Competent Authority Report

Programme for Inclusion of Active Substances in Annex I to Council Directive 98/8/EC

Permethrin (PT 8)

CAS-No. 52645-53-1

DOCUMENT IIIA (A1-A3)

Bayer Environmental Science

Sumitomo Chemical (UK) Plc.

Rapporteur: Ireland

November 2013

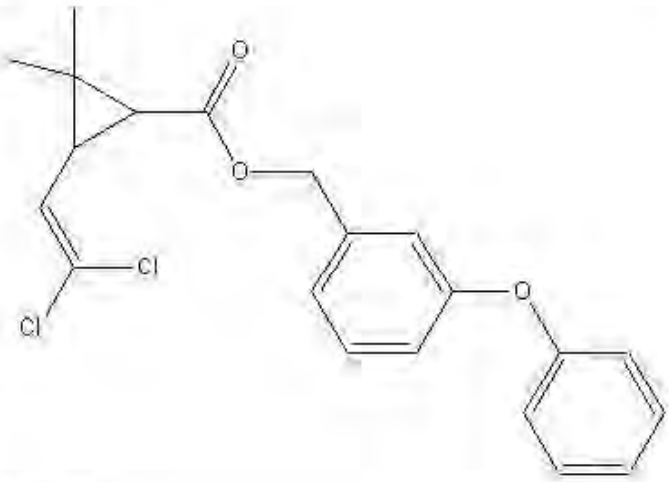
Permethrin PT8

Document IIIA (A1-A3)

CONTENTS

Section A1 **Annex Point IIA1**	**Applicant**		
1.1 **Applicant**	Name: Address: Contact Person: Telephone: Fax number: E-mail address: Name: Address: Contact Person: Telephone: Fax number: E-mail address:	Sumitomo Chemical (UK) plc Horatio House, 77-85 Fulham Palace Rd LONDON W6 8JA UK [redacted] Bayer Environmental Science 16 rue Jean-Marie Leclair CP106 69266 Lyon France [redacted]	
1.2 **Manufacturer of Active Substance** (if different)	Name: Address: Telephone: Fax number: Location of manufacturing plant:	Bilag Industries Limited Plot #306/3, II Phase, GIDC Vapi – 396 195, Gujarat, India [redacted] Gujarat, India	X
1.3 **Manufacturer of Product(s) (if different)**	None		

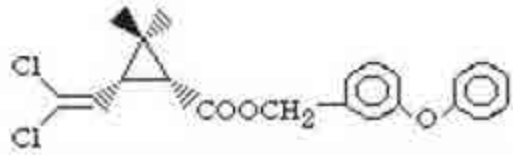
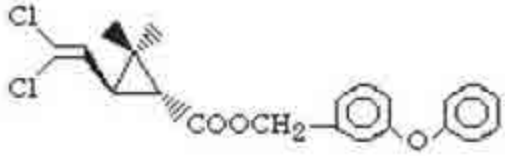
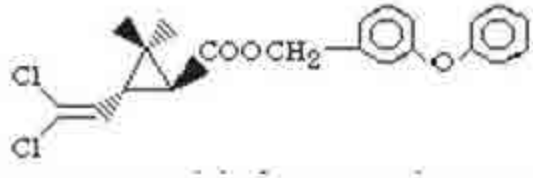
Section A2 Identity of Active Substance

Subsection (Annex Point)			Official use only
2.1	Common name (IIA2.1)	Permethrin	
2.2	Chemical name (IIA2.2)	3-phenoxybenzyl (1RS)-cis,trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate	
2.3	Manufacturer's development code number(s) (IIA2.3)	NRDC 143, 21Z73	
2.4	CAS No and EC numbers (IIA2.4)		
2.4.1	CAS-No	52645-53-1	
2.4.2	EC-No	258-067-9	
2.4.3	Other	CIPAC 331	
2.5	Molecular and structural formula, molecular mass (IIA2.5)		
2.5.1	Molecular formula	$C_{21}H_{20}Cl_2O_3$	
2.5.2	Structural formula		X
2.5.3	Molecular mass	391.29	

Section A2	Identity of Active Substance					
2.6	**Method of manufacture of the active substance (IIA2.1)**	See Confidential data				
2.7	**Specification of the purity of the active substance, as appropriate (IIA2.7)**	g/kg	g/l	% w/w 95.8% min	% v/v	X
2.8	**Identity of impurities and additives, as appropriate (IIA2.8)**	see separate standard format in confidential file				
2.8.1	**Isomeric composition**	% *cis*-isomer 22.93% min % *trans*-isomer 70.03% min				X
2.9	**The origin of the natural active substance or the precursor(s) of the active substance (IIA2.9)**	Precursors manufactured				

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date	19/11/2013
Materials and methods	**X – Structural formula** Permethrin has four stereoisomers: 1Rcis, 1Scis, 1Rtrans, and 1Strans. Two pairs of diastereomers (each consisting of a non-racemic pair of enantiomers) are present in a ratio of *ca.* 25:75. 1Rcis isomer –  1Scis isomer –  1Rtrans isomer –  1Strans isomer – 
Conclusion	Permethrin has four stereoisomers.
Reliability	1
Acceptability	Acceptable.
Remarks	No further data required

COMMENTS FROM ...

Date
Results and discussion
Conclusion
Reliability
Acceptability
Remarks

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	31/10/2012
Materials and methods	**X - Manufacturer of Active Substance** Bilag is a Toll-manufacturer for Bayer. Although Bilag (Vapi) is the manufacturing site, Bayer Environmental Science is the actual manufacturer of the technical material.
Conclusion	Bayer Environmental Science is the manufacturer of the technical material.
Reliability	1
Acceptability	Acceptable.
Remarks	No further data required
	COMMENTS FROM ...
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	16/11/2013
Materials and methods	**X - Specification of the purity of the active substance, as appropriate & Isomeric composition** 27 batches of the Bilag production were examined. See details in the Confidential Section of the CAR.
Conclusion	Technical specification for Bayer source of permethrin: Min. 95% w/w of total active. Total cis range: 22 – 28% ratio Total trans range: 72-78% ratio 1Rcis range: 5.0 – 10.0% w/w. 1Scis range: 15-20% w/w. 1Rtrans range: 45 – 55% w/w. 1Strans range: 17 – 27 % w/w.
Reliability	1
Acceptability	Acceptable for the purposes of Annex I inclusion.
Remarks	No further data required
	COMMENTS FROM ...
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section A3 **Physical and Chemical Properties of Active Substance**

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.1 Melting point, boiling point, relative density (IIA3.1)								
3.1.1 Melting point								X
Melting pt. 1	Fisher-Johns melting point apparatus	Cis isomer 99.7%	55.7-56.3°C	Average of 3 determinations	Y	1	Alvarez, M.; 1989	
Melting pt. 2	Fisher-Johns melting point apparatus	Trans isomer 99.6%	45.7-46.3°C	Average of 3 determinations	Y	1	Alvarez, M.; 1989	
3.1.2 Boiling point								
Boiling pt. 1	Calculated	No data	437°C	See Justification A3.1.2	N/A	3	EPIWIN	X
Boiling pt. 2	Secondary source	No data	220°C (6.67 Pa)	EHC data	No data	4	Meister et al; 1990	
Boiling pt. 3	Secondary source	No data	200°C (1.33 Pa)	EHC data	No data	4	Meister et al; 1990	
3.1.3 Bulk density/ relative density	OECD109	Batch 002/96,38 94% (w/w)	1.207 (25°C)	Mean of 5 replicate measurements	Y	1	Tamiliselvan, C; 1997a	X
3.2 Vapour pressure (IIA3.2)								X
Vapour pressure 1	Gas saturation	Cis isomer 99.7%	25°C: 2.88 µPa	-	Y	1	Alvarez, M.; 1989	
Vapour pressure 2	Gas saturation	Trans isomer 99.6%	25°C: 0.92 µPa	-	Y	1	Alvarez, M.; 1989	
3.2.1 Henry´s Law Constant (Pt. I-A3.2)	Calculation	N/A	**$K > 4.5.10^{-2}$ Pa m^3 mol^{-1}**	Calculation	N/A	1	Bascou, J.P, 2007	X
3.3 Appearance (IIA3.3)	-	-	-	-	-	-	-	X

Section A3 **Physical and Chemical Properties of Active Substance**

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.3.1 Physical state	Direct visual examination	Based on 52:48 cis:trans mixture of 96.3% purity	Viscous liquid (Liquid, Solid or mixture of liquid and solid)	Appearance of isomer mixtures not expected to vary	Y	2	Alvarez, M.; 1989	
3.3.2 Colour	ASTM D1544-80	Based on 52:48 cis:trans mixture of 96.3% purity	Yellow brown (Gardner 17+)	Appearance of isomer mixtures not expected to vary	Y	2	Alvarez, M.; 1989	
3.3.3 Odour		Based on 52:48 cis:trans mixture of 96.3% purity	Characteristic pyrethroid odour (aromatic)	Appearance of isomer mixtures not expected to vary	Y	2	Alvarez, M.; 1989	
3.4 Absorption spectra (IIA3.4)								
UV/VIS	UV Spectrometry	25:75 cis trans ≥99.0%	See IUCLID entry (Section 1.1.2)	Isomers mixed in 25:75 ratio	N	2	White, D.F, et al 2004	X
IR	IR spectrometry	Pure cis-permethrin (99.3 % (w/w)) and pure trans permethrin (99.0 % (w/w))	Results are in full agreement with the proposed structure of the test item. spectra provided	-	Y	1	Walker, JA and O'Connor BJ 2007	
NMR	NMR Spectrometry	Pure cis-permethrin (99.3 % (w/w)) and pure trans permethrin (99.0 % (w/w))	Results are in full agreement with the proposed structure of the test item. spectra provided	-	N[1]	1	Guebert C., 2007	

Section A3 **Physical and Chemical Properties of Active Substance**

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
MS	Mass Spectrometry	Pure cis-permethrin (99.3 % (w/w)) and pure trans permethrin (99.0 % (w/w))	results are in full agreement with the proposed structure of the test item. spectra provided	-	N[1]	1	Guebert C., 2007	
3.5 Solubility in water (IIA3.5)	Measured (20°C) - Official guideline method L383A A6	25:75 cis trans ≥99.0%	<4.95 µg l^{-1}	-	Y	1	White, D.F, et al 2004	
3.6 Dissociation constant	Spectrophotometric	Technical 25:75 cis:trans ratio	7.03 – 7.42	Range of 5 analyses	Y	1	Tamiliselvan, C; 1997b	
3.7 Solubility in organic solvents, including the effect of temperature on solubility (IIIA3.1)	CIPAC method MT 181 'Solubility in Organic Solvents':	Technical 25:75 cis:trans ratio 97.3%	20°C Hexane >250g/L Toluene >250g/L Dichloromethane >250g/L Methanol >250g/L Acetone >250g/L Ethyl acetate >250g/L 30°C Hexane >250g/L Toluene >250g/L		Y	1	Forster B, 2007	
3.8 Stability in organic solvents used in b.p. and identity of relevant breakdown products (IIIA3.2)	-	Technical 25:75 cis:trans ratio	A methanolic solution of permethrin exposed to light for 4 weeks showed no evidence of decomposition	-	N	2	Lines, C; 1986	

Section A3 **Physical and Chemical Properties of Active Substance**

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.9 Partition coefficient n-octanol/water (IIA3.6)	Generator Column Method (OPPTS 830.7560)	Technical 25:75 cis:trans ratio 94,5% (W/W)	Log Pow = 6.1 at 20°C		N	2	Wollenton C, 1987 Robson C.G and Pearson F.J 1995	X
3.10 Thermal stability, identity of relevant breakdown products (IIA3.7)	-	Technical 25:75 cis:trans ratio	Permethrin is thermally stable when stored at temperatures up to and including 50°C for twelve months	-	N	2	Lines, C; 1986	
3.11 Flammability, including auto-flammability and identity of combustion products (IIA3.8)	Measured - Official guideline method L383A A15	Technical 25:75 cis:trans ratio	Determined not to have an auto-ignition temperature below 400°C	-	Y	1	Tremain S P 2004	
3.12 Flash-point (IIA3.9)	Closed cup equilibrium - Official guideline method L383A A9	Technical 25:75 cis:trans ratio	219 ± 2°C at 101.325 kPa	-	Y	1	Tremain S P 2004	
3.13 Surface tension (IIA3.10)	-	-	-	Not required – see justification A3.13	-	-	-	X
3.14 Viscosity (-)	-	-	-	Not required – see justification A3.14	-	-	-	X
3.15 Explosive properties (IIA3.11)	Predicted - Official guideline method L383A A14	Not applicable	Predicted negative	-	Y	1	Tremain S P 2004	X
	Measured – ASTM E680-79	Technical grade 52:48 cis:trans	No ignition up to maximum drop height	Drop weight impact sensitivity test	N	2	Alvarez, M.; 1989	X

Section A3 **Physical and Chemical Properties of Active Substance**

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.16 Oxidizing properties (IIA3.12)	Predicted - Draft guideline method L383A A21	Not applicable	Predicted negative	-	Y	1	Tremain S P 2004	
3.17 Reactivity towards container material (IIA3.13)	Predicted – based on pH, structure and experience	Not applicable	Predicted not reactive to epoxy-coated steel containers	-	Y	1	Tremain S P 2004	
1- The analytical evaluation of the study was conducted in a GLP compliant laboratory of Bayer CropScience AG, Product Technology Analytics Frankfurt. Study was finalized 09/2007. Raw data and related documents are filed and stored in GLP/GMP Archive Building BCS Frankfurt, G864, Industriepark Höchst, 65926 Frankfurt am Main, Germany.								

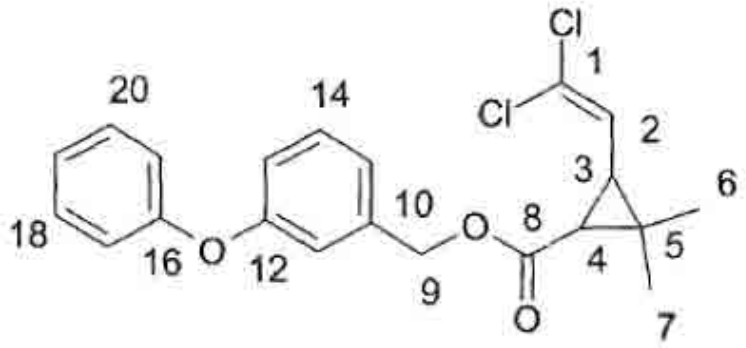
Table 3.4.1 UV Absorbance of permethrin

Medium	Concentration ($mol.dm^{-3}$)	Approximate wavelength (nm)	Molar absorption coefficient ($dm^3.mol^{-1}.cm^{-1}$)
Acidic (0.1M HCl)	5.14×10^{-4}	272 277	1.92×10^{-3} 1.84×10^{3}
Neutral	5.14×10^{-4}	272 277	1.90×10^{-3} 1.82×10^{3}
Alkaline (0.1M NaOH)	5.14×10^{-4}	272 278	1.86×10^{-3} 1.73×10^{3}

Table 3.4.2 IR Spectral data permethrin

Vibrational Frequency (cm^{-1})	Vibrational Mode	Functional Group
~3150 to ~3000	C – H , stretching	Aromatic groups, cyclopropane group and alkene group.
~3000 to ~2850	C – H , stretching	Alkane groups
~1750 to ~1710	C = O, stretching	Ester group
~1675 to ~1620	C = C, stretching	alkene group
~1660 to ~1430	C = C (aromatic)	Aromatic groups
~1480 to ~1340	C – H , deformation	Alkane groups
~1260 to ~1140	C - O, stretching	Diaryl ether group
~1200 to ~1140	C - O, stretching	Ester group
~880 to ~780	C – H , out of plane deformation	alkene group
~810 to ~680	C – H , out of plane deformation	Aromatic groups
~800 to ~700	C – Cl, stretching	Halogenated group

Table 3.4.3 NMR Spectral data permethrin



^{1}H NMR data for permethrin (cis)

Chemical Shift (δ ppm)	Multiplicity	Assignment
7.37-7.30	overlapped	Aromatic : H (18,19,20)
7.26	singulet	$CDCl_3$
7.12	Triplet of triplets	Aromatic : H (14)
7.08	doublet	Aromatic : H (13 or 15)
7.04-7.00	overlapped	Aromatic H (11, 17,21)
6.96	doublet of doublets	Aromatic : H (13 or 15)
6.26	doublet	H_2
5.09, 5.05	doublet, doublet	Ar-CH_2-O (9)
2.05	triplet	H_3
1.89	doublet	H_4
1.25	singlet	2xCH_3 (6,7)
0.0	singlet	TMS

^{1}H NMR data for permethrin (trans)

