Competent Authority Report

According to Directive 98/8/EC

lambda-Cyhalothrin

CAS 91465-08-6

Active substance in Biocidal Products, Product Type 18 (Insecticide)

Notifier: Syngenta European Center

DOCUMENT III-A

Sections 1-3: Applicant, Identity and Physical and Chemical Properties

Rapporteur Member State: Sweden

Final May 2011

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KEMI

Kemikalieinspektionen

Swedish Chemicals Agency

Table of Contents; DOC III-A Sections 1-3

Borttaget: September

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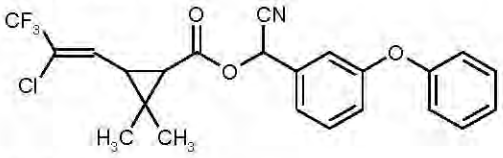
Section A1 Applicant

Annex Points IIA, I.1.1 to 1.2

1.1	**Applicant**	Name:	Syngenta Limited Syngenta European Regional Center
		Address:	Guildford GU2 7YH United Kingdom
		Contact person:	[redacted]
		Telephone:	[redacted]
		Fax number:	[redacted]
		E-mail address:	[redacted]
1.2	**Manufacturer of Active Substance (if different)**	Name:	Syngenta Crop Protection AG
		Address:	4002 Basel Switzerland
		Contact person:	[redacted]
		Telephone:	[redacted]
		Fax number:	[redacted]
		E-mail address:	[redacted]
		Location of manufacturing plant:	[redacted]
1.3	**Manufacturer of product(s) (if different)**	See appropriate Section B1 for details of the manufacturer of the biocidal products.	

Section A2 Identity of Active Substance

Annex Points IIA, II.2.1 to 2.9

Subsection			Official use only
2.1	Common name (IIA2.1)	*Lambda*-cyhalothrin	
2.2	Chemical name (IIA2.2)	**IUPAC nomenclature** : alpha-cyano-3-phenoxybenzyl-3-(2-chloro-3,3,3-trifluoropropeny)-2,2-dimethylcyclopropanecarboxylate **CA nomenclature :** 1-alpha(S*),3-alpha(Z)]-cyano(3-phenoxyphenyl)methyl-3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate (9CI)	X1
2.3	Manufacturer's development code number(s) (IIA2.3)	PP321	
2.4	CAS No and EC numbers (IIA2.4)		
2.4.1	CAS-No	91465-08-6	
2.4.2	EC-No	Not listed	X2
2.4.3	Other	CIPAC: 463	
2.5	Molecular and structural formula, molecular mass (IIA2.5)		
2.5.1	Molecular formula	$C_{23}H_{19}ClF_3NO_3$	
2.5.2	Structural formula		X3
2.5.3	Molecular mass	449.9	
2.6	Method of manufacture of the active substance (IIA2.1)	Confidential information, see Annex Confidential Data and Information	
2.7	Specification of the purity of the active substance, as appropriate (IIA2.7)	900 g/kg minimum content	X4

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Section A2 Identity of Active Substance

Annex Points IIA, II.2.1 to 2.9

2.8	**Identity of impurities and additives, as appropriate (IIA2.8)**	Confidential information, see Annex Confidential Data and Information
2.9	**The origin of the natural active substance or the precursor(s) of the active substance (IIA2.9)**	Not applicable as the chemical is manufactured synthetically.

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date	January 2007
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

Borttaget: September

Borttaget: 0

Section A2 **Identity of Active Substance**

Annex Points IIA, II.2.1 to 2.9

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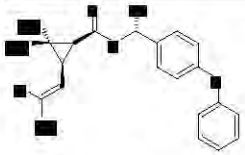

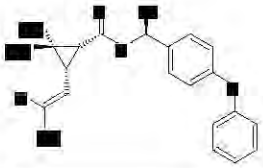

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Section A2.10 **Exposure data in conformity with Annex VIIA to Council Directive 92/32/EEC (OJ No L, 05.06.1992, p.1) amending Council Directive 67/548/EEC**

Annex Point IIA II.2.10

2.10.1 Human exposure towards active substance

Official use only

2.10.1.1 Production

i) Description of process

The manufacturing process is detailed in the Confidential section of the dossier.

Lambda-cyhalothrin is produced in [redacted] there is no anticipated exposure to plant personnel during manufacture.

