portugal - incl. Amendment 1 vom 14.11.2001 RA-2045/00 ! MO-01-020775 ! 0050-00 ! 0244-00 ! 0245-00 ! R-19223 GLP: Yes Published: No 04.03.2010 GLP: Y ASB k.A. BVL-2846736 RIP2003-267	N	Y		ADAMA

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KCA 6.3	Schöning, R.; Sur, R.	2001	Determination of residues of beta-cyfluthrin on barley following spray application of Bulldock 025 EC in France, Italy and Portugal RA-2031/00 ! MO-01-019665 ! 0030-00 ! 0227-00 ! 0228-00 ! R-19254 GLP: Yes Published: No ASB k.A. BVL-2637568 RIP2003-273	N	J		ADAMA

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