Chemical Shift (δ ppm)	Multiplicity	Assignment
7.37-7.30	overlapped	Aromatic : H (18,19,20)
7.26	singulet	$CDCl_3$
7.12	Triplet of triplets	Aromatic : H (14)
7.08	doublet	Aromatic : H (13 or 15)
7.04-7.00	overlapped	Aromatic H (11, 17,21)
6.96	doublet of doublets	Aromatic : H (13 or 15)
5.60	doublet	H_2
5.08, 5.12	doublet, doublet	Ar-CH_2-O (9)
2.25	doublet of doublets	H_3
1.65	doublet	H_4
1.27	quartet	CH_3 (6 or 7)
1.18	quartet	CH_3 (6 or 7)
0.0	singlet	TMS

^{13}C NMR data for permethrin (cis)

Chemical shift (ppm)	assignments	multiplicity	Chemical shift (ppm)	assignments	multiplicity
0	TMS	singlet	122.69	15 or 13	Doublet
14.94	6 or 7	Quartet	123.48	14	Doublet
27.67	5	Singlet	124.78	2	Doublet
28.36	6 or 7	Quartet	129.81	18,20	Doublet
31.79	4	Doublet	129.93	19	Doublet
32.70	3	Doublet	137.95	10	Singlet
65.77	9	Triplet	156.93	16	Singlet
118.3	11	Doublet	157.56	12	Singlet
118.4	13 or 15	Doublet	170.27	8	Singlet
120.79	1	Singlet			

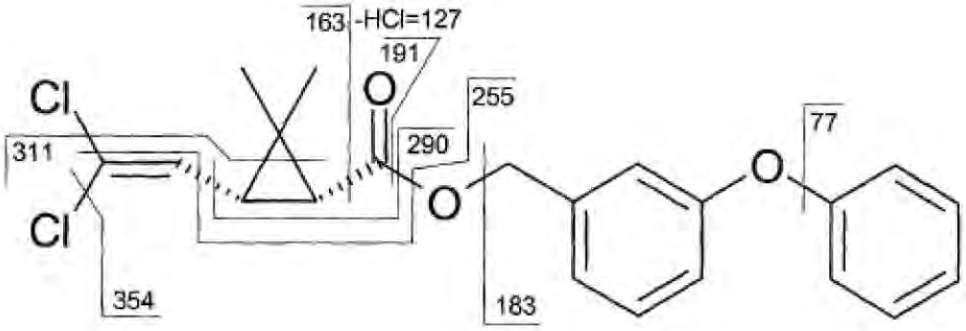
^{13}C NMR data for permethrin (trans)

Chemical shift (ppm)	assignments	multiplicity	Chemical shift (ppm)	assignments	multiplicity
0	TMS	singlet	122.69	13 or 15	Doublet
20.08	6 or 7	Quartet	123.50	14	Doublet
22.59	6 or 7	Quartet	126.89	2	Doublet
29.12	5	singlet	129.81	18,20	Doublet
33.01	3	Doublet	129.91	19	Doublet
34.68	4	Doublet	137.97	10	Singlet
66.01	9	Triplet	156.92	16	Singlet
118.3	11,13 or 15	overlapped	157.57	12	Singlet
119.07	17,21	Doublet	170.88	8	Singlet
122.17	1	Singlet			

Table 3.4.3 MS Spectral data permethrin

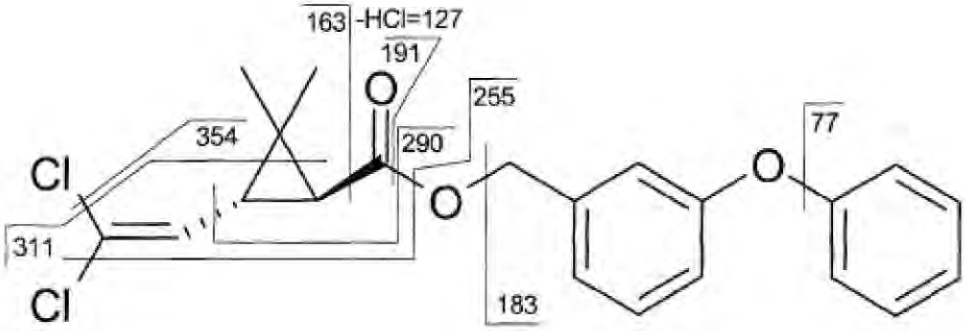
Fragmentation Scheme of CIS-PERMETHRIN (BCS-AA10041)

CIS-PERMETHRIN (BCS-AA10041): M^+ = 390 (2 Cl)



Fragmentation Scheme of TRANS-PERMETHRIN (BCS-AA10042)

TRANS-PERMETHRIN (BCS-AA10042): M^+ = 390 (2 Cl)



Section A3.1.2	BOILING POINT	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure** [ ]	**Technically not feasible** [X] **Scientifically unjustified** [ ] **Other justification** [X]	
Detailed justification:	The Meister et al (1990) reference quotes a value of 200 – 220 °C for boiling point determination, but no detail on the original reference can be found in the document or the open literature. EPIWIN calculation based upon an adapted Stein & Brown method estimates a boiling point of 438°C. Recent work on the hazardous physical-chemical properties of permethrin technical (Tremain, S.P; 2004) indicates a flash point of 219°C and no observations of auto-ignition were made below 400°C. Based on these empirical observations, it is probable that the value of 200°C is anomalous, and the estimated value of 438°C is more predictive of the true boiling point of permethrin. Therefore, it is proposed that since the likely boiling point of permethrin is above 360°C it is justified not to undertake testing, as discussed in the Guidance on Data Requirements, which requires measurement of boiling point only up to 360°C.	
Undertaking of intended data submission [ ]	Not applicable	

Evaluation by Competent Authorities		
Section	**A3.1.1**	**Melting Point**
		EVALUATION BY RAPPORTEUR MEMBER STATE
Date		15/06/2011
Evaluation of applicant's justification		X – Melting Point: The Bayer/Sumitomo study has been conducted on the individual cis and trans isomers and not the 25:75 isomeric test material. However, Tagros have provided a study using purified active substance with the correct isomeric ratio (99.30%, cis:trans ratio of 25:75). The Tagros melting point = 33°C – 35°C.
Reliability		1
Acceptability		Acceptable
Conclusion		The Bayer/Sumitomo was not conducted using the correct test material, however there is an acceptable Tagros study available.
Remarks		No further data required
		COMMENTS FROM OTHER MEMBER STATE
Date		
Evaluation of applicant's justification		
Conclusion		
Remarks		

Evaluation by Competent Authorities		
Section	**A3.1.2**	**Boiling Point**
		EVALUATION BY RAPPORTEUR MEMBER STATE
Date		15/06/2011
Evaluation of applicant's justification		X – Boiling Point: Tagros have provided an acceptable boiling point study (305°C using purified active with a min. Purity of 99.3%, cis:trans 25:75). The applicants are data sharing in relation to phys.chem. studies.
Conclusion		Bayer/Sumitomo did not carry out a boiling point study, however Tagros have an acceptable study available.
Reliability		1
Acceptability		Acceptable
Remarks		No further data required
		COMMENTS FROM OTHER MEMBER STATE
Date		
Evaluation of applicant's justification		
Conclusion		
Remarks		

Evaluation by Competent Authorities	
Section A3.1.3	Bulk density/relative density
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	15/06/2011
Evaluation of applicant's justification	**X - Bulk density/relative density:** The Bayer/Sumitomo relative density study did not use purified active substance as the test substance, however Tagros have an acceptable study available. The Tagros relative density = 1.2250 (99.3%, 25:75 cis:trans).
Conclusion	The Bayer/Sumitomo study used the wrong test substance for the test. The Tagros relative density = 1.2250 (99.3%, 25:75 cis:trans).
Reliability	1
Acceptability	Acceptable
Remarks	No further data required.
	COMMENTS FROM OTHER MEMBER STATE
Date	
Evaluation of applicant's justification	
Conclusion	
Remarks	

Evaluation by Competent Authorities	
Section A3.2	Vapour pressure
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	15/06/2011
Evaluation of applicant's justification	<u>X – Vapour pressure:</u> The Bayer/Sumitomo vapour pressure study used the individual isomers instead of the 25:75 test material. However the Bayer/Sumitomo vapour pressure results can be used to calculate the Henry's Law Constant for the 25:75 test material. It should also be noted that Tagros have conducted a vapour pressure study using the correct test material (vapour pressure = 2.155×10^{-6} Pa at 20°C, using purified active substance with a min. purity of 99.3%, cis:trans 25:75).
Conclusion	The Bayer/Sumitomo study used the wrong test substance for their vapour pressure study. The Tagros vapour pressure result = 2.155×10^{-6} Pa at 20°C (99.3%, 25:75 cis:trans).
Reliability	1
Acceptability	Acceptable
Remarks	No further data required.
	COMMENTS FROM OTHER MEMBER STATE
Date	
Evaluation of applicant's justification	
Conclusion	
Remarks	

	Evaluation by Competent Authorities
3.2.1	**Henry,s Law Constant**
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	12/05/08
Evaluation of applicant's justification	<u>X – Henry's Law Constant:</u> Based on the v.p. values given for pure cis- and pure trans- isomers at 25°C, see 3.2 above, the v.p. value of a 25:75 isomeric mix was calculated to be $0.57x10^{-6}$ Pa at 20°C (by extrapolation) Water solubility value is <4.95µg/l at 20°C. Using these values: K = $>4.5x10^{-2}$ Pa m^3 mol^{-1}
Conclusion	K = $>4.5x10^{-2}$ Pa m^3 mol^{-1} based on experimental data provided for vapour pressure and water solubility. Based on this value and the value for vapour pressure the molecule is considered to be volatile
Reliability	1
Acceptability	Acceptable
Remarks	No further data required
	COMMENTS FROM OTHER MEMBER STATE
Date	
Evaluation of applicant's justification	
Conclusion	
Remarks	

	Evaluation by Competent Authorities
3.3	**Appearance**
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	15/06/2011
Evaluation of applicant's justification	**X – Appearance:** The Bayer/Sumitomo study did not use the correct test material. There is an acceptable Tagros study available that uses the correct test material.
Conclusion	The Bayer/Sumitomo study did not use the correct test material. The Tagros study is available and is considered acceptable.
Reliability	1
Acceptability	Acceptable
Remarks	No further data required
	COMMENTS FROM OTHER MEMBER STATE
Date	
Evaluation of applicant's justification	
Conclusion	
Remarks	

	Evaluation by Competent Authorities
3.4	**Absorption spectra**
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	12/05/08
Evaluation of applicant's justification	**X - Absorption spectra:** UV Data acceptable. No absorbance >290nm.
Conclusion	UV/VIS study acceptable
Reliability	1
Acceptability	Acceptable
Remarks	No further data required
	COMMENTS FROM OTHER MEMBER STATE
Date	
Evaluation of applicant's justification	
Conclusion	
Remarks	

	Evaluation by Competent Authorities
3.6	**Dissociation constant**
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	10/10/05
Evaluation of applicant's justification	**X - Dissociation constant:** Test substance was permethrin manufactured by M/s Mitsu Industries Ltd. The purity is 94%, cis:trans isomer ratio is not given. The procedure was similar to OECD 112. No GLP compliance statement, no temperature given.
Conclusion	Because the molecule is not expected to dissociate no further data is required.
Reliability	1
Acceptability	Acceptable
Remarks	
	COMMENTS FROM OTHER MEMBER STATE
Date	
Evaluation of applicant's justification	
Conclusion	
Remarks	

	Evaluation by Competent Authorities
Section 3.9 (IIA 3.6)	**Partition coefficient n-octanol/water**
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	11/10/05
Evaluation of applicant's justification	<u>X - Partition coefficient n-octanol/water:</u> The Bayer/Sumitomo study should have been conducted using purified active substance, however there is an acceptable Tagros study available. The mean partition coefficient (log Pow) of Pure Tagros material at 25± 1 °C in water = 4.67 +/- 0.01.
Conclusion	The Bayer/Sumitomo study did not use the correct test material. The mean partition coefficient (log Pow) of Pure Tagros material at 25± 1 °C in water = 4.67 +/- 0.01.
Reliability	1
Acceptability	Acceptable
Remarks	No further data required
	COMMENTS FROM OTHER MEMBER STATE
Date	
Evaluation of applicant's justification	
Conclusion	
Remarks	

Section A3.13	SURFACE TENSION	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] Limited exposure [ ]	Technically not feasible [ ] Scientifically unjustified [X] Other justification [ ]	
Detailed justification:	OECD Guideline 115 for determining the Surface Tension of Aqueous Solutions states "Substances with a water solubility lower than 1 mg/l need not be tested". The water solubility of permethrin is reported as being between $<4.95 \times 10^{-3}$ mg l^{-1} and therefore fulfils the criteria for exclusion	
Undertaking of intended data submission [ ]	Not applicable	

Evaluation by Competent Authorities		
Section	**A3.13**	**SURFACE TENSION**
		EVALUATION BY RAPPORTEUR MEMBER STATE
Date		11/10/05
Evaluation of applicant's justification		Accept justification that substances with a water solubility <1mg/l need not be tested
Conclusion		
Remarks		No data required
		COMMENTS FROM OTHER MEMBER STATE
Date		
Evaluation of applicant's justification		
Conclusion		
Remarks		

Section A3.14	VISCOSITY	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure** [X]	**Technically not feasible** [ ] **Scientifically unjustified** [..] **Other justification** [...]	
Detailed justification:	The requirement for kinematic viscosity is to enable classification for aspiration hazard (Technical Notes for Guidance on the generation and submission of Chemistry data in support of the approval of non-agricultural pesticides). Technical grade permethrin is a dense liquid (1.207) with a melting point between 46-63°C, and is, by observation, highly viscous. The very low vapour pressure (between 1 and 3 $\times 10^{-6}$Pa), Henrys constant (2.88×10^{-7} atm-m^3/mole) and saturated vapour concentration (2.6×10^{-9} ppm) are all indicative that permethrin would not be classified as an aspiration hazard. Therefore, a justification for non-submission of data on the basis of limited exposure is proposed.	
Undertaking of intended data submission [ ]		

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	13/05/08
Evaluation of applicant's justification	
Conclusion	No requirement for Viscosity
Remarks	No further data required
	COMMENTS FROM OTHER MEMBER STATE
Date	
Evaluation of applicant's justification	
Conclusion	
Remarks	

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	16/06/2011
Evaluation of applicant's justification	<u>X - Explosive properties:</u> The applicants (Tagros and Bayer) are data sharing in relation to their phys.chem. studies. Tagros have an experimental study demonstrating that permethrin is not explosive. No further data is required. The experimental result is also supported by a theoretical assessment of the permethrin molecular structure.
Conclusion	Permethrin will not classify as being explosive.
Reliability	1
Acceptability	Acceptable
Remarks	No further data required.
	COMMENTS FROM OTHER MEMBER STATE
Date	
Evaluation of applicant's justification	
Conclusion	
Remarks	

Appendix I to Doc III-A1-A3

Bayer Environmental Science is an affiliated company of Bayer CropScience, therefore the studies submitted by Bayer Environmental Science are owned by Bayer CropScience AG.

Reference List Doc. III-A1-A3. sorted by reference no.