[redacted]

ii) Workplace description

Production is subject to health and safety regulations and requirements of good occupational hygiene practice involving the use of engineering/procedural controls to prevent or minimise exposure hazards prior to use of PPE and RPE.

Consideration of these requirements has been included in design of the plant, cleanliness of the workplace and equipment, working practices and personal hygiene requirements. Control of exposure to any active substance which can be hazardous by ingestion, absorption or inhalation is to a standard that eliminates human health risks.

For synthesis and formulation of the active ingredient, an occupational exposure standard has been set by the manufacturer as the primary mechanism for controlling atmospheric exposure based on available toxicological data and suitable safety factors for extrapolation from animal data to a human standard. The OES for *lambda*-cyhalothrin is 0.04 mg/m^3 for an 8 hour time weighted average exposure, based on a dog NOAEL value of 0.5 mg/kg bw/day; worker body weight of 70 kg and a shift inhalation volume of 10m^3.

The control strategy includes prohibition of eating and drinking within areas where chemicals are handled, to avoid accidental ingestion. Skin contact is prevented by partial or total enclosure of the manufacturing systems and in addition, suitable PPE is required where a dermal contamination risk is perceived.

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iii) Inhalation exposure

The OES for *lambda*-cyhalothrin is 0.04 mg/m^3 for an 8 hour time weighted average exposure, based on a dog NOAEL value of 0.5 mg/kg bw/day; worker body weight of 70 kg and a shift inhalation

Section A2.10 **Exposure data in conformity with Annex VIIA to Council Directive 92/32/EEC (OJ No L, 05.06.1992, p.1) amending Council Directive 67/548/EEC**

Annex Point IIA II.2.10

	volume of 10m^3. The hygiene monitoring records measuring workplace and personal exposures from atmospheric contamination against the OES indicate that 99% of fixed workplace exposure and 100% of personal exposures are less than the OES. The active substance is practically non-volatile however containment measures include use of partial or total enclosure during manufacture and appropriate extraction systems.
iv) Dermal exposure	The cleanliness of the workplace is monitored by wipe-down swab analysis. Semi-quantitative positive results lead to revision of cleaning regimens and consequently reduce risk of dermal contamination. *Lambda* –cyhalothrin has a low intrinsic dermal permeability (<1% in 24 hours) but may persist on skin after washing. Since cases of subjective facial sensation (paraesthesia) may occur, measure to prevent dermal contact are required.

2.10.1.2 Intended use(s)

1. Professional users

i) Description of application process	The product is a capsule suspension (CS) formulation that is sprayed onto surfaces or into cracks and crevices in and around animal houses or other buildings. Applications are made by professional operators.
ii) Workplace description	OXYFLY 10 CS is sprayed overhead, upwards and downwards onto walls and floors and into cracks and crevices where pests may be present. Demand/ICON 10 CS is sprayed overhead, upwards and downwards onto walls and floors and into cracks and crevices where pests may be present. Low pressure spray application (50 mL product/200 m^2) using a hand held knapsack sprayer. PPE for profesional users assumed to include wearing of gloves.
iii) Inhalation exposure	Systemic exposure via inhalation exposure estimated to be 0.0015 mg/kg bw/day. See Documents II B1 and II B2. and II C.
iv) Dermal exposure	Systemic exposure via dermal exposure estimated to be 0.00006 mg/kg bw/day. Total Systemic Exposure (dermal and inhalation) : 0.0016 mg/kg bw/day equivalent to MOS of 156. See Documents II B1 and II B2. and II C.

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Section A2.10 **Exposure data in conformity with Annex VIIA to Council Directive 92/32/EEC (OJ No L, 05.06.1992, p.1) amending Council Directive 67/548/EEC**