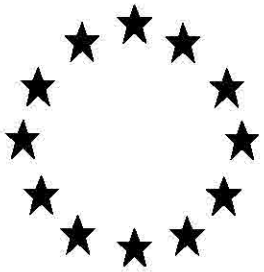
Section No/ Reference No	**Author (s)**	**Year**	**Title. Source, Report No. GLP /(Un) Published**	**Data Protection Claimed (Yes/No)**	**Owner**
2	Gangolli, S. (Ed)	1999	The Dictionary of Substances and their Effects, Volume 6. (2nd Edition). Publ. The Royal Society of Chemistry.	No	N/A
2	Meister et al (1983), Worthing & Walker (1987), FAO/WHO (1980), Wells et al (1986)	1990	Environmental Health Criteria 94: Permethrin. IPCS. World Health Organisation. Not GLP; Published	No	N/A
2,4	Heubach, G.	1982	Plant Protection/Designs of a Substance. Hoechst. Report No. HEU-366; Not GLP; Unpublished	Yes	Sumitomo Chemical
2,5	Heubach, G.	1982	Plant Protection/Designs of a Substance. Hoechst. Report No. HEU-366; Not GLP; Unpublished	Yes	Sumitomo Chemical
3,1,1	Alvarez, M	1989	Permethrin: Physical Properties; FMC Corportation Report No. P-2242; GLP; Unpublished	Yes	Sumitomo Chemical
3,1,2	Meister et al (1983), Worthing & Walker (1987), FAO/WHO (1980), Wells et al (1986)	1990	Environmental Health Criteria 94: Permethrin. IPCS. World Health Organisation. Not GLP; Published	No	N/A
3,1,3	Tamilselvan, C.	1997a	Density of permethrin Technical. Jai Research Foundation. Report No. DEN/PMT/28; GLP; Published	Yes	Bayer CropScience AG
3,2	Alvarez	1989	Permethrin: Physical Properties; FMC Corportation Report No. P-2242; GLP; Unpublished	Yes	Sumitomo Chemical
3.2.1	Bascou,JP	2007	Permethrin 25/75 Henry's law calculation, September, 10th 2007, non GLP; unpublished.	Yes	Bayer CropScience AG
3.3	Alvarez	1989	Permethrin: Physical Properties; FMC Corportation Report No. P-2242; GLP; Unpublished	Yes	Sumitomo Chemical

Section No/ Reference No	**Author (s)**	**Year**	**Title. Source, Report No. GLP /(Un) Published**	**Data Protection Claimed (Yes/No)**	**Owner**
3,4	White, D.F et al	2004	Permethrin: Determination of general Physico-Chemical properties; Safepharm Laboratories Report 1430/016; GLP; Not Published	Yes	Sumitomo Chemical
3,4	Walker, JA and O'Connor BJ	2007	*cis* –permethrin and trans-permethrin : infrared spectra, SPL project number 2491/0001, GLP, Not published	Yes	Bayer CropScience AG
3,4	Guebert C.,	2007	Spectral Data (1H-NMR, 13C-NMR, MS) of the isomers *cis*-permethrin (BCS-AA10041) and trans-permethrin (BCS-AA10042)of permethrin (AE F032639), study identification AF07/101, nonGLP, not published	Yes	Bayer CropScience AG
3,5	White, D.F et al	2004	Permethrin: Determination of general Physico-Chemical properties; Safepharm Laboratories Report 1430/016; GLP; Not Published	Yes	Sumitomo Chemical
3,6	Tamilselvan, C.	1997b	Dissociation constants of permethrin Technical in water. Jai Research Foundation. Report No. 260/JRF/PC/97; GLP; Unpublished	Yes	Bayer CropScience AG
3,7	Forster, B	2008	Biocidal testing for solvent solubility; CEMAS report n°CEMS-3768, GLP, Not published	Yes	Bayer CropScience AG
3.8	Lines, C	1986	Results of a Three-Year Storage Test on permethrin. The Wellcome Foundation, Ltd. Report No. DASD 86-6 (Unpublished)	Yes	Sumitomo Chemical
3,9	Wollenton C,		Physico-chemical data : permethrin water solubility and octanol-water partition coefficient, Zeneca Agrochemical, Report number CW092287. GLP; Not Published	Yes	Bayer CropScience AG
3,9	Robson C.G and Pearson F.J		1995, addendum to MRID 42377601, Permethrin : Physico-chemical study on technical grade active ingredient, Response to EPA; Project id RJ1141B, not GLP; Not Published	Yes	Bayer CropScience AG
3,10	Lines, C.B. & Balderson, K. E.	1986	Results of a Three-Year Storage Test on permethrin. The Wellcome Foundation, Ltd. Report No. DASD 86-6	Yes	Sumitomo Chemical
3,11	Tremain S P	2004	Permethrin: Determination of hazardous Physico-Chemical properties; Safepharm Laboratories Report 1430/017; GLP; Not Published	Yes	Sumitomo Chemical

Section No/ Reference No	**Author (s)**	**Year**	**Title. Source, Report No. GLP /(Un) Published**	**Data Protection Claimed (Yes/No)**	**Owner**
3,12	Tremain S P	2004	Permethrin: Determination of hazardous Physico-Chemical properties; Safepharm Laboratories Report 1430/017; GLP; Not Published	Yes	Sumitomo Chemical
3,15	Tremain S P	2004	Permethrin: Determination of hazardous Physico-Chemical properties; Safepharm Laboratories Report 1430/017; GLP; Not Published	Yes	Sumitomo Chemical
3,15	Alvarez, M	1989	Permethrin: Physical Properties; FMC Corportation Report No. P-2242; GLP; Unpublished	Yes	Sumitomo Chemical
3,16	Tremain S P	2004	Permethrin: Determination of hazardous Physico-Chemical properties; Safepharm Laboratories Report 1430/017; GLP; Not Published	Yes	Sumitomo Chemical
3,17	Tremain S P	2004	Permethrin: Determination of hazardous Physico-Chemical properties; Safepharm Laboratories Report 1430/017; GLP; Not Published	Yes	Sumitomo Chemical

Competent Authority Report

Programme for Inclusion of Active Substances in Annex I to Council Directive 98/8/EC



Permethrin (PT 8)

CAS-No. 52645-53-1

DOCUMENT IIIA (A4)

Bayer Environmental Science

Sumitomo Chemical (UK) Plc.

Rapporteur: Ireland

November 2013

Permethrin PT8

Document IIIA (A4)

CONTENTS

Section A4.1(1) Annex Point IIA4.1/4.2 & IIIA-IV.1

Analytical Methods for Detection and Identification
Methods for quantifying permethrin active Ingredient and impurities)

Key Study

1. REFERENCE

Official use only

1.1	**Reference**	Ann, W (2006). CIPAC Method 331 TC/m/-, Published
1.2	**Data protection**	
1.2.1	**Data owner**	Public data
1.2.2	**Companies with letters of access**	
1.2.3	**Criteria for data protection**	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I

2. GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	No (not relevant)
2.2	**GLP**	No (not relevant)
2.3	**Deviation**	No

3 MATERIALS AND METHODS

3.1	**Preliminary treatment**	
3.1.1	**Enrichment**	Homogenise the sample. When the sample is waxy solid or partly waxy solid homogenise it by warming it to melt and by stirring. Prepare sample solutions in duplicate for each sample. Weigh (to the nearest 0.1 mg) 90 to 110 mg (w mg) of permethrin into a vial or stoppered flask (100 ml). Add by pipette internal standard solution (5 ml) and dissolve completely. Add by measuring cylinder acetone (45 ml) and mix well (Solutions SA and SB).
3.1.2	**Cleanup**	None.
3.2	**Detection**	
3.2.1	**Separation method**	Gas chromatograph equipped with a split/splitless injection Column fused silica, 30 m x 0.25 (i.d.) mm, film thickness: 0.25 µm, coated with crosslinked dimethyl; polysiloxane (DB-1 or equivalent) Injection system : Injector split injection ; Split flow approximately 100 ml/min; Injection volume 1 µl Detector flame ionisation Temperatures Column oven 240°C Injection port 265°C Detector 265°C Carrier gas helium, 30 cm/sec Retention times triphenyl phosphate: about 6.5 min permethrin: *cis*-permethrin; about 12.4 min *trans*-permethrin; about 12.9 min
3.2.2	**Detector**	A flame ionisation detector.

Section A4.1(1) Annex Point IIA4.1/4.2 & IIIA-IV.1	Analytical Methods for Detection and Identification Methods for quantifying permethrin active Ingredient and impurities)	
	Key Study	
3.2.3 Standard(s)	internal standard : triphenyl phosphate	
3.2.4 Interfering substance(s)		
3.3 Linearity		
3.3.1 Calibration range	Analytical methods described in CIPAC handbooks are regarded as validated and do not require revalidation.	
3.3.2 Number of measurements	Analytical methods described in CIPAC handbooks are regarded as validated and do not require revalidation.	
3.3.3 Linearity	Analytical methods described in CIPAC handbooks are regarded as validated and do not require revalidation.	
3.4 Specifity: interfering substances	Analytical methods described in CIPAC handbooks are regarded as validated and do not require revalidation.	X
3.5 Recovery rates at different levels	Analytical methods described in CIPAC handbooks are regarded as validated and do not require revalidation.	
3.5.1 Relative standard deviation	Analytical methods described in CIPAC handbooks are regarded as validated and do not require revalidation.	
3.6 Limit of determination	Limit of determination or detection of the active substance in the active substance technical material is not meaningful.	
3.7 Precision		
3.7.1 Repeatability	Repeatability r = 9 g/kg at 953 g/kg active ingredient content = 9 g/kg at 951 g/kg active ingredient content Reproducibility R = 23 g/kg at 953 g/kg active ingredient content = 18 g/kg at 951 g/kg active ingredient content	
3.7.2 Independent laboratory validation	Not required	
	4 APPLICANT'S SUMMARY AND CONCLUSION	
4.3 Materials and methods	The content of permethrin in the test samples are determined by capillary GC using flame ionisation detection and triphenyl phosphate as internal standard, and the *trans*-isomer ratio is calculated from the chromatogram obtained. The content of permethrin is the total content of *cis*- and *trans*-isomers.	
4.4 Conclusion	Determination of *cis*- and *trans* permethrin is performed according to the CIPAC method permethrin 331	
4.4.1 Reliability	1	
4.4.2 Deficiencies	No	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	21/11/13
Materials and methods	CIPAC Method Specificity was addressed by retention time matching of reference standards and technical material. The was no interference at the retention time of interest. Identity was confirmed by NMR and MS.
Conclusion	
Reliability	1
Acceptability	Acceptable
Remarks	No further data required in relation to the CIPAC method of analysis. It should be noted that the applicant also provided a validated chiral method of analysis for the determination of enantiomers in technical permethrin. The validation data for the chiral method is provided in the Confidential Section of the CAR.
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion. Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A4.1(3)	**Analytical Methods for Detection and Identification**
Annex Point IIA4.1/4.2 & IIIA-IV.1	**Methods for quantifying permethrin active Ingredient and impurities**

Key Study

		Official use only
	1 REFERENCE	
1.1 Reference	Wink, O.; Felde, T. 2008, BES number M-300179-01-1. Non GLP. Unpublished Same method used in the 5 batch analysis performed by Chhatre, A.S in 2000 (see 4.1 (1) Wink, O.; Felde, T.2008, BES number M-300189-01-1. Non GLP. Unpublished	
1.2 Data protection	Yes	
1.2.1 Data owner	Bayer CropScience AG	
1.2.2 Companies with letters of access	None	
1.2.3 Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I	
	2 GUIDELINES AND QUALITY ASSURANCE	
2.1 Guideline study	Directive 91/414/EEC, Annex II and III; Directive 96/46/EC Analytical Methods and US – EPA Product Properties Guideline OPPTS 830.1800	
2.2 GLP	No	

Information presented in this summary is considered as confidential therefore it is fully presented in the confidential document.

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	21/12/12
Materials and methods	See Confidential Section A.4
Conclusion	
Reliability	1
Acceptability	Acceptable.
Remarks	No further data required.
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion. Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A4.1(4)	**Analytical Methods for Detection and Identification**
Annex Point IIA4.1/4.2 & IIIA-IV.1	**Method for quantifying two by-products in permethrin samples,**

Key Study

			Official use only
		1 REFERENCE	
1.1	**Reference**	Junker, H, Gübert C, 2008, Analytical method N°AM020108FP1, non GLP, unpublished. Dr. M. Cichy, C. Guebert, 2008; Validation of GC-method AM020108FP1 non GLP, unpublished	
1.2	**Data protection**	yes	
1.2.1	**Data owner**	Bayer CropScience AG	
1.2.2	**Companies with letters of access**		
1.2.3	**Criteria for data protection**	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	EU 91/414/EEC Annex II, 4.1 OPPTS 830.1800	
2.2	**GLP**	no	
2.3	**Deviations**	None	

Information presented in this summary is considered as confidential therefore it is fully presented in the confidential document.

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	15/07/09
Materials and methods	Accept data supplied by notifier. See Confidential Section A.4
Conclusion	
Reliability	1
Acceptability	Acceptable
Remarks	No further data required
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion. Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section 4.1(5) Annex Point IIA4.1/4.2	Analytical Methods for Detection and Identification Methods for quantifying permethrin active Ingredient and impurities	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] Limited exposure [ ]	Technically not feasible [X] Scientifically unjustified [ ] Other justification [ ]	

Information presented in this summary is considered as confidential therefore it is fully presented in the confidential document.

Section A4.1(6)	**Analytical Methods for Detection and Identification**
Annex Point IIA4.1/4.2 & IIIA-IV.1	**Methods for quantifying permethrin active Ingredient and impurities**

Additional information

			Official use only
		1 REFERENCE	
1.1	**Reference**	Chhatre, A.S; 2000; Quantification of Active Ingredient and impurities of permethrin Technical (5-batch analysis) by GC-MS. Bilag Industries internal report no. C008551; Not GLP; Unpublished.	X
1.2	**Data protection**	Yes	
1.2.1	**Data owner**	Bayer CropScience AG	
1.2.2	**Companies with letters of access**	None	
1.2.3	**Criteria for data protection**	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	The methodology described was reported in the above reference, which describes a method suitable for the analysis of permethrin technical.	
2.2	**GLP**	No.	
		3 MATERIALS AND METHODS	
3.1	**Preliminary treatment**	An internal standard of 4 g/l n-octacosane was prepared in dichloromethane. Approximately 100 mg of permethrin technical was accurately weighed into a 100 ml volumetric flask, and 25 ml of internal standard added. The flask was made up to volume with DCM. A standard solution of Analytical Reference Standard of permethrin is prepared in a similar fashion.	
3.1.1	**Enrichment and clean-up**	The method described is for the quantification of Active Ingredient and impurities of permethrin Technical, as such no enrichment or clean-up was performed.	
3.2	**Detection**		
3.2.1	**Separation method**	Capillary Gas Chromatography Column: DB-1 Carrier gas: Helium @ 1.1 ml/min Temps: Column: Injector: MS interface: Sample volume 1 µl	
3.2.2	**Detector**	Mass Spectrometer	
3.2.3	**Standard(s)**	Standards of 1.0, 10, 200, 600 and 1000 mg/l were prepared in DCM for determination of the linear range.	
3.2.4	**Interfering substance(s)**	None.	

Section A4.1(6)	**Analytical Methods for Detection and Identification**
Annex Point IIA4.1/4.2 & IIIA-IV.1	**Methods for quantifying permethrin active Ingredient and impurities**

Additional information

3.2.5	**Quantification**	External and internal standards
3.3	**Linearity**	
3.3.1	**Calibration range**	Standards of 1.0, 10, 200, 600 and 1000 mg/l were prepared in DCM for determination of the linear range.
3.3.2	**Number of measurements**	Single injections
3.3.3	**Linearity**	R^2 values for *cis*- and *trans*- isomers individually and summed gave a value of 1, indicating the calibration was linear over the given range.
3.4	**Specifity: interfering substances**	None. The method achieved separation between *cis*- and *trans*-permethrin, and the following impurities; • **See Confidential Information for details**
3.5	**Recovery rates at different levels**	Not performed
3.5.1	**Relative standard deviation**	Not performed
3.6	**Limit of determination**	Not performed
3.7	**Precision**	(based on analysis of 5 sample preparations, single replication) 0.0088% (as a % of RSD)
3.7.1	**Repeatability**	Not performed
3.7.2	**Independent laboratory validation**	Not performed

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1	**Materials and methods**	The reference describes in detail a capillary GC method suitable for the separation of *cis*- and *trans*-permethrin from impurities expected in technical grade material, including the use of internal and external standards over a 10^3 concentration range. Specific data on detection are not supplied, although the reference states detection is via Mass Spectrometry.
4.2	**Conclusion**	Although this study was not audited to the standards of GLP, it was reported according to the principles of GLP, including the inclusion of individual chromatograms (with associated peak area data) to allow verification of derived results.
4.2.1	**Reliability**	2
4.2.2	**Deficiencies**	No GLP accreditation, does not specify MS conditions.

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	21/12/12
Materials and methods	See the Confidential Section of the CAR for fully validated methods of analysis.
Conclusion	The analytical methods and their validation presented in the Confidential Section of the CAR are considered acceptable.
Reliability	1
Acceptability	Acceptable.
Remarks	*No further data required.*
	COMMENTS FROM ...
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section A4.1(7)	**Analytical Methods for Detection and Identification**
Annex Point IIA4.1/4.2 & IIIA-IV.1	**Methods for quantifying total permethrin (*cis*- and *trans*-isomers) in permethrin formulations**

Key Study

		Official use only
	1. REFERENCE	
1.1 Reference	No Author; 1980; Determination of permethrin in Liquid and Powder Formulations. Report No. E1/390/80; Not GLP; Unpublished	X
1.2 Data protection	No	
1.2.1 **Data owner**	Sumitomo Chemicals (UK) PLC	
Companies with letters of access	Bayer Environmental Science	
1.2.3 Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I	
	2 GUIDELINES AND QUALITY ASSURANCE	
2.1		
2.2		
2.3		
	2. MATERIALS AND METHODS	
3.1 Preliminary treatment		
3.1.1 Enrichment	None	
3.1.2 Cleanup	None	
3.2 Detection		
3.2.1 Separation method	Gas Liquid Chromatography Column: 1.5m × 4mmid glass Packing: 2% OV210 on 80 to 100 mesh GasChromQ Column. Temp: 220°C Injector Temp: No data Detector Temp: No data Carrier gas: Nitrogen at 60 ml min^{-1} Sample size: 5 µl	
3.2.2 Detector	Flame Ionisation Detector	
3.2.3 Standard(s)	Internal Standard: Di-n-hexyl phthalate External Standards: Technical permethrin of known purity Prepare an approximately 10 g l^{-1} solution of the internal standard in ethyl acetate(1). Dilute solution ×10 in ethyl acetate (2). **Standard solution**: Accurately weigh approximately 0.2 g of technical permethrin into a 100 ml volumetric flask, add 10.0 ml of internal standard and dilute to volume with ethyl acetate.	

Section A4.1(7)	**Analytical Methods for Detection and Identification**
Annex Point IIA4.1/4.2 & IIIA-IV.1	**Methods for quantifying total permethrin (*cis*- and *trans*-isomers) in permethrin formulations**

Key Study

		Test solution (liquid formulations): Accurately weigh sufficient sample to contain approximately 0.2 g of technical permethrin into a 100 ml volumetric flask, add 10.0 ml of internal standard (1) and dilute to volume with ethyl acetate. **Test solution (powder formulations)**: Accurately weigh sufficient sample to contain approximately 0.2 g of technical permethrin into a 250 ml volumetric flask, add 100 ml of internal standard (2) and dilute to volume with ethyl acetate. Stopper and shake vigorously for 1 hour. Allow to settle.
3.2.4	**Interfering substance(s)**	No data
3.2.5	**Quantification**	For *cis*- and *trans*-isomers and impurities in permethrin samples: detection via FID. Permethrin (*cis* and *trans*) quantified as a ratio of peak response in the standards against the samples, as normalised against internal standard response.
3.3	**Linearity**	
3.3.1	**Calibration range**	No data
3.3.2	**Number of measurements**	No data
3.3.3	**Linearity**	No data
3.4	**Specifity: interfering substances**	No data
3.5	**Recovery rates at different levels**	No data
3.5.1	**Relative standard deviation**	No data
3.6	**Limit of determination**	No data
3.7	**Precision**	
3.7.1	**Repeatability**	No data
3.7.2	**Independent laboratory validation**	No

Section A4.1(7)	**Analytical Methods for Detection and Identification**
Annex Point IIA4.1/4.2 & IIIA-IV.1	**Methods for quantifying total permethrin (*cis*- and *trans*-isomers) in permethrin formulations**

Key Study

4 APPLICANT'S SUMMARY AND CONCLUSION

4.2 Materials and methods	The method employs a packed bed gas-liquid chromatography technique to separate the individual *cis* and *trans* components present in a formulation, and quantifies them against external standards
4.3 Conclusion	The method described provides a robust chromatographic method for the determination of permethrin isomers formulated samples. The separation technology is based upon a packed bed gas liquid chromatography, and is therefore likely to be robust and reproducible. Measurement and quantification are based upon a universal detector (FID), which would detect any organic components in the solution (within the usual limitations of GC as defined by molecular size, solubility, and volatility). No data are included in the report to describe reproducibility, but the inclusion of an internal standard is generally recognised as being a suitable method to improve reproducibility. No limits of quantification were defined, because the purpose of the analysis described was not to detect low concentration in the matrix, but to quantify major components in a formulated sample.
4.3.1 Reliability	2
4.3.2 Deficiencies	No

	Determination of permethrin in Liquid and Powder Formulations
	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	21/11/13
Materials and methods	Method is not acceptable. No linearity, accuracy, repeatability or specificity data provided.
Conclusion	No relevant validation data has been supplied
Reliability	4
Acceptability	Not acceptable
Remarks	When products are evaluated at MS level then acceptable validated methods of analysis for a.s. in the biocidal products must be supplied. It was decided at the EU Technical Meeting that chiral methods of analysis for permethrin should be provided for product formulations 6 months before product authorisation.
	COMMENTS FROM ...
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section A4.2(1) **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**Analytical methods: soil, air, water, animal and human body fluids and tissues** **Methods for quantifying permethrin residues in soil**

Key Study

Official use only

		1 REFERENCE
1.1	**Reference**	Brumhard, B.; 2008; Analytical method 01081 for the determination of residues of permethrin (AE F032639) in soil by HPLC-MS/MS; Report N°MR-07/355 BES N°M-296886-01-1; Unpublished
1.2	**Data protection**	Yes
1.2.1	**Data owner**	Bayer CropScience AG
1.2.2	**Companies with letters of access**	
1.2.3	**Criteria for data protection**	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I
		2 GUIDELINES AND QUALITY ASSURANCE
2.1	**Guideline study**	EC Guidance Document on Residue Analytical Methods, SANCO/825/00 rev.7 of March 17, 2004 BBA Guideline: Residue Analytical Methods for Post-Registration Control Purposes of July 21, 1998 Commission Directive 96/46/EC amending Council Directive 91/414/EEC of 16 July 1996
2.2	**GLP**	Yes
2.3	**Deviations**	None
		3 MATERIALS AND METHODS
3.1	**Preliminary treatment**	
3.1.1	**Enrichment**	Soil samples (20 g of the soil) were extracted with acetonitrile/water (4:1, v/v) and 10 mmol ammonium formate using a microwave extractor.
3.1.2	**Cleanup**	The extract was cleaned up by centrifugation before injection.
3.2	**Detection**	
3.2.1	**Separation method**	Reversed phase chromatography coupled with tandem mass spectrometry (MS/MS) with electrospray ionisation. Instrument: Agilent 1100 or equivalent Injector: HTC PAL, CTC Analytics or equivalent Column: Synergi 2µ Polar RP, length 50 x 2 mm (or equivalent) Injection Volume: 25 µL or as needed for the sensitivity Oven temperature: 60 °C Mobile Phase: Bin Pump A: methanol/water/formic acid,

Section A4.2(1) **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**Analytical methods: soil, air, water, animal and human body fluids and tissues** **Methods for quantifying permethrin residues in soil**

Key Study

	(100:900:0.12, v/v/v)+ 10 mM Ammonium formate Bin Pump B: Methanol Iso Pump C: methanol/water/formic acid, (500:500:0.12, v/v/v)+ 10 mM Ammonium formate The mobile phase composition is given in Table A4.2(1)-1 Flow (into MS): 0.35 mL/min Retention times: Permethrin approx. 2.9 min
3.2.2 Detector	The detection by MS/MS was performed on a triple-quadrupole tandem mass spectrometer, equipped with a Turbo IonSpray (ESI) interface operated in positive ion mode and multiple reaction monitoring (MRM). Low unit mass resolution was established and maintained in the mass resolving quadrupoles by maintaining a full width at half-maximum (FWHM) of about 1.4 amu. Optimal collisionally-activated dissociation (CAD) conditions for fragmentation of the pseudomolecular ions of the analyte were applied with nitrogen as the collision gas. The parent ion for detection of permethrin (408 m/z) is related to the ammonium adduct $[M+NH4]^+$ of the compound. Detector: Triple Quadrupole Tandem Mass Spectrometer, IONICS EP 10+ with turbo-ionspray interface (performance-enhanced Sciex API-365), mass selective detector (MS/MS), or any equivalent HPLC-MS/MS System Interface: Turbo-IonSpray (ESI) Gas Temperature: 350 °C or as needed for the sensitivity Scan Type: MRM (Multiple Reaction Monitoring).
3.2.3 Standard(s)	Internal Standard: None External Standards: Technical permethrin of known purity
3.2.4 Interfering substance(s)	The high selectivity of the method resulted from the HPLC separation in combination with MS/MS detection. Two MRM transitions were monitored for permethrin (m/z 408 →183 for quantitation and m/z 408 → 355 for confirmation).No signals / peaks interfering with the detection of the analyte were observed in extracts of untreated blank control specimens.
3.2.5 Quantification	Quantitation of the analyte concentrations was accomplished by mean of the external standard method.
3.3 Linearity	
3.3.1 Calibration range	For both mass transitions of permethrin the correlation between the injected amount of substance and the detector response was linear for standards in matrix and in solvent within a range of 1 µg/L to 100 µg/L (corresponding to a concentration in soil of 2 to 200 µg/kg).
3.3.2 Number of measurements	Not reported
3.3.3 Linearity	The correlation coefficients of the 1/x weighted linear regression

Section A4.2(1) **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**Analytical methods: soil, air, water, animal and human body fluids and tissues** **Methods for quantifying permethrin residues in soil**

Key Study

		ranged from 0.9992 to 0.9999.
3.4	**Specifity: interfering substances**	Apparent residues in control samples were below 0.3 × LOQ. The recoveries were not corrected for interferences. Two MRM transitions were monitored for each matrix tested, m/z 408 → 183 for quantitation and m/z 408 → 355 for confirmation of permethrin. Therefore, this HPLC-MS/MS method is regarded as highly specific.
3.5	**Recovery rates at different levels**	Recovery rates were determined at fortification levels of 5 µg/kg (= LOQ level), and 50 µg/kg. Recovery experiments were conducted by separate fortification of untreated control samples with defined amounts of permethrin prior to analysis. For this purpose two soil types, one from Höfchen and one from Laacher Hof were fortified with a solution of permethrin. Results are presented in Table A4.2(1)-2 and Table A4.2(1)-3
3.5.1	**Relative standard deviation**	92% ± 7.6% at the LOQ level (for the quantifier mass transition) 97% ± 4.5% at 10 x LOQ (for the quantifier mass transition)
3.6	**Limit of determination**	The limit of quantitation (LOQ) for permethrin is 5.0 µg/kg in soil. The limit of determination (LOD) is 1.5 µg/kg.
3.7	**Precision**	
3.7.1	**Repeatability**	As a measure for the precision of the method, the intra-laboratory repeatability (n = 5) is given as relative standard deviation (% RSD) for all sample materials at fortification levels of 5 and 50 µg/kg.. The RSD of the repeatability tests at each recovery set ranged from 1.3 to 7.3% for the quantifier mass transition. (1.3 to 7.1% for the confirmatory method)
3.7.2	**Independent laboratory validation**	Not performed

Section A4.2(1) **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**Analytical methods: soil, air, water, animal and human body fluids and tissues** **Methods for quantifying permethrin residues in soil**

Key Study

1

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1 Materials and methods

The present method validation was performed for the determination of the active ingredient permethrin (AE F032639) in soil by HPLC-MS/MS using two MRM transitions.
Soil samples of 20 g are extracted in a microwave extractor with 40 mL of a mixture of acetonitrile/water (4/1, v/v) + 10 mmol ammonium formiate. Then a subsample is centrifuged to remove fine particles of the soil. Identification and quantitation of the test item is done by high performance liquid chromatography using MS/MS detection in the Multiple Reaction Monitoring mode.
The method was validated using a silt loam soil (Höfchen) and a sandy loam soil (Laacher Hof).
Specificity: Apparent residues in control samples were below 0.3 × LOQ. The recoveries were not corrected for interferences. Two MRM transitions were monitored for each matrix tested, m/z 408 → 183 for quantitation and m/z 408 → 355 for confirmation of permethrin. Therefore, this HPLC-MS/MS method is regarded as highly specific.
Linearity: The mass spectrometric detector showed linear correlation between concentration and peak area for solvent as well as matrix matched standards in the range of about 1 to 100 µg/L for permethrin (corresponding to about 2 to 200 µg/kg sample equivalents) with a correlation coefficient between 0.9992 and 0.9999 for permethrin.
LOQ and LOD: The limit of quantitation (LOQ) for permethrin is 5.0 µg/kg in soil. The limit of determination (LOD) is 1.5 µg/kg.
Blank Values: The blank values in all control samples were below 1.5 µg/kg (<1/3 x LOQ), demonstrating that no relevant background level of permethrin was present in the test systems.
Recovery Rates (Accuracy): Mean recoveries for each fortification level and the overall mean recovery were within the 70 - 110% range for all matrices
Repeatability (Precision): Relative standard deviations were below 20% for all sample materials.

4.2 Conclusion

The method meets all guideline criteria to determine residues of permethrin in soil at the LOQ of 5.0 µg/kg using two mass transitions.

4.2.1 Reliability

1

4.2.2 Deficiencies

none.

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	21/10/08
Materials and methods	The method using HPLC/MS/MS analysed residues of permethrin in silt loam (Höfchen) and sandy loam (Laacher Hof) soil types. The method was validated to a LOQ of 5.0µg/kg
Conclusion	Accept applicants version of method. The method of analysis is acceptable for monitoring permethrin residues in soil.
Reliability	1
Acceptability	Acceptable
Remarks	No further data required
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion. Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A4.2(1)-1 The mobile phase time table

Time [min]	A [%, v/v]	B [%, v/v]	Flow (Column) [mL/min]	Into MS	Into Waste
0.0	30	70	0.35	Iso pump	Bin pump
0.1	30	70	0.35		
2.0				Bin Pump	Iso Pump
5.0	0	100	0.35		
8.0	0	100	0.35		
8.1	30	70	0.35		
10.0				Iso pump	Bin pump
12.0	30	70	0.35		
12.0	Stop time				

Table A4.2(1)-2 Recoveries for permethrin (Quantifier Mass Transition m/z 183)

Soil	Fortification Level (FL) [µg/kg]	Recoveries (Single Values) [%]					Mean per FL [%]	RSD [%]	Mean overall [%]	RSD overall [%]
Höfchen	5	92	93	97	105	89	95	6.4	98	5.4
	50	103	100	100	101	102	101	1.3		
Laacher Hof	5	98	89	91	82	82	88	7.3	91	5.7
	50	92	94	92	95	94	93	1.6		
Overall	5								92	7.6
	50								97	4.5
	mean								**95**	**6.7**

Table A4.2(1)-3 Recoveries for permethrin (Confirmatory Mass Transition m/z 355)

Soil	Fortification Level (FL) [µg/kg]	Recoveries (Single Values) [%]					Mean per FL [%]	RSD [%]	Mean overall [%]	RSD overall [%]
Höfchen	5	93	93	98	108	91	96	7.1	98	5.2
	50	102	99	100	100	102	101	1.3		
Laacher Hof	5	98	90	92	83	83	89	7.0	91	5.1
	50	91	93	92	94	93	93	1.5		
Overall	5								93	7.8
	50								97	4.5
	mean								95	**6.5**

Section A4.2(24) **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**Analytical methods: soil, air, water, animal and human body fluids and tissues** **Methods for quantifying permethrin residues and metabolites in soil**

Additional information

			Official use only
		1 REFERENCE	
2.1	**Reference**	Nagel, W.D; 1993; Analytical method for the determination of permethrin, Dichlorovinyl Acid and m-Phenoxybenzoic acid Residue in/on Soil; FMC Agricultural Chemical Group; P-2703M; August 1993; Unpublished Validation data in : Hatfield, M.W, 1996b, interim final report "Aquatic dissipation of permethrin in California and North Carolina. American Agricultural Services Inc., Study No. AA940907." BES report C003413; GLP; Unpublished	
2.2	**Data protection**	Yes	
2.3	**Data owner**	Sumitomo Chemical (UK) Ltd	
2.3.1	**Companies with letters of access**	Bayer Environmental Science	
2.3.2	**Criteria for data protection**	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.4	**Guideline study**	Pesticide Assessment Guidelines Subdivision 0,171-4: Residue, Analytical Method	
2.5	**GLP**	No	
2.6	**Deviations**	No	
		3 MATERIALS AND METHODS	
3.1	**Preliminary treatment**		
3.1.1	**Enrichment**	Soil samples were extracted with 7:3 acetonitrile:water which was subsequently partitioned with aqueous alkaline hexane. The permethrin was associated with the hexane fraction, while the two metabolites were associated with the aqueous fraction.	
3.1.2	**Cleanup**	The hexane fraction was cleaned up using a silica solid phase extraction (SPE) cartridge. The aqueous fraction was acidified and partitioned against methylene chloride. After concentration, the methylene chloride fraction was derivatised using pentafluorobenzyl bromide, extracted into hexane, which was then cleaned up with silica solid phase extraction (SPE) cartridge.	
3.2	**Detection**		
3.2.1	**Separation method**	Permethrin; Samples were separated via wide-bore capillary GC (15 m x 0.53 mm cross-bonded trifluoropropylmethyl silicone	

Section A4.2(24) **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**Analytical methods: soil, air, water, animal and human body fluids and tissues** **Methods for quantifying permethrin residues and metabolites in soil**

Additional information

		capillary) using a temperature gradient from 210 to 260°C at 5°C per minute. The validation performed by Hartfield used a fused silica megabore capillary column (30mx0.53mm, 1.0 µm film thickness). Dichlorovinyl Acid and m-Phenoxybenzoic acid; Samples were separated via capillary GC (15 m x 0.25 mm 5% phenyl 95% methyl silicone capillary) using a temperature gradient from 170 to 270°C at 10°C per minute. The validation performed by Hartfield used fused silica capillary column (30mx0.25mm, 0.25 µm film thickness)
3.2.2	**Detector**	Permethrin; Electron Capture Detector (ECD) with argon/methane make-up gas Dichlorovinyl Acid and m-Phenoxybenzoic acid; Mass Selective Detector operated in single ion mode monitoring at 163 amu and 394 amu.
3.2.3	**Standard(s)**	Samples were quantified via external standardisation. No internal standards were employed.
3.2.4	**Interfering substance(s)**	No interfering substances identified
3.3	**Linearity**	
3.3.1	**Calibration range**	*cis* permethrin : 20-400 pg injected *trans* permethrin : 20-400 pg injected *cis* DCVA : 20-80 pg injected *trans* DCVA : 20-80 pg injected mPBAcid : 20-80 pg injected
3.3.2	**Number of measurements**	7 measurements for *cis* and *trans* permethrin. 6 measurements for *cis* and *trans* DCVA and mPBA.
3.3.3	**Linearity**	The responses for *cis* and *trans* permethrin, *cis* and *trans* DCVA and mPBA were shown to be linear with the following correlation coefficient r: *cis* permethrin : 0.999305 *trans* permethrin : 0.999381 *cis* DCVA : 0.997389 *trans* DCVA : 0.994708 mPBAcid : 0.986877 The calibration curves are given in Figures 1 to 6
3.4	**Specifity: interfering substances**	No interfering substances identified
3.5	**Recovery rates at different levels**	Recovery experiments were undertaken at ranges from 0.05 to 0.25 mg kg^{-1} permethrin and metabolites (n=37). The average ± SD recoveries were;

Section A4.2(24) **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**Analytical methods: soil, air, water, animal and human body fluids and tissues** **Methods for quantifying permethrin residues and metabolites in soil**

Additional information

85 ± 9% (*cis* permethrin)
96 ± 8% (*trans* permethrin)
90 ± 9% (*cis* DCVA)
87 ± 8% (*trans* DCVA)
94 ± 8% (mPBAcid)
Recovery experiments undertaken at ranges from 0.01 to 0.50 mg kg^{-1} permethrin and metabolites in the dissipation study

analyte	overall mean ans standard deviation	range of recoveries
cis-permethrin	94% ±16% (n=12)	69-110%
trans-permethrin	94% ±16% (n=12)	68-114%
cis-DCVA	100% ±19% (n=12)	69-138%
trans-DCVA	92% ±16% (n=12)	75-120%
PBA	98% ±19% (n=12)	76-133%

3.5.1 Relative standard deviation
Given above (Section 3.5)

3.6 Limit of determination
0.025 mg kg^{-1} from the validation of the method itself.
0.01 mg kg^{-1} from the validation of the dissipation study.