Annex Point IIA II.2.10

2. Non-professional users including the general public	See Documents II B1 and II B2. and II C. Primary exposure to professional users is by skin contact or by inhalation during application of OXYFLY 10CS or Demand/Icon 10CS during application by spraying. There are no secondary exposure scenarios for adults or children entering buildings sprayed with liquid insecticides in EU Guidance documents	
(i) via inhalational contact	OXYFLY 10CS and Demand/Icon 10CS are CS formulations containing the same active ingredient. Inhalation exposure to *lambda*-cyhalothrin may occur during mixing/loading and application. However, applications are made at low pressure and high water volumes as a medium or coarse spray generating droplets of median diameter of 210 µm or larger (EU Guidance Document Table 5 Point 2.2.3 Section 3.5 of Part 2 June 2002) with a low proportion of droplets of respirable size (approximate diameter of 50 µm or less) reducing the potential for inhalation exposure. Professional users are also expected to wear PPE. Non-users are not expected to be present during application. Children and adults may enter treated buildings after application but *lambda*-cyhalothrin is not volatile (vapour pressure of the active substance is, estimated by extrapolation, 2×10^{-10} kPa at 20°C) and the risk of inhalation exposure to dried residues of *lambda*-cyhalothrin after application for all non-users is considered to be negligible. Total Systemic Exposure (dermal and inhalation) : 0.0016 mg/kg bw/day equivalent to MOS of 156 for professional users. For non-professionals and the general public the level of secondary exposure is considerably lower than for applicators and hence the margin of safety is likely to be considerably higher.	
(ii) via skin contact	Dermal exposure to *lambda*-cyhalothrin may occur during mixing/loading and application though professional users are expected to wear PPE. Non-users are not expected to be present during application. Children and adults may enter treated buildings after application but the risk of dermal exposure to residues of *lambda*-cyhalothrin after application for all non-users is considered to be negligible.	
(iii) via drinking water	A parametric value for drinking water of Cmax water = 60 µg/l is proposed. In practice, on the basis of the data on the fate of *lambda*-cyhalothrin in the environment, it is unlikely that *lambda*-cyhalothrin will be present in water abstracted for drinking water following normal use of the insecticide.	**X1**

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Section A2.10 **Exposure data in conformity with Annex VIIA to Council Directive 92/32/EEC (OJ No L, 05.06.1992, p.1) amending Council Directive 67/548/EEC**

Annex Point IIA II.2.10

(iv) via food	Unlikely to reach the mouth of professional users. Therefore, the risk during use is considered to negligible. Non-users are not expected to be present during application. Children and adults may enter treated buildings after application but the risk of oral exposure to dried residues of *lambda*-cyhalothrin after application for all non-users is considered to be negligible. The products are not sprayed in areas used for food preparation or open food storage.

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	Not relevant.
Materials and methods	[redacted]
Conclusion	
Reliability	
Acceptability	
Remarks	[redacted]

Section A3 Physical and Chemical Properties of Active Substance

Annex Points IIA, III.3.1.1 to 3.13, Annex Points IIIA, III.1 to 2 and TnsG Chapter 3, Part A, Point 3.6 and Point 3.14

Subsection (Annex Point)	Method	Purity/ Specification	Results	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								
	OECD 102	Pure PP321 Batch ASJ/PP/No123 Purity: 99.0%	**The melting point of the test substance was determined to be: 49.2°C**	-	Y	1	A 3.1.1(01) Wollerton, C. 1984	X1
3.1.2 Boiling point	OECD 103	Pure PP321 Batch ASJ/PP/No123 Purity: 99.0%	**No boiling point at atmospheric or reduced pressure. Decomposition occurs at 239°C at 1 mm Hg pressure.**	-	Y	1	A 3.1.2(01) Wollerton, C. 1984	X2
	EEC A.2, ebulliometry and DSC	Technical PP321 Batch P28 Purity: not stated	**Decomposes at approximately 270 °C at atmospheric pressure**		Y	1	A 3.1.2(02) Jackson, W.A. 1994	X
3.1.3 Bulk density/ relative density	OECD 103	Technical PP321 P28 Batch 1144 Purity: not stated	**1.288 at 20°C**	-	Y	1	A 3.1.3(01) Jackson, W.A. 1994	X X3

Section A3 Physical and Chemical Properties of Active Substance

Annex Points IIA, III.3.1.1 to 3.13, Annex Points IIIA, III.1 to 2 and TnsG Chapter 3, Part A, Point 3.6 and Point 3.14