3.7 Precision
The precision of the method was acceptable, with %RSD less than 20% for *cis* and *trans* permethrin, *cis* and *trans* DCVA and mPBA in the different validations.

3.7.1 Repeatability
ILV was not undertaken in this study.

3.7.2 Independent laboratory validation
None performed

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1 Materials and methods
Soils are extracted with acetonitrile:water which is then partitioned with hexane to isolate the permethrin fraction. The metabolites in the aqueous phase are acidified and extracted with methylene chloride for derivatisation. The derivatised metabolites are extracted with hexane. Both hexane extracts are cleaned up with normal phase SPE, and analysed.
Parent material is analysed using megabore capillary GC with ECD detection.
Metabolites are analysed using capillary GC with MSD in SIM.

4.2 Conclusion
The results would indicate the separation method may be suitable for residue analysis, and the extraction efficiency indicates confidence in quantitative recovery.

4.2.1 Reliability
2

4.2.2 Deficiencies
The references describe in detail a suitable extraction method for permethrin and metabolites in soil, and recoveries indicate the methods are quantitative.

	Evaluation by Competent Authorities
	Methods for quantifying permethrin residues in soil
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	20/06/2011
Materials and methods	A method has been presented for residues of permethrin, dichlorovinyl acid and m-Phenoxybenzoic acid in soil. Permethrin is analysed using capillary GC with ECD detection. Acceptable linearity, repeatability and recovery data was presented. Chromatograms supplied demonstrated that no interfering peaks occur at the retention times of *cis*- and *trans*- permethrin. Residues of dichlorovinyl acid and m-Phenoxybenzoic acid were derivatized using pentafluorobenzyl bromide and analysed using GC with MSD detection operated in single ion mode monitoring at 163amu and 394amu. Acceptable linearity, repeatability and recovery data was presented. It is recommended that at least three ions with an m/z value greater than 100amu, and two ions with an m/z greater than 200amu are required for MSD detection. Data for one other ion would be required The recovery rates obtained refer to recovery over the range 0.025mg/kg to 0.5mg/kg, thus 0.025mg/kg is considered to be the LOQ for all three residues.
Conclusion	The method would be considered acceptable for the relevant permethrin metabolites in soil if a further ion with a m/z ratio > 100 was used for method validation. Analysis of residues of permethrin, dichlorovinyl acid and m-phenoxybenzoic acid in soil were achieved to an LOQ of 0.025mg/kg.
Reliability	3
Acceptability	Not acceptable.
Remarks	It should be noted that Bayer/Sumitomo already have an acceptable HPLC-MS/MS method of analysis for monitoring parent permethrin in soil. No further data required.
	COMMENTS FROM ...
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Figure 1: Extraction regime for soil samples

B Method Flow Scheme

FIGURE 1

METHOD FLOW SCHEME for cis- and trans-PERMETHRIN, cis- and trans-DCVA, and M-PBacid in SOIL

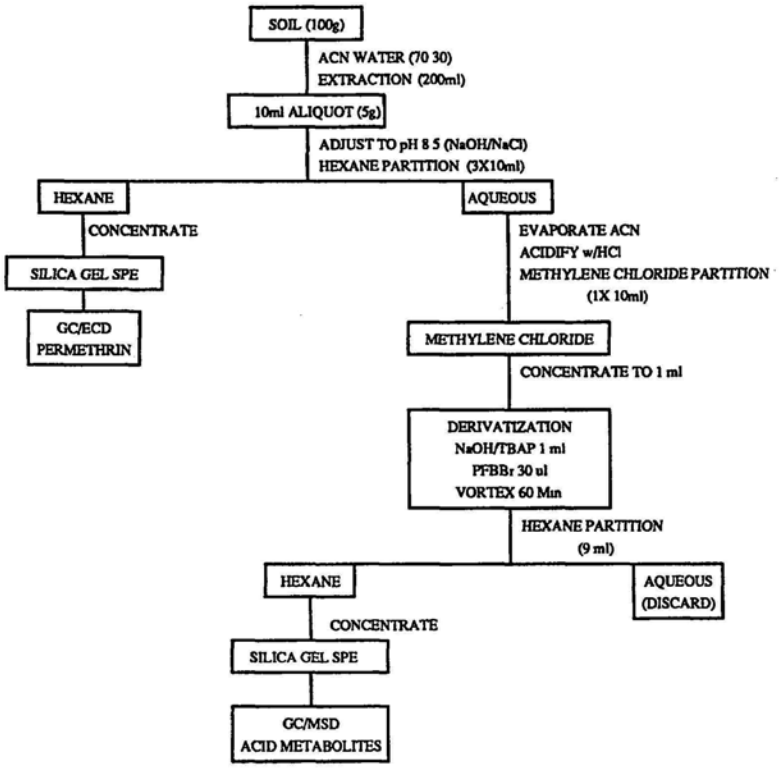


Fig 2: Typical calibration curve for *cis*-permethrin

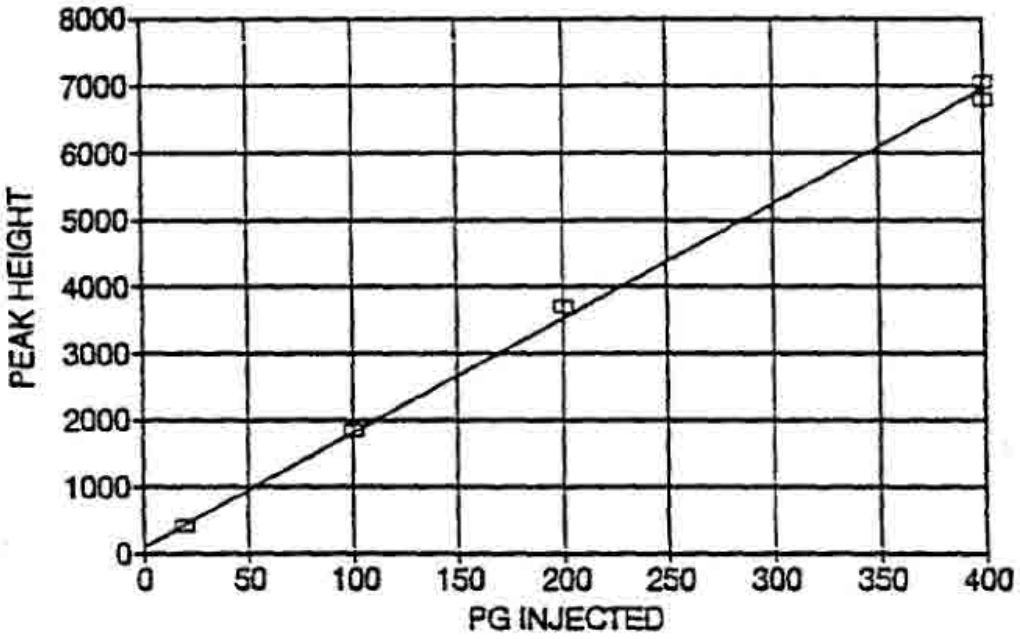


Fig 3: Typical calibration curve for *trans*-permethrin

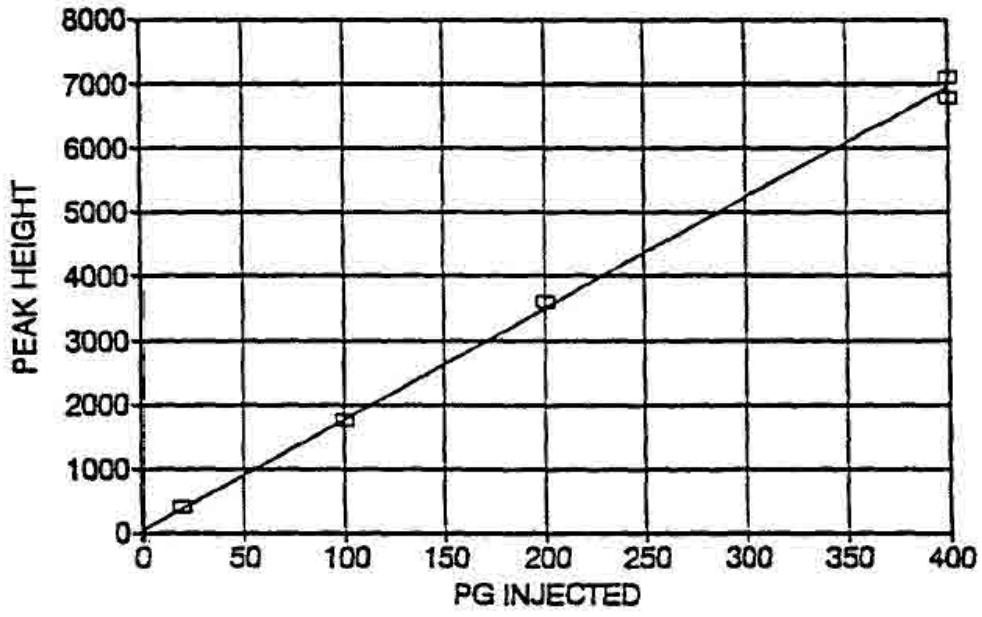


Fig 4: Typical calibration curve for *cis*-DCVA

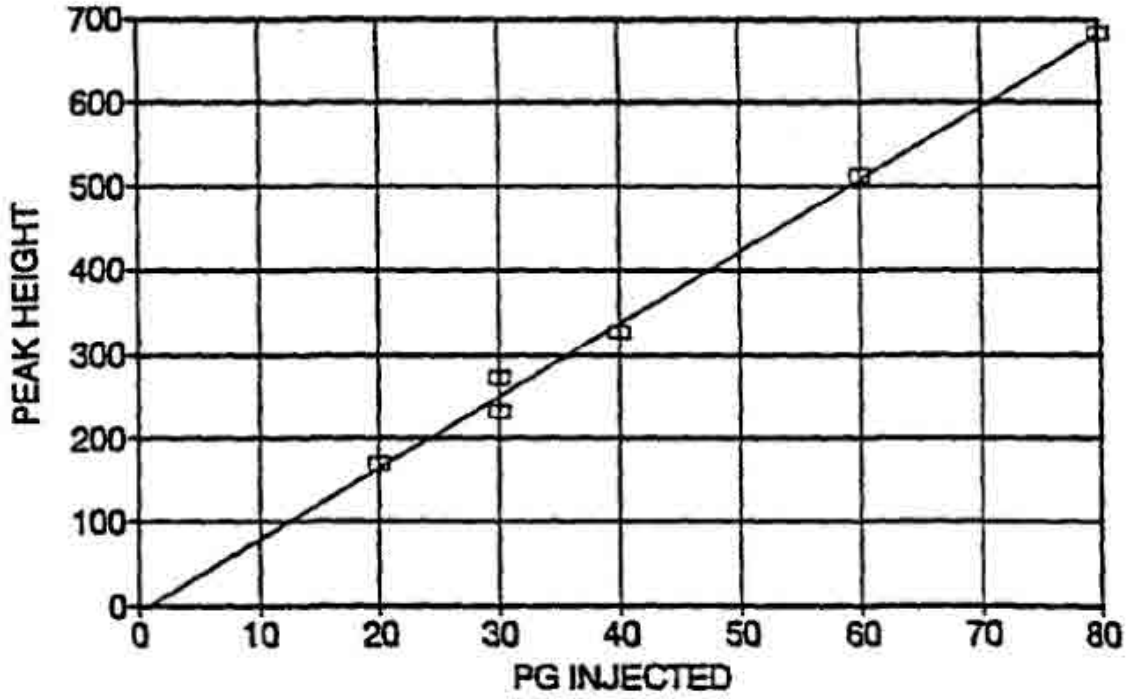


Fig 5: Typical calibration curve for *trans*-DCVA

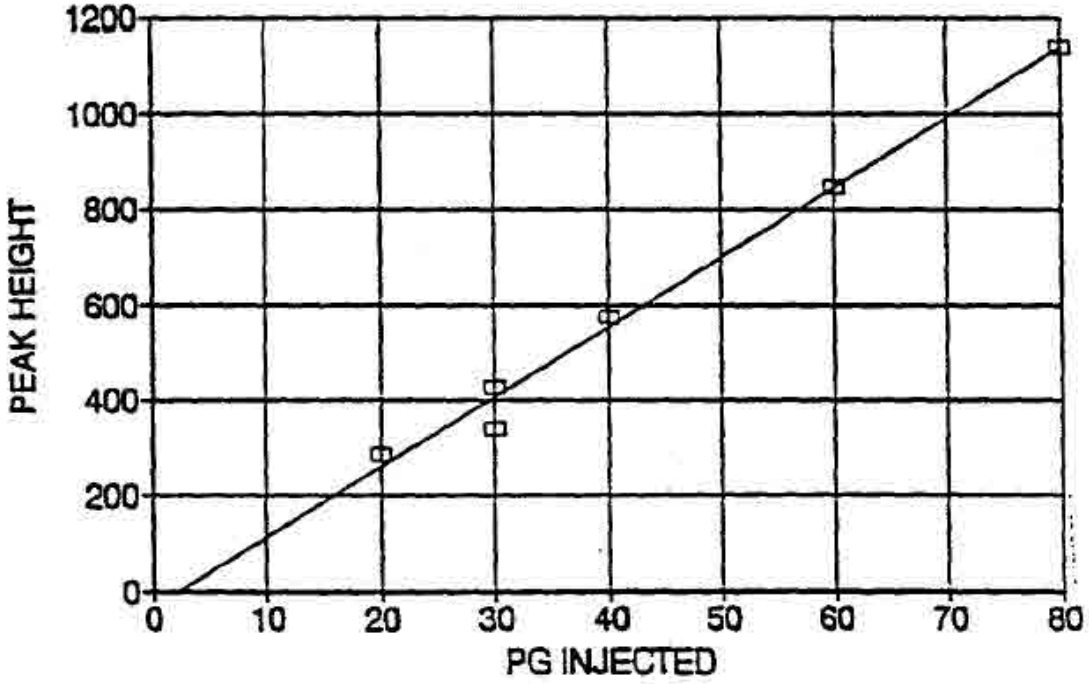
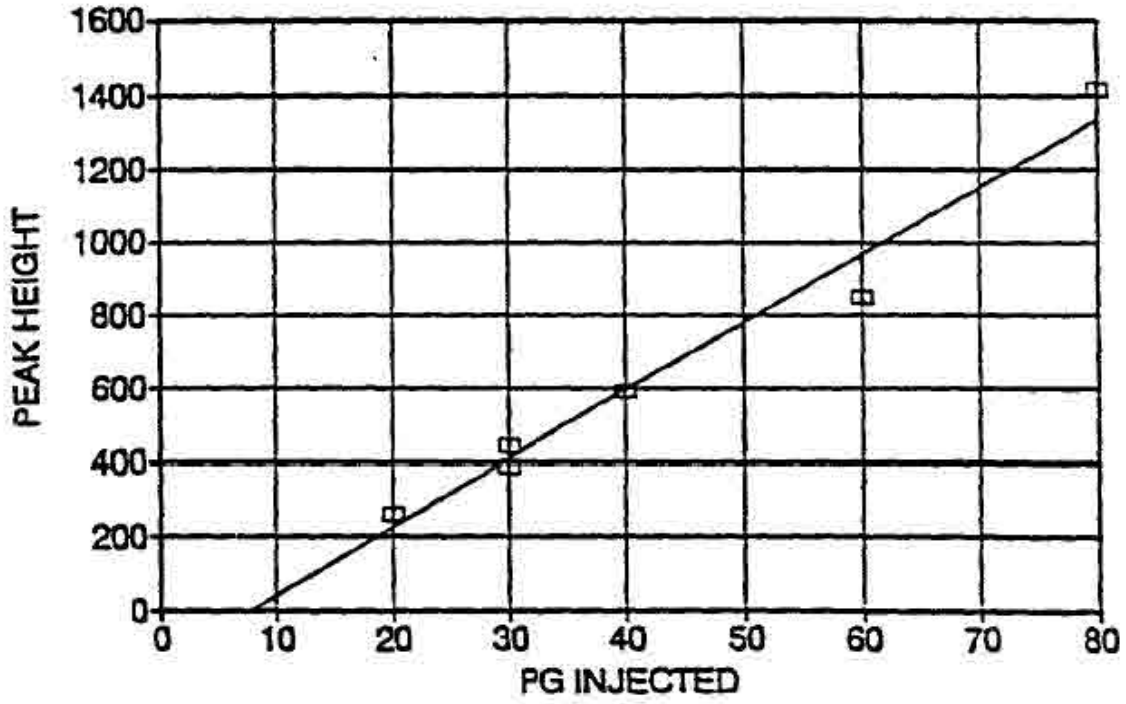


Fig 6: Typical calibration curve for mPBA



Section 4.2(3)	**Analytical methods: soil, air, water, animal and human body fluids and tissues**
BPD Data set IIA/ Annex Point IV.4.2	**Residues of two metabolites, permethric acid (DCVA) and 4-fluoro-3-phenoxybenzoic acid (FPBacid) in soil**

Additional information

			Official use only
		1 REFERENCE	
1.1	**Reference**	Gronberg, R and Pfankuche, L (1983). An Analytical Residue Method for Baythroid and its Major Metabolites in Soil. Mobay Chemical Corporation, Report No. 85886 BES Ref: MO-02-007541,Report date: 15 June 1983,Unpublished	
1.2	**Data protection**	Yes	
1.2.1	**Data owner**	Bayer CropScience AG	
1.2.2			
1.2.3	**Criteria for data protection**	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Yes EC Directive 91/414/EEC, Annex II and III	
2.2	**GLP**	No	
2.3	**Deviations**	No	
		3 MATERIALS AND METHODS	
3.1	**Preliminary treatment**		
3.1.1	**Enrichment**	The method involves extractions using methanol, water and 1N hydrochloric acid.	
3.1.2	**Cleanup**	Acid/base partition clean up steps were used prior to analysis of cyfluthrin by GC and the metabolites by HPLC. After the first four extractions, cyfluthrin and the acid metabolites were separated by a chloroform/bicarbonate partition.	
3.2	**Detection**		
3.2.1	**Separation method**	GC columns: 60 cm x 2 mm i.d. borosilicate glass packed with 15% DC 200 on 80/100 mesh Gas Chrom. Q; or 54 cm x 2 mm i.d. borosilicate glass packed with 5% SE 30 on 80/100 mesh Chromosorb W; or 54 cm x 2 mm i.d. borosilicate glass packed with 15% UCW 982 on 80/100 mesh Chromosorb W. HPLC columns: 5 micron, analytical (25 cm x 4.6 mm i.d.) or preparative (25 cm x 10 mm i.d.) column	
3.2.2	**Detector**	UV detector at 230nm for HPLC method to determine metabolites	
3.2.3	**Standard(s)**	External standard	
3.2.4	**Interfering substance(s)**	None. There were no interferences from any compounds as shown by the chromatograms.	

Section 4.2(3)	**Analytical methods: soil, air, water, animal and human body fluids and tissues**
BPD Data set IIA/ Annex Point IV.4.2	**Residues of two metabolites, permethric acid (DCVA) and 4-fluoro-3-phenoxybenzoic acid (FPBacid) in soil**

Additional information

3.3	**Linearity**	
3.3.1	**Calibration range**	0.01 mg/kg to 0.1 mg/kg
3.3.2	**Number of measurements**	5 single determinations were made.
3.3.3	**Linearity**	The responses for both DCVA and FPB-acid were shown to be linear from 0.01 mg/kg to 0.1 mg/kg.
3.4	**Specifity: interfering substances**	No significant interferences from the sample matrix were detected at the retention times corresponding to the metabolites, DCVA and FPBacid.
3.5	**Recovery rates at different levels**	Recovery of DCVA and FPB-acid at the same fortification levels ranged from 70% to 110% (mean= 87%) and 70% to 114% (mean = 85%), respectively.
3.5.1	**Relative standard deviation**	FPBacid: % RSD = 16.7%, n=11 DCVA: % RSD = 13.1%, n=11
3.6	**Limit of determination**	LOQ = 0.05 mg/kg for each of the analytes in soil samples.
3.7	**Precision**	
3.7.1	**Repeatability**	The precision of the method was acceptable, with %RSD of 16.7% for FPBacid, and 13% for DCVA.
3.7.2	**Independent laboratory validation**	ILV was not undertaken in this study.

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1	**Materials and methods**	The analytical method for determining the two metabolites, DCVA and FPB-acid in soil samples, involved extractions with methanol, water and 1N hydrochloric acid. A series of acid/base partition clean up steps were used prior to analysis of DCVA and FPB-acid by HPLC analysis.
4.2	**Conclusion**	Recovery of DCVA and FPB-acid ranged from 70% - 110% and 70% - 114%, respectively. There were no interferences. The method is suitable for determination of the metabolites, DCVA and FPB-acid in soil samples.
4.2.1	**Reliability**	1
4.2.2	**Deficiencies**	none.

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	20/06/2011
Materials and methods	Metabolites of cyfluthrin, permethric acid (DCVA) and 4-fluoro-3-phenoxybenzoic acid (FPBacid) were analysed using HPLC with UV detection at 230nm. No details of analytical standards were supplied, no confirmatory test was carried. Only an outline of the method was given, full details would be required to assess the relevance of suitability of the method in relation to residues of permethrin. Residues of 4-fluoro-3-phenoxybenzoic acid (FPBacid) would not occur as a result of permethrin treatment.
Conclusion	
Reliability	3
Acceptability	Not acceptable
Remarks	It should be noted that Bayer/Sumitomo already have an acceptable HPLC-MS/MS method of analysis for monitoring parent permethrin in soil. No further data required.
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion. Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A4.2(4)	**Analytical methods: soil, air, water, animal and human body fluids and tissues**
Annex Point IIA4.1/4.2 & IIIA-IV.1	**Methods for quantifying permethrin in air**

Key Study

Official use only

		5 REFERENCE
5.1	**Reference**	Bacher, R; 2008; Permethrin: Analytical method for determination in air; Report N°.P/B 1389G, BES ref M-296331-01-1, GLP; unpublished
5.2	**Data protection**	Yes
5.2.1	**Data owner**	Bayer CropScience AG
5.2.2	**Companies with letter of access**	
5.2.3	**Criteria for data protection**	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I
		6 GUIDELINES AND QUALITY ASSURANCE
6.1	**Guideline study**	EU Directive 91/414/EEC Annex II (Part A, Section 4.2.4), as amended by Commission Directive 96/46/EC. EC Guidance document on residue analytical methods, SANCO/825/00 rev. 7 (17/03/04).
6.2	**GLP**	Yes
6.3	**Deviations**	None
		7 MATERIALS AND METHODS
7.1	**Preliminary treatment**	
7.1.1	**Enrichment**	Air sampling uses adsorption tubes filled with two layers of XAD porous polymer. Particles and aerosols are trapped by filtration or impact onto the adsorbent material. After sampling of air (6 hours at about 1.5 L/min), the front adsorbent portion was extracted three times with about 3 mL of acetone. The extracts were combined and the volume was adjusted to 10 mL.
7.1.2	**Cleanup**	none
7.2	**Detection**	
7.2.1	**Separation method**	Reversed phase high performance liquid chromatography Column Temperature: 20 °C Injection Volume: 20 µL Mobile Phase: A –0.1 % formic acid + 5mM ammonium formate in water B –0.1 % formic acid + 5mM ammonium formate in methanol Flow Rate: 300 µL/min

Gradient:

Time, min	A, %	B, %
0.0	60	40
3.0	0	100

Section A4.2(4) Annex Point IIA4.1/4.2 & IIIA-IV.1	**Analytical methods: soil, air, water, animal and human body fluids and tissues** **Methods for quantifying permethrin in air**

Key Study

	10.0	0 100
	10.1	60 40
	13.0	60 40

Retention times: Permethrin approx. 6.9 to 7 min

7.2.2 Detector	The detection by MS/MS was performed on a mass spectrometer, equipped with a Turbo lonSpray (ESI) interface operated in positive ion mode and multiple reactions monitoring (MRM).
7.2.3 Standard(s)	Internal Standard: None External Standards: Technical permethrin of known purity
7.2.4 Interfering substance(s)	The LC/MS/MS chromatograms of the blank control specimens showed no signals (< 1 µg/m3) at the retention time of permethrin.
7.2.5 Quantification	Quantification of the analyte was accomplished by the external standard method. The concentration of permethrin in air (C_{Air}, in µg/m3) in the air specimen was calculated as follows: C_{Air} fortified = Amount fortified on the cartridge / VAir C_{Air} found = (CEnd x VEnd x DF) / (VAir x 1000 ng/µg) with: C_{End}: Concentration determined by LC/MS/MS in the final extract, in ng/mL V_{End}: Final extract volume, 10 mL V_{Air}: Air sampling volume, in m³ DF: Dilution factor, 10 Recoveries (in %) are calculated as follows: Rec. = (C_{Air} found / C_{Air} fortified) x 100 %
7.3 Linearity	
7.3.1 Calibration range	Linear LC/MS/MS calibration functions were established by injecting standard solutions (20 µL) and using the 183 m/z and the 355 m/z daughter ion peak areas for separate quantification/confirmation. Calibration levels ranged from 5.0 ng/mL to 500 ng/mL.
7.3.2 Number of measurements	Not reported
7.3.3 Linearity	The calibration functions calculated by regression analysis gave correlation coefficients r of >0.997

Section A4.2(4) **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**Analytical methods: soil, air, water, animal and human body fluids and tissues** **Methods for quantifying permethrin in air**

Key Study

7.4	**Specifity: interfering substances**	Quantification is performed by LC/MS/MS using the signal for two daughter ions (183 m/z and 355 m/z), both formed from the ammonium adduct of permethrin ion observed at 408 m/z. The chromatograms of the control specimens showed no signals (<1 µg/m3) at the retention time of permethrin.
7.5	**Recovery rates at different levels**	The layer A of sampling cartridges was fortified with permethrin at the LOQ or at the 10-fold LOQ. Subsequently, the sampling of air was performed for 6 hours with ambient air and warm, humid air (approx. 35 °C, approx. 100 % relative humidity). Five replicates per fortification level and sampling condition were analysed using LC/MS/MS. See Table A4.2(4)-1
7.5.1	**Relative standard deviation**	The average recoveries for the analyte, for both sampling conditions, fortification levels and MS/MS transitions after air sampling ranged between 87 % and 92 %, the relative standard deviations were always ≤6 %.
7.6	**Limit of determination**	The method achieves a limit of quantification (LOQ) of 5 µg/m^3.
7.7	**Precision**	
7.7.1	**Repeatability**	Above recovery data confirm precision of method.
7.7.2	**Independent laboratory validation**	ILV was not undertaken in this study

8 APPLICANT'S SUMMARY AND CONCLUSION

8.1	**Materials and methods**	The objective of this study was to validate an analytical method for the determination of permethrin in air, achieving a limit of quantification (LOQ) of ≤5 µg/m3 and to demonstrate the applicability of the method at higher concentration levels (10 x LOQ). Air is sucked through XAD adsorption tubes at about 1.5 L/min for 6 hours (total air sampling volume about 0.5 m^3). Subsequently, the adsorption material is extracted with acetone. The extract is diluted with methanol/water (1/2 v/v) and finally analysed by liquid chromatography with tandem mass spectrometric detection (LC/MS/MS), monitoring two parent-daughter ion transitions. The analytical method was validated with ambient air and warm, humid air (approximately 35 °C, approx. 100 % relative humidity) at fortification levels of 2.5 µg/adsorption tube and 25 µg/adsorption tube, corresponding to 5 µg/m^3 (LOQ) and approximately 50 µg/m^3 (10xLOQ). Fortification was performed directly onto the XAD adsorption material.

Section A4.2(4) Annex Point IIA4.1/4.2 & IIIA-IV.1	**Analytical methods: soil, air, water, animal and human body fluids and tissues** **Methods for quantifying permethrin in air**

Key Study

8.2 Conclusion	An LC/MS/MS based analytical method was successfully validated for the determination of permethrin in air with a limit of quantification of 5 µg/m^3.
8.2.1 Reliability	1
8.2.2 Deficiencies	none

Evaluation by Competent Authorities
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted

	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	21/10/08
Materials and methods	The method using HPLC/MS/MS analysed residues of permethrin in air and was validated to a LOQ of 5.0µg/m^3
Conclusion	Accept applicants version of method
Reliability	1
Acceptability	Acceptable
Remarks	No further data required
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion. Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A4.2(4)-1 Summary of Method Validation Results

Specimen Type	Fortified		Recovery	Permethrin	
	µg	µg / m^3		408 m/z --> 183 m/z	408 m/z --> 355 m/z
Extraction Efficiency	25	--	Av.	81%	80%
			n	2	2
Storage Stability Over Night Refrigerated	25	--	Av.	89%	88%
			n	2	2
Storage Stability over 7 Days Refrigerated	25	--	Av.	87%	87%
			n	2	2
Sampling with Ambient Air	2.5	5.0	Av.	87%	88%
			RSD	5%	6%
			n	5	5
	25	48	Av.	90%	90%
			RSD	4%	4%
			n	5	5
Sampling with Warm, Humid Air	2.5	4.8	Av.	92%	91%
			RSD	4%	2%
			n	5	5
	25	49	Av.	91%	90%
			RSD	3%	4%
			n	5	5

Av.: Average. RSD: relative standard deviation. n: Number of results included. For overall av. And RSD, see tables.

Section A4.2(5) Annex Point IIA4.1/4.2 & IIIA-IV.1	**Analytical methods: soil, air, water, animal and human body fluids and tissues** **Methods for quantifying permethrin residues in water**

Key Study

			Official use only
		1 REFERENCE	
1.1	**Reference**	Krebber, R and Braune, M; 2008; Analytical method 01075 for the determination of permethrin (AE F032639) in drinking water and surface water by HPLC-MS/MS. No Report MR-07/341.BES N°M-296400-01-1; Unpublished	
1.2	**Data protection**	Yes	
1.2.1	**Data owner**	Bayer CropScience AG	
1.2.2	**Companies with letter of access**		
1.2.3	**Criteria for data protection**	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Guidance document on residue analytical methods, Sanco/825/00 rev.7 of March 17, 2004 BBA guideline : Residue Analytical methods for post registration control purposes of July 21, 1998 Commission directive 96/46/EC amending council directive 91/414/EEC of 16 July 1996	
2.2	**GLP**	Yes	
2.3	**Deviations**	none	
		3 MATERIALS AND METHODS	
3.1	**Preliminary treatment**		
3.1.1	**Enrichment**	Water samples are diluted with 25% of acetonitrile and formic acid is added to the samples to a final concentration of 0,1 mL/L. Subsamples are analysed by direct injection.	
3.1.2	**Cleanup**	None	
3.2	**Detection**		
3.2.1	**Separation method**	Reversed phase high performance liquid chromatography Instrument: Agilent 1100, Agilent Technologies or equivalent Injector: HTC PAL, CTC Analytics or equivalent Column: Synergi 2u Polar RP, length 50 x 2 mm (or equivalent) with precolumn; Phenomenex or equivalent Injection Volume: e.g. 100 µL or as needed for the sensitivity Oven temperature: e.g. 60 °C Mobile Phase: Bin Pump A: Deionized water/ methanol, 900/100, v/v + 10 mM ammonium formate + 120 µL/L formic acid Bin Pump B: Methanol	

Section A4.2(5) Annex Point IIA4.1/4.2 & IIIA-IV.1	Analytical methods: soil, air, water, animal and human body fluids and tissues Methods for quantifying permethrin residues in water