Subsection (Annex Point)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.2 Vapour pressure (IIA3.2)	OECD 104	Pure PP321 Batch ASJ/PP/No123 Purity: 99.0%	**The vapour pressure of pure *lambda*-cyhalothrin has been estimated as 2×10^{-10} kPa at 20°C, by extrapolation.**	Gas saturation method	Y	1	A 3.2(01) Wollerton, C. 1984	X4
3.2.1 Henry's Law Constant (IIA3.2)	-	-	**Henry's Law Constant 2×10^{-2} Pa m3/mol**	-	-	-	-	X5
3.3 Appearance (IIA3.3)								X6
3.3.1 Physical state	-	Pure PP321 Batch ASJ/PP/No123 Purity: 99.0%	**Solid**	-	Y	1	A 3.3.1(01) Wollerton, C. 1984	
	-	Technical PP321 Batch P13 Purity: 96.5%	**Solid**	-	Y	1		X
3.3.2 Colour	-	Pure PP321 Batch ASJ/PP/No123 Purity: 99.0%	**White**	-	Y	1	A 3.3.2(01) Wollerton, C. 1984	

Section A3 Physical and Chemical Properties of Active Substance

Annex Points IIA, III.3.1.1 to 3.13, Annex Points IIIA, III.1 to 2 and TnsG Chapter 3, Part A, Point 3.6 and Point 3.14

Subsection (Annex Point)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
	-	Technical PP321 Batch P13 Purity: 96.5%	**Beige**	-	Y	1		X
3.3.3 Odour	-	Pure PP321 Batch ASJ/PP/No123 Purity: 99.0%	**No characteristic odour**	-	Y	1	A 3.3.3(01) Wollerton, C. 1984	
		Technical PP321 Batch P13 Purity: 96.5%	**No characteristic odour**	-	Y	1		X
3.4 Absorption spectra (IIA3.4)		Pure PP321 Batch ASJ/PP/No123 Purity: 99.0%		-	Y	1	A 3.4 (01) Wollerton, C. 1984	X7
UV/VIS	Methanol solution		**The molar extinction coefficients were determined to be:** **λ nm — ext. coeff.** **254 — 1090** **277 — 2070**	Some absorption has been observed above 290 nm.	Y	1		X8

Section A3 Physical and Chemical Properties of Active Substance

Annex Points IIA, III.3.1.1 to 3.13, Annex Points IIIA, III.1 to 2 and TnsG Chapter 3, Part A, Point 3.6 and Point 3.14

Subsection (Annex Point)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
IR	KBr pellet		**Spectra consistent with structure**	-	Y	1		X9
NMR			**Spectra consistent with structure**	-	Y	1		X10
MS	EI		**Spectra consistent with structure**	-	Y	1		X11
3.5 Solubility in water (IIA3.5)								
Water solubility 1	Generator column method	Pure PP321 Batch ASJ/PP/No123 Purity: 99.0%	**Pure water: 0.005 mg/L at 20°C (pH 6.5)** **pH 5 buffer: 0.004 mg/L at 20°C** **pH 9.2 buffer: 0.004 mg/L at 20°C**	-	Y	1	A 3.5 (01) Wollerton, C. 1984	X12
3.6 Dissociation constant (-)	-	Pure PP321 Batch ASJ/PP/No123 Purity: 99.0%	***Lambda*-cyhalothrin does not dissociate in water**	-	Y	1	A 3.6 (01) Wollerton, C. 1984	X13

Section A3 Physical and Chemical Properties of Active Substance

Annex Points IIA, III.3.1.1 to 3.13, Annex Points IIIA, III.1 to 2 and TnsG Chapter 3, Part A, Point 3.6 and Point 3.14

Subsection (Annex Point)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.7 Solubility in organic solvents, including the effect of temperature on solubility (IIIA3.1)	OECD 105	Technical PP321 Batch P13 Purity: 96.5%	**The solubility of *Lambda*-cyhalothrin is greater than 500 g/L in methanol, acetone, dichloromethane, toluene, ethyl acetate and hexane.**	-	Y	1	A 3.7 (01) Wollerton, C. 1984	X X14
3.8 Stability in organic solvents used in b.p. and identity of relevant breakdown products (IIIA3.2)	Based on the storage stability of the formulated products (Documents IIIB1 3.7 and IIIB2 3.7), lambda cyhalothrin is considered chemically stable in the solvent which is used/present in the product.							X15
3.9 Partition coefficient n-octanol/water (IIA3.6)	Generator column	Pure PP321 Batch ASJ/PP/No123 Purity: 99.0%	**log P_{ow} = 7.0 (20°C)**	-	Y	1	A 3.9 (01) Wollerton, C. 1984	X16
3.10 Thermal stability, identity of relevant breakdown products (IIA3.7)	OECD 102	Pure PP321 Batch ASJ/PP/No123 Purity: 99.0%	**Decomposes above 275°C.**	Combustion products are likley to be oxides of carbon and water. It is possible that small amounts of florinated substances or cyanides maybe produced.	Y	1	A 3.10 (01) Wollerton, C. 1984	X17

Section A3 Physical and Chemical Properties of Active Substance

Annex Points IIA, III.3.1.1 to 3.13, Annex Points IIIA, III.1 to 2 and TnsG Chapter 3, Part A, Point 3.6 and Point 3.14

Subsection (Annex Point)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
	EEC A4	PP321 P28 Batch 1144 Purity: not stated	**Decomposes above 270°C.**	-	Y	1	A 3.10 (02) Jackson, W.A. 1994	X X18
3.11 Flammability, including auto-flammability and identity of combustion products (IIA3.8)	Depending on the purity and the manufacturing process, lambda-cyhalothrin is either a low melting point solid or a viscous liquid. It is therefore considered that flash point, not flammability, is the most relevant parameter for classification purposes. Therefore, flammability data are not presented.							X19
	EEC A15	PP321 P28 Batch 1144 Purity: not stated	**Auto-ignition temperature: 380°C**	-	Y	1	A 3.11 (01) Jackson, W.A. 1994	X X20
3.12 Flash-point (IIA3.9)	EEC A9	Pure PP321 P28 Batch 1144 Purity: not stated	**Flash point 83 ± 2°C**	-	Y	1	A 3.12 (01) Jackson, W.A. 1994	X X21
3.13 Surface tension (IIA3.10)	EEC A5 Wilhelmy plate method	Technical PP321 Batch P13 Purity: 96.5%	**Surface tension of aqueous solutions at 25°C by the Wilhelmy plate method was determined to be: σ = 71.3 mN/m.**	*Lambda*-cyhalothrin is not regarded as a surface active substance because the surface tension is >60 mN/m.	Y	1	A 3.13 (01) Wollerton, C. 1984	X X22

Section A3 Physical and Chemical Properties of Active Substance

Annex Points IIA, III.3.1.1 to 3.13, Annex Points IIIA, III.1 to 2 and TnsG Chapter 3, Part A, Point 3.6 and Point 3.14

Subsection (Annex Point)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.14 Viscosity (-)	Not applicable because *Lambda*-cyhalothrin is not a liquid.							X23
3.15 Explosive properties (IIA3.11)	EEC A14	PP321 P28 Batch 1144 Purity: not stated	***Lambda*-cyhalothrin is not considered an explosive in accordance with EEC Method A. 14**	-	Y	1	A 3.15 (01) Jackson, W.A. 1994	X X24
3.16 Oxidising properties (IIA3.12)	EEC A17	PP321 P28 Batch 1144 Purity: not stated	***Lambda*-cyhalothrin is not considered to have oxidising properties in accordance with EEC Method A. 17**	-	Y	1	A 3.16 (01) Jackson, W.A. 1994	X25
3.17 Reactivity towards container material (IIA3.13)	EPA OPPTS 830.6313 Stability in contact with metals and metal ions	ASSF364A, Lambda Cyhalothrin Technical Batch FLO11300	***Lambda*-cyhalothrin is chemically stable in the presence of iron and aluminium metals and salts for at least 114 days.**	*Lambda*-cyhalothrin does not react with iron or aluminium containers.	Y	1	A 3.17 (01) Johnson, N. 2002	X26

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Section A3 Physical and Chemical Properties of Active Substance

Annex Points IIA, III.3.1.1 to 3.13, Annex Points IIIA, III.1 to 2 and TnsG Chapter 3, Part A, Point 3.6 and Point 3.14

Subsection (Annex Point)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
	-	Technical PP321 Batch P37	***Lambda*-cyhalothrin (originally manufactured in 2001) was stored in a container at ambient conditions. A certificate of analysis [ref. IIIA 3.17 (02)] prepared in 2003 showed the purity to be 83.6% w/w. The same material was re-analysed in 2006 [ref. IIIA 3.17 (03)] and the purity was 82.8% w/w.**	The report concludes that the stability of *Lambda*-cyhalothrin was confirmed, indicating that it did not react with the containers.	Y	1	A 3.17 (02) McIntyre, A.D. 2003 A 3.17 (03) Foster, B. 2006	X27

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Section A3 Physical and Chemical Properties of Active Substance