Key Study

		Iso Pump C: Deionized water/ methanol, 500/500, v/v The mobile phase composition is given in table A4.2(5)-1 Flow (Column): 0.35 mL/min Flow (into MS): 0.35 mL/min Retention times: Permethrin approx. 2.9 min
3.2.2	Detector	The detection by MS/MS was performed on a triple-quadrupole tandem mass spectrometer, equipped with a Turbo lonSpray (ESI) interface operated in positive ion mode and multiple reaction monitoring (MRM). Gas Temperature: 380 °C or as needed for the sensitivity
3.2.3	Standard(s)	Internal Standard: None External Standards: Technical permethrin of known purity
3.2.4	Interfering substance(s)	None, The high selectivity of the method resulted from the HPLC separation in combination with MS/MS detection. Two MRM transitions were monitored for the analyte. No signals/peaks interfering with the detection of the analyte was observed in solutions of untreated control specimens.
3.2.5	Quantification	The measured concentration is calculated by comparison of the analyte response to a standard calibration curve (1/x weighted).
3.3	Linearity	
3.3.1	Calibration range	The method/detector response was linear within the range of 0.04 µg/L -10 µg/L
3.3.2	Number of measurements	Not reported
3.3.3	Linearity	Correlation coefficient r > 0.9995 for all MRM transitions.
3.4	Specifity: interfering substances	The control chromatograms generally have no peaks above the chromatographic background and the spiked sample chromatograms contain only the analyte peak of interest. Peaks were well defined and symmetrical.
3.5	Recovery rates at different levels	Because of the direct measurement of fortified samples without separate extraction and clean-up steps it is not possible to determine recovery rates in a classical way and therefore, an estimate of the accuracy of the analytical technique was made by an assessment of the linearity of matrix calibration and by determination of the repeatability of sample analysis. However, for additional demonstration of the reliability of the method, the validation samples were evaluated like recovery rates. The results are shown in Table A4.2(5)-2, with the confirmatory method in Table A4.2(5)-3. The overall mean recovery and RSD are given Table A4.2(5)-4.
3.5.1	Relative standard deviation	The relative standard deviation was 5.1% (n= 10) for the primary method and 4.1% for the confirmatory method (n = 10).
3.6	Limit of	The lowest fortification level experimentally providing a mean

Section A4.2(5) Annex Point IIA4.1/4.2 & IIIA-IV.1	Analytical methods: soil, air, water, animal and human body fluids and tissues Methods for quantifying permethrin residues in water
	Key Study
determination	recovery between 70 % and 110 % with a relative standard deviation of < 20% is per definition corresponding to the limit of quantitation (LOQ). The limit of quantitation for permethrin quantification ion and confirmatory ion in surface water is 0.05 µg/L. The limit of detection for permethrin quantification ion and confirmatory ion in surface water was determined to be 0.02 µg/L.
3.7 Precision	
3.7.1 Repeatability	For method validation surface water samples were fortified with permethrin (fortification levels 0.05 µg/L and 0.5 µg/L). From each test solution five aliquots were taken and injected twice into the HPLC-MS/MS instrument. The peak areas and retention times for permethrin in surface water were determined and are listed in Table A4.2(5)-5. As a measure for the precision of the method, the intra-laboratory repeatability (n = 10) is given as relative standard deviation (% RSD) for surface water samples at fortification levels of 0.05 µg/L and 0.5 µg/L. The relative standard deviation for the peak area of the quantification ion was between 1.7 % and 2.2 % for both concentration levels. The relative standard deviation for the retention time was < 0.4 % for all MRM transitions and levels. The results of the method validation were confirmed using a second MRM transition for confirmation. The relative standard deviation for the peak area of the confirmatory ion was between 3.2 % and 4.3 % for the both concentration levels. The relative standard deviation for the retention time was < 0.3 % for both levels. Results for the peak areas and retention times of the confirmatory method are shown in Table A4.2(5)-6
3.7.2 Independent laboratory validation	No
	4 APPLICANT'S SUMMARY AND CONCLUSION
4.1 Materials and methods	The method 01075 describes the determination of the active ingredient permethrin in drinking and surface water by HPLC-MS/MS using two MRM transitions. A validation for drinking water was not necessary because the limit of quantitation for surface water is below the drinking water limit of 0.1 µg/L. Acetified water samples are diluted with acetonitrile and determined by direct injection into the HPLC-MS/MS instrument using positive ionisation mode without further cleanup. Concentrations were quantified using external matrix-matched standard solutions.

Section A4.2(5) Annex Point IIA4.1/4.2 & IIIA-IV.1	**Analytical methods: soil, air, water, animal and human body fluids and tissues** **Methods for quantifying permethrin residues in water**

Key Study

	Specificity: Apparent concentrations in control samples were below 0.3 x LOQ. Two MRM transitions were monitored for permethrin (m/z 408 —> m/z 183 for quantitation and m/z 408 —> m/z 355 for confirmation). Therefore, the HPLC-MS/MS method is highly specific and an additional confirmatory method is not necessary. Linearity: The correlation between the injected amount of substance and the detector response was linear (1/x weighted) for aqueous standard solutions ranging from 0.04 µg/L to 10 µg/L. The correlation coefficients were > 0.9995 for both MRM transitions. LOQ and LOD: The limit of quantitation (LOQ) for permethrin is 0.05 µg/L in surface water. The limit of detection (LOD) is 0.02 µg/L. Recovery Rates (Accuracy): Mean recoveries for each fortification level and the overall mean recoveries were within the 70 % - 110 % range for both MRM transitions. Repeatability (Precision): Relative standard deviations were below 20 % for both MRM transitions.
4.2 Conclusion	The method was validated for the determination of permethrin in drinking and surface water and meet EU requirements in all respects. The method was linear in the range of 0.04µg/l to 10.0µg/l, its accuracy and precision were confirmed, and there were no interferences.
4.2.1 Reliability	1
4.2.2 Deficiencies	No

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	20/06/2011
Materials and methods	The method using HPLC/MS/MS analysed residues of permethrin in drinking and surface water and was validated to a LOQ of 0.05µg/l for both drinking and surface water No method was supplied to determine residues of metabolites in water
Conclusion	Accept applicants version of method for permethrin residues.
Reliability	1
Acceptability	Acceptable
Remarks	No further data required.
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion. Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 4.2/5-1 : The mobile phase time table

Time Table:

Time [min]	A [%, v/v]	B [%, v/v]	Into MS	Into Waste
0.0	30	70		0 min – 2.0 min
0.1	30	70		
5.0	0	100	2.0 min – 10.0 min	
8.0	0	100		10.0 min – 12.0 min
8.1	30	70		
12.0	Stop time			

Table A4.2(5)-2 : Recovery Rates for permethrin (m/z 408 -^ m/z 183)

Sample Material	Fortification Level (FL) [µg/L]	Recoveries % (Single Values)					Mean [%] per FL	RSD [%]	Mean [%] overall	RSD [%] overall
Permethrin in Surface Water	0.05	103	99	101	100	105	102	2.0	97	5.1
		102	101	101	105	101				
	0.5	95	92	92	92	95	93	1.8		
		90	93	92	92	95				

RSD: Relative Standard Deviation

Table A4.2(5)-3 : Recovery Rates for permethrin (m/z 408 —> m/z 355)

Sample Material	Fortification Level (FL) [µg/L]	Recoveries % (Single Values)					Mean [%] per FL	RSD [%]	Mean [%] overall	RSD [%] overall
Permethrin in Surface Water	0.05	103	104	99	91	97	98	4.2	97	4.1
		93	101	99	96	100				
	0.5	96	95	92	93	98	95	3.3		
		90	93	95	96	101				

FL: Fortification Level, RSD: Relative Standard Deviation

Table A4.2(5)-4 : Recoveries, Relative Standard Deviations (RSD) and Number of Replicates (n)

Analyte	Matrix	Fortification Level [µg/L]	Mean Recovery [%]	RSD [%]	*n*	Overall Mean Recovery [%]	Overall RSD [%]
Permethrin m/z 408 → 183	Surface water	0.05	102	2.0	10	97	4.6
		0.5	93	1.8	10		
Permethrin m/z 408 → 355		0.05	98	4.2	10		
		0.5	95	3.3	10		

Table A4.2(5)-5 : Method Validation for permethrin (m/z 408 -^ m/z 183)

Sample Material	Fortification Level (FL) [µg/L]	Peak Area (Single Values [Area Counts])					Mean [Area Counts]	RSD [%]	Retention Time	
									Mean [min]	RSD [%]
Permethrin in Surface Water	0.05	6582	6319	6437	6386	6750	6518	2.2	2.87	0.4
		6558	6454	6481	6746	6463				
	0.5	65616	63571	63514	63182	65347	63965	1.7	2.88	0.3
		62284	64274	63191	63423	65246				

RSD: Relative Standard Deviation

Table A4.2(5)-6 : Method Validation for permethrin (m/z 408 —> m/z 355)

Sample Material	Fortification Level (FL) [µg/L]	Peak Area (Single Values [Area Counts])					Mean [Area Counts]	RSD [%]	Retention Time	
									Mean [min]	RSD [%]
Permethrin in Surface Water	0.05	2827	2869	2734	2502	2659	2703	4.3	2.86	0.3
		2554	2777	2723	2633	2755				
	0.5	25753	25573	24885	25031	26368	25547	3.2	2.87	0.3
		24297	25060	25534	25717	27253				

FL: Fortification Level, RSD: Relative Standard Deviation

Section A4.2(6)	**Analytical methods: soil, air, water, animal and human body fluids and tissues**
Annex Point IIA4.1/4.2 & IIIA-IV.1	**Methods for quantifying permethrin residues in urine**

Additional information

Official use only

1 REFERENCE

1.1 Reference	Clare, R.A & Doig, M.V.; 1986; An analytical method for the estimation of absorbed permethrin in man by measurement of its metabolites 88H73 and 34W86 in urine. Wellcome Foundation Report BDGC/86/03/C; Not GLP; Unpublished
1.2 Data protection	No
1.2.1 Data owner	Sumitomo Chemicals (UK) PLC.
1.2.2 Companies with letter of access	Bayer Environmental Science
1.2.3 Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I
2	
2.1	
2.2	
2.3	

3 MATERIALS AND METHODS

3.1 Preliminary treatment	Permethrin is rapidly metabolised *in vivo* and the major metabolites are *cis*- and *trans*-3-(2,2-dichlorovinyl)-2,2-dimethyl cyclopropane carboxylic acid (ClVA, or chlorsanthemic acid), which are excreted in the urine. It is therefore possible to monitor permethrin exposure by monitoring levels of *cis* and *trans* ClVA in urine.
3.1.1 Enrichment and clean-up	1 Pipette 1 ml urine sample into a 10 ml glass tube 2 Add 100 µl citrate buffer, pH 5 (1M aq. Citric acid, adjusted to pH 5 with 10M aq. KOH) 3 Add 100 µl enzyme preparation (β-glucuronidase/aryl sulphatase from *Helix pomatia*) 4 Cap tubes, vortex mix 5 Incubate for at least 12 hours at 37°C 6 Cool to room temperature 7 Add 10 µl of internal standard (Section 3.2.3) 8 Add 200 µl of glycerol:water 1:1 9 Add 200 µl 2M citric acid 10 Vortex mix 11 Add 2ml hexane, cap tubes and shake on a mechanical shaker at approx. 275 strokes min^{-1} for 30 minutes 12 Centrifuge at 2000 rpm for 10 minutes 13 Transfer hexane layer to clean tubes 14 Add 200 µl of methanolic BF_3 (approx 14% BF_3 in

Section A4.2(6) Annex Point IIA4.1/4.2 & IIIA-IV.1

Analytical methods: soil, air, water, animal and human body fluids and tissues

Methods for quantifying permethrin residues in urine

Additional information

MeOH)

15 Place in dry block heater at 100 to 105°C for 50 minutes with occasional shaking – allow to cool

16 Add 1 ml sodium phosphate (sat'd Na_2HPO_4)

17 Shake manually for 30 seconds

18 Transfer hexane to 2 ml autosampler vials and cap

3.2 Detection

3.2.1 Separation method

Two-dimensional (wide capillary/trap/capillary) Gas Liquid Chromatography

Column 1: 15m × 0.53 mmid fused silica cross-linked DB5 (1.5 µm thickness)

Column 2: 25m × 0.25 mmid fused silica cross-linked CPS1 (0.5 µm thickness)

Column. Temp: Initial 113°C, hold for 3.9 min, ramp 8°C min^{-1} to 7.1 min, ramp 30°C min^{-1}, final oven temp 185°C

Injector Temp: 200°C

Carrier gas: Helium at 15 ml min^{-1}

Sample size: 1 µl

inlet pressure: 120 kPa

Trap 2.7 to 4.3 min (*cis*- and *trans*-ClVA, 5.9 to 7.4 min (int. std)

3.2.2 Detector

VG16F Mass spectrometer

Source temp: 220°C

Interface temp: 200°C

Electron energy 60eV

Emission current 200 µA

Accelerating V 4kV

Mass spectrometer monitoring in Selective Ion Monitoring mode, monitoring for the following ions;

163.0078 ClVA isomers $(M-59)^+$ loss of CH_3OCO

171.9886 Dibromo analogue $(M-138)^+$ loss of CH3OCO + Br

3.2.3 Standard(s)

Internal Standard: A dibromo analogue of *cis*-CIVA

External Standards: *cis*- and *trans*-CIVA

Standard solutions: Approximately 10 mg of the standards were weighed accurately and dissolved in methanol to give 100 µg ml^{-1} solutions.

1 ml of the *trans*- was mixed with 0.25 ml of the *cis*, and diluted to 50 ml with control urine to give a solution containing 2000/500 nl/ml of *trans*/*cis*. 20, 15, 10 and 5 ml aliquots were diluted to 25 ml with control urine and prepared as described in Section 3.1.1.

3.2.4 Interfering substance(s)

Because of the sample clean-up, column switching, and detector

Section A4.2(6) Annex Point IIA4.1/4.2 & IIIA-IV.1	Analytical methods: soil, air, water, animal and human body fluids and tissues Methods for quantifying permethrin residues in urine
	Additional information
	selectivity, there were no interfering substances.
3.2.5 Quantification	Quantification was by external standards, normalised for IS recovery.
3.3 Linearity	
3.3.1 Calibration range	100 to 400 ng ml^{-1} (*cis*-ClVA), 400 to 1600 ng ml^{-1} (*trans*-ClVA)
3.3.2 Number of measurements	No data
3.3.3 Linearity	10 to 500 ng ml^{-1} (*cis*-ClVA), 40 to 2000 ng ml^{-1} (*trans*-ClVA)
3.4 Specifity: interfering substances	No data
3.5 Recovery rates at different levels	No data
3.5.1 Relative standard deviation	No data
3.6 Limit of determination	The minimum detection limit was set at 20 ng ml^{-1} because of the observed levels in the human samples. The authors state the *cis* was detectable at levels well below 20 ng ml^{-1}.
3.7 Precision	
3.7.1 Repeatability	Within day variation of samples spiked with 100 and 400 ng ml^{-1} *cis* and trand ClVA produced coefficients of variation (n=6) of 8 and 13%. Repeat injections of a single sample gave CofV of a similar magnitude.
3.7.2 Independent laboratory validation	No

Section A4.2(6) Annex Point IIA4.1/4.2 & IIIA-IV.1	**Analytical methods: soil, air, water, animal and human body fluids and tissues** **Methods for quantifying permethrin residues in urine**

Additional information

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1 Materials and methods

The method describes an enzyme digestion, to deconjugate and reform ClVA (carboxylic acid), followed by extraction to an organic solvent and derivatisation to form the methyl ester.

The derivatised samples are analysed by two column capillary GC, with the ClVA and internal standard methyl esters cold trapped from the first column and switched to a second. The separation allows adequate distinction between *cis* and *trans* isomers of permethrin degradates and other contaminants which may appear in the urine samples. Detection is on a Mass Spectrometer set for Selective Ion Monitoring.

4.2 Conclusion

The method described provides a specialised (two column with cold trapping) chromatographic method, with measurement and quantification based upon a GC-MS system, with the MS working in SIM.

4.2.1 Reliability

2

4.2.2 Deficiencies

No

	Evaluation by Competent Authorities
	Methods for quantifying permethrin residues in urine
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	18/10/05
Materials and methods	Method analyses residues of methyl ester derivatives of *cis*- and *trans*-3-(2,2-dichlorovinyl)-2,2-dimethyl cyclopropane carboxylic acid (CIVA). The method was calibrated over the range 100-400ng ml^{-1} (*cis*-CIVA) and 400-1600ng ml^{-1} (*trans*-CIVA), r^2 = >0.999 Chromatograms provided demonstrated that there are no interfering peaks at the relevant Rt values. No recovery data was presented
Conclusion	No further data required. The molecule does not classify as toxic or highly toxic
Reliability	3/4
Acceptability	Not acceptable
Remarks	No further data required. The molecule does not classify as toxic or highly toxic
	COMMENTS FROM ...
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section A4.3 **Annex Point III-XI.1**	**Analytical methods for residues in/on food or feedstuffs**	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	**Technically not feasible [ ] Scientifically unjustified [ ]**	
Limited exposure [ ]	**Other justification [X]**	
Detailed justification:	The biocidal products are not used in a manner which may cause contact with food or feedstuffs. No food or feedstuffs contamination is expected. Therefore, An analytical method for the determination of Permethrin residues in/on food or feedstuffs and other products is not required.	
	.	
Undertaking of intended data submission [ ]	Not applicable	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	22/10/08	
Evaluation of applicant's justification	Since the proposal is for non-crop use then analytical methods for residues in food of plant and/or animal tissue are not required.	
Conclusion	Accept justification by notifier	
Remarks	If in the future products containing permethrin are proposed for use in a situation where food may be contaminated then the issue of analytical methods for residues in food would need to be addressed.	
	COMMENTS FROM OTHER MEMBER STATE (specify)	
Date	Give date of comments submitted	
Evaluation of applicant's justification	Discuss if deviating from view of rapporteur member state	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A4.3 (2)	**Analytical methods for residues in/on food or feedstuffs**
Annex Point IIA4.1/4.2 & IIIA-IV.1	**Methods for quantifying permethrin residues in food and feed**

Additional information

		Official use only
	1 REFERENCE	
1.1 Reference	EPA; September 2000; Method 1656; Organo-halide pesticides in wastewater, soil, sludge, sediment and tissue by GC/HSD. EPA-821-R-00-017.; Not GLP; Published	
1.2 Data protection		
1.2.1 Data owner	No data protection claimed	
1.2.2 Companies with letter of access	No data protection claimed	
1.2.3 Criteria for data protection	No data protection claimed	
	2	
2.1		
2.2		
2.3		
	3 MATERIALS AND METHODS	
3.1 Preliminary treatment		
3.1.1 Enrichment	Samples are homogenized while still frozen, where practical. Each analysis requires 10 g of tissue (wet weight). Therefore, homogenize at least 30 g of tissue to allow for the Matrix Spike (MS) and for re-extraction of a second aliquot of the same homogenized sample, if re-analysis is required. When whole fish analysis is required, the entire fish is homogenized. Homogenize the sample in a tissue homogenizer or grind in a meat grinder. Cut tissue too large to feed into the grinder into smaller pieces. To assure homogeneity, grind three times. Transfer approximately 10 g (wet weight) of homogenized tissue to a clean, tared, 400- to 500-mL beaker. Record the weight to 3 significant figures. Spike 1.0 mL of the surrogate spiking solution (tetrachloro-m-xylene or decachlorobiphenyl at a concentration of 2 µg/mL in acetone) into the sample. Transfer the remaining homogenized tissue to a clean jar with a fluoropolymer lined lid. Seal the jar and store the	

Section A4.3 (2)		Analytical methods for residues in/on food or feedstuffs
Annex Point IIA4.1/4.2 & IV.1	IIIA-	Methods for quantifying permethrin residues in food and feed

		Additional information
		tissue at <-10°C. Return any tissue that was not homogenized to its original container and store at <-10°C. Preparation of Quality Control (QC) aliquots. For each sample, weigh two 10-g (± 1 g) aliquots of the tissue reference matrix (Corn or other vegetable oil. Fish oil may be used provided it is demonstrated to be free of the analytes of interest and interfering substances at the detection limit of this Method.) into clean 400- to 500-mL beakers. One aliquot will serve as the blank and the other as the Ongoing Precision and Recovery (OPR) standard. Spike 1.0 mL of the surrogate spiking solution into each aliquot. OPR - Spike a combined QC standard (for multiresidue analysis) or permethrin QC standard (for permethrin analysis) into one of the aliquots. MS - Prepare an aliquot at the concentration required.
3.1.2	Cleanup	Tissue extraction and determination of lipid content. **Pre-extraction of the apparatus;** Charge a clean extraction thimble with 5.0 g of silica. Place the thimble in a clean extractor. Place 30 to 40 mL of methylene chloride:hexane (1:1) mixture in the receiver and 200 to 250 mL of methylene chloride:hexane (1:1) mixture in the flask. Pre-extract by heating the flask until the methylene chloride:hexane (1:1) mixture is boiling. When properly adjusted, one to two drops of methylene chloride:hexane (1:1) mixture will fall per second from the condenser tip into the receiver. Extract the apparatus for a minimum of three hours. After pre-extraction, cool and disassemble the apparatus. Rinse the thimble with methylene chloride:hexane (1:1) mixture and allow to air dry. **Sample extraction;** Add 30 to 40 g of powdered anhydrous sodium sulphate to each of the sample and QC aliquots and mix thoroughly. Cover the beakers with aluminum foil and allow to equilibrate for 12-24 hours. Remix prior to extraction to prevent clumping. Reassemble the pre-extracted Soxhlet apparatus and add a fresh charge of methylene chloride:hexane to the reflux flask. Transfer the sample/sodium sulfate mixture to the Soxhlet thimble, and install the thimble in the Soxhlet apparatus. Rinse the beaker with several portions of solvent mixture

Section A4.3 (2)	Analytical methods for residues in/on food or feedstuffs
Annex Point IIA4.1/4.2 & IIIA-IV.1	Methods for quantifying permethrin residues in food and feed

Additional information

and add to the thimble. Fill the thimble/receiver with solvent. Extract for 18 to 24 hours.
After extraction, cool and disassemble the apparatus. Filter each extract through Whatman #41 paper into a 500-mL Kuderna-Danish (K-D) evaporator flask equipped with a 10-mL concentrator tube. Rinse the extraction apparatus with 30 to 50 mL of methylene chloride and add to the K-D flask.

Percent lipid determination;

Concentrate the tissue extract to near dryness using the K-D apparatus, and complete the removal of the solvent using a nitrogen blowdown procedure and a water bath temperature of approximately 60°C. Weigh the receiver, record the weight, and return the receiver to the blowdown apparatus, concentrating the residue until a constant weight is obtained. Record the weight of the receiver, boiling chips, and residue.

Redissolve the residue in methylene chloride and quantitatively transfer to a vial for GPC cleanup, retaining the boiling chips in the receiver.
Allow the receiver and chips to dry and weigh the receiver (including the boiling chips). Calculate the lipid content of the sample, blank, and OPR to the nearest three significant figures as follows:

$$\text{Percent lipid} = \frac{\text{Weight of residue (g)}}{\text{Weight of tissue (g)}} \times 100$$

GPC Cleanup;

Place 70 to 75 g of SX-3 Bio-beads in a 400- to 500-mL beaker. Cover the beads with methylene chloride and allow to swell overnight (12 hours minimum). Transfer the swelled beads to a column and pump solvent through the column, from bottom to top, at 4.5 to 5.5 mL/min prior to connecting the column to the detector.
After purging the column with solvent for one to two hours, adjust the column head pressure to 7 to 10 psig, and purge for 4 to 5 hours to remove air. Maintain a head pressure of 7 to 10 psig. Connect the column to the detector.
Column calibration.
Load 5 mL of a calibration solution (Solution containing 300 mg/mL corn oil, 15 mg/mL bis (2-ethylhexyl) phthalate, 1.4 mg/mL pentachlorophenol, 0.1 mg/mL perylene, and 0.5 mg/mL sulphur) into the sample loop. Inject the calibration solution and record the signal from

Section A4.3 (2)	Analytical methods for residues in/on food or feedstuffs
Annex Point IIA4.1/4.2 & IIIA-IV.1	Methods for quantifying permethrin residues in food and feed

Additional information

the detector. The elution pattern will be corn oil, bis (2-ethylhexyl) phthalate, pentachlorophenol, perylene, and sulphur.
Set the "dump time" to allow greater than 85% removal of the corn oil and greater than 85% collection of the phthalate. Set the "collect time" to the peak minimum between perylene and sulfur.
Verify the calibration with the calibration solution after every 20 extracts. Calibration is verified if the recovery of the pentachlorophenol is greater than 85%. If calibration is not verified, the system shall be recalibrated using the calibration solution, and the sample batch (those samples affected by the calibration) shall be re-extracted and cleaned up using a calibrated GPC system.
Extract cleanup - GPC requires that the column not be overloaded. The column specified in this Method is designed to handle a maximum of 0.5 g of high molecular weight material in a 5-mL extract. If the extract is known or expected to contain more than 0.5 g, the extract is split into fractions for GPC and the fractions are combined after elution from the column. The solids content of the extract may be obtained gravimetrically by evaporating the solvent from a 50-µL aliquot.
Filter the extract or load through the filter holder to remove particulates. Load the extract onto the column.
Elute the extract using the calibration data determined.
Collect the eluate in a clean 400- to 500-mL beaker.
Rinse the sample loading tube thoroughly with methylene chloride between extracts to prepare for the next sample. If a particularly dirty extract is encountered, a 5.0-mL methylene chloride blank must be run through the system to check for carry-over.
Concentrate the extract via K-D and exchange into hexane. Adjust the final volume to 0.5 ml for analysis.

3.2 Detection

3.2.1 Separation method

Gas Liquid Chromatography
Column: 30m x 0.5 mmid fused silica DB-608 (or equivalent)
Column. Temp: 150°C for 0.5 min, 150 to 270°C at 5°C /min, hold at 270°C
Injector Temp: 275°C
Detector Temp: 300°C
Carrier gas: Helium at 7 ml min^{-1}
Sample size: 1.0 µl Split/splitless injection

3.2.2 Detector

Ni^{63} Electron Capture Detector

Section A4.3 (2)	**Analytical methods for residues in/on food or feedstuffs**
Annex Point IIA4.1/4.2 & IIIA-IV.1	**Methods for quantifying permethrin residues in food and feed**

Additional information

3.2.3	**Standard(s)**	Internal Standard: tetrachloro-m-xylene or decachlorobiphenyl at a concentration of 2 µg/mL in acetone External Standards: Technical permethrin of known purity **Standard solutions**: Prepare a range of standards of technical grade material in hexane to cover 200 to 4000 ng ml^{-1} (0.2 to 4 mg l^{-1}).
3.2.4	**Interfering substance(s)**	The method describes further clean-up stages using SPE, Florisil and alumina should interferences occur. An optional sulphur removal stage is also included, although this is more appropriate for soil/sediment samples.
3.2.5	**Quantification**	Detection via ECD. Permethrin quantified as a ratio of peak response in the external standards against the samples.
3.3	**Linearity**	
3.3.1	**Calibration range**	200 to 4000 ng ml^{-1} (0.2 to 4 mg l^{-1}).
3.3.2	**Number of measurements**	Not specified
3.3.3	**Linearity**	Authors state calibration standards should be within the linear range
3.4	**Specifity: interfering substances**	None
3.5	**Recovery rates at different levels**	
3.5.1	**Relative standard deviation**	Acceptable values for performance tests are quoted as;

Spike level (ng/ml)	Calibration Recovery (%)	Ongoing Verification (%)	Max RSD (%)
Cis-Permethrin	10000	40	70-130 41-157
Trans-Permethrin	10000	40	70-130 50-150

3.6	**Limit of determination**	200 ng/l
3.7	**Precision**	
3.7.1	**Repeatability**	Repeatability is verified by the inclusion of Quality Control and Ongoing Precision and Recovery standards
3.7.2	**Independent**	The method has been prepared by the EPA for use in all

Section A4.3 (2)	Analytical methods for residues in/on food or feedstuffs
Annex Point IIA4.1/4.2 & IIIA-IV.1	Methods for quantifying permethrin residues in food and feed

	Additional information
laboratory validation	laboratories involved in the analysis of organo-halide pesticides in a variety of matrices.
	4 APPLICANT'S SUMMARY AND CONCLUSION
4.1 Materials and methods	Fish and other tissue samples are homogenized and dried with sodium sulfate, then extracted using methylene chloride:hexane (1:1) in a Soxhlet extractor. The extract is dried over sodium sulfate and concentrated using a Kuderna-Danish evaporator. Cleanup procedures include gel permeation chromatography (GPC), Florisil and alumina column chromatography, solid-phase cartridge, and sulfur removal. After cleanup, the extract is concentrated to 1.0 mL (0.5 mL if GPC has been used). A 1-µL aliquot of the extract is injected into the gas chromatography (GC). The analytes are separated on a wide-bore, fused-silica capillary column and detection is *via* an electron capture detector. Quantitative analysis is performed using an authentic standard to produce a calibration factor or calibration curve, and using the calibration data to determine the concentration of permethrin in the extract. The concentration in the sample is calculated using the sample weight or volume and the extract volume. Quality is assured through reproducible calibration and testing of the extraction and GC systems.
4.2 Conclusion	The method described provides an extensive extraction and clean-up process for permethrin in tissue samples, including optional clean-up stages should the nature of the sample require it. A robust chromatographic method for the determination of permethrin in extracts based upon a capillary gas liquid chromatography is therefore likely to be robust and reproducible. Measurement and quantification are based upon a halogen-specific detector (ECD), which would detect any halogen containing organic components in the solution (within the usual limitations of GC as defined by molecular size, solubility, and volatility). No data are included in the report to describe reproducibility and robustness, but the broad acceptability of the EPA methods, the well studied/understood nature of the extraction and analytical techniques and the inclusion

Section A4.3 (2)	Analytical methods for residues in/on food or feedstuffs
Annex Point IIA4.1/4.2 & IIIA-IV.1	Methods for quantifying permethrin residues in food and feed

		Additional information
		of several quality control measures within the methodology would suggest that the method is suitable for permethrin analysis in tissue samples.
4.2.1	Reliability	2
4.2.2	Deficiencies	No

	Evaluation by Competent Authorities
	Methods for quantifying permethrin residues in food and feed
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	18/10/05
Materials and methods	EPA Method 1656 has been presented for the determination of residues of permethrin in animal tissue. The full outline of the method has been presented. No validation data has been submitted to demonstrate the effectiveness of the method for analysis of permethrin residues in animal tissue. It has not been suggested that this method is appropriate for analysis of permethrin residues in plant material.
Conclusion	Since the proposal is for non-crop use then analytical methods for residues in food of plant and/or animal tissue are not required. If in the future products containing permethrin are proposed for use in a situation where food may be contaminated then the issue of analytical methods for residues in food would need to be addressed.
Reliability	3
Acceptability	Acceptable in the present context
Remarks	No further data required
	COMMENTS FROM ...
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

APPENDIX 1 TO DOC III-A4

Bayer Environmental Science is a an affiliated company of Bayer CropScience, therefore the studies submitted by Bayer Environmental Science are owned by Bayer CropScience AG.

Reference List Doc. III-A4. sorted by reference no.

Section No/ Reference No	Author (s)	Year	Title. Source, Report No. GLP /(Un) Published	Data Protection Claimed (Yes/No)	Owner
4,1(1)	Ann.	2006	CIPAC Method 331 TC/m/-, Published	No	
4,1(3)			See confidential document	Yes	Bayer CropScience AG
4,1(4)			See confidential document	Yes	Bayer CropScience AG
4,1(6)	Chhatre, A.S.	2000	Quantification of Active Ingredient and impurities of permethrin technical (5-batch analysis) by GC-MS. Bilag Industries internal report no. C008551; GLP; Unpublished.	Yes	Bayer CropScience AG
4,2(7)	No Author	1980a	Determination of permethrin in Liquid and Powder Formulations Report No. E1/390/80; Not GLP; Unpublished	Yes	Sumitomo Chemical
4,2(1)	Brumhard, B	2008	Analytical method 01081 for the determination of residues of permethrin (AE F032639) in soil by HPLC-MS/MS; Report N°MR-07/355 BES N°M-296886-01-1; Unpublished	Yes	Bayer CropScience AG
4,2(2)	Nagel, W.D	1993	Analytical method for the determination of permethrin, Dichlorovinyl Acid and m-Phenoxybenzoic acid Residue in/on Soil; FMC Agricultural Chemical Group; P-2703M; August 1993; Unpublished	Yes	Sumitomo Chemical
4,2(2)	Hatfield, M.W	1996b	Interim final report "Aquatic dissipation of permethrin in California and North Carolina. American Agricultural Services Inc., Study No. AA940907." BES report C003413; GLP; Unpublished	Yes	Bayer CropScience AG
4,2(3)	Gronberg, R and Pfankuche, L	1983	An Analytical Residue Method for Baythroid and its Major Metabolites in Soil. Mobay Chemical Corporation, Report No. 85886 BES Ref: MO-02-007541,Report date: 15 June 1983,Unpublished	Yes	Bayer CropScience AG

Section No/ Reference No	Author (s)	Year	Title. Source, Report No. GLP /(Un) Published	Data Protection Claimed (Yes/No)	Owner
4,2(4)	Bacher, R	2008	Permethrin: Analytical method for determination in air; Report N°.P/B 1389G, BES ref M-296331-01-1, GLP; unpublished	Yes	Bayer CropScience AG
4,2(5)	Krebber, R and Braune, M	2008	Analytical method 01075 for the determination of permethrin (AE F032639) in drinking water and surface water by HPLC-MS/MS. No Report MR-07/341.BES N°M-296400-01-1; Unpublished	Yes	Bayer CropScience AG
4,2(6)	Clare, R.A & Doig, M.V.	1986	An Analytical Method or the Estimation of Absorbed permethrin in Man by Measurement of its Metabolites 88H73 and 34W86 in Urine. The Wellcome Foundation Ltd. Report No. BDGC/86/03/C; Not GLP; Unpublished	Yes	Sumitomo Chemical
4,3(2)	No authors	2000	EPA; September 2000; Method 1656; Organo-halide pesticides in wastewater, soil, sludge, sediment and tissue by GC/HSD. EPA-821-R-00-017.; Not GLP; Published	No	

Competent Authority Report

Programme for Inclusion of Active Substances in Annex I to Council Directive 98/8/EC

Permethrin (PT 8)

CAS-No. 52645-53-1

DOCUMENT IIIA (A5)

Bayer Environmental Science

Sumitomo Chemical (UK) Plc.

Rapporteur: Ireland

August 2009

Permethrin PT8

Document IIIA (A5)

CONTENTS