Annex Points IIA, III.3.1.1 to 3.13, Annex Points IIIA, III.1 to 2 and TnsG Chapter 3, Part A, Point 3.6 and Point 3.14

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	August 2006
Evaluation of data submitted under section A3	[redacted]

Borttaget: September

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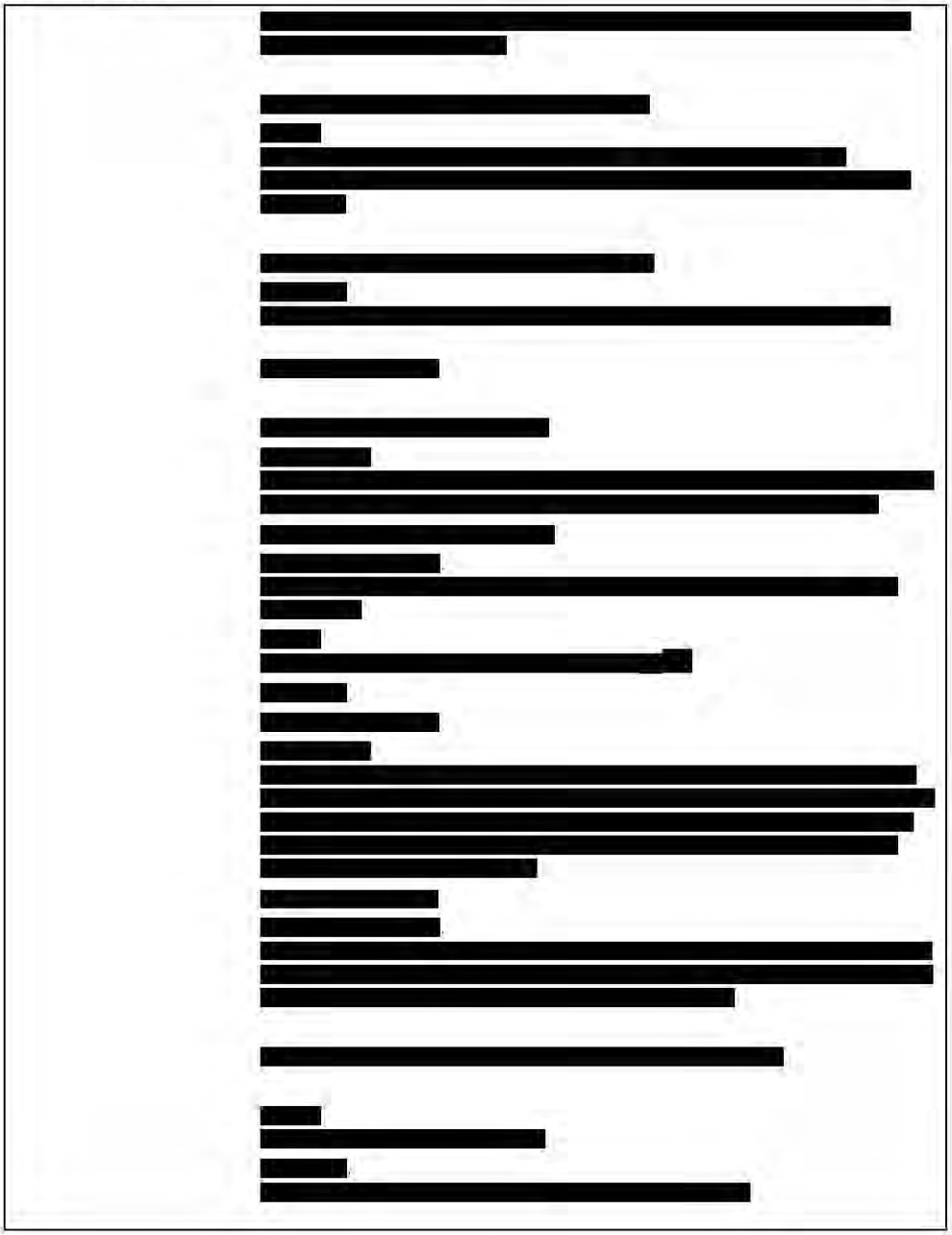
Section A3 **Physical and Chemical Properties of Active Substance**

Annex Points IIA, III.3.1.1 to 3.13, Annex Points IIIA, III.1 to 2 and TnsG Chapter 3, Part A, Point 3.6 and Point 3.14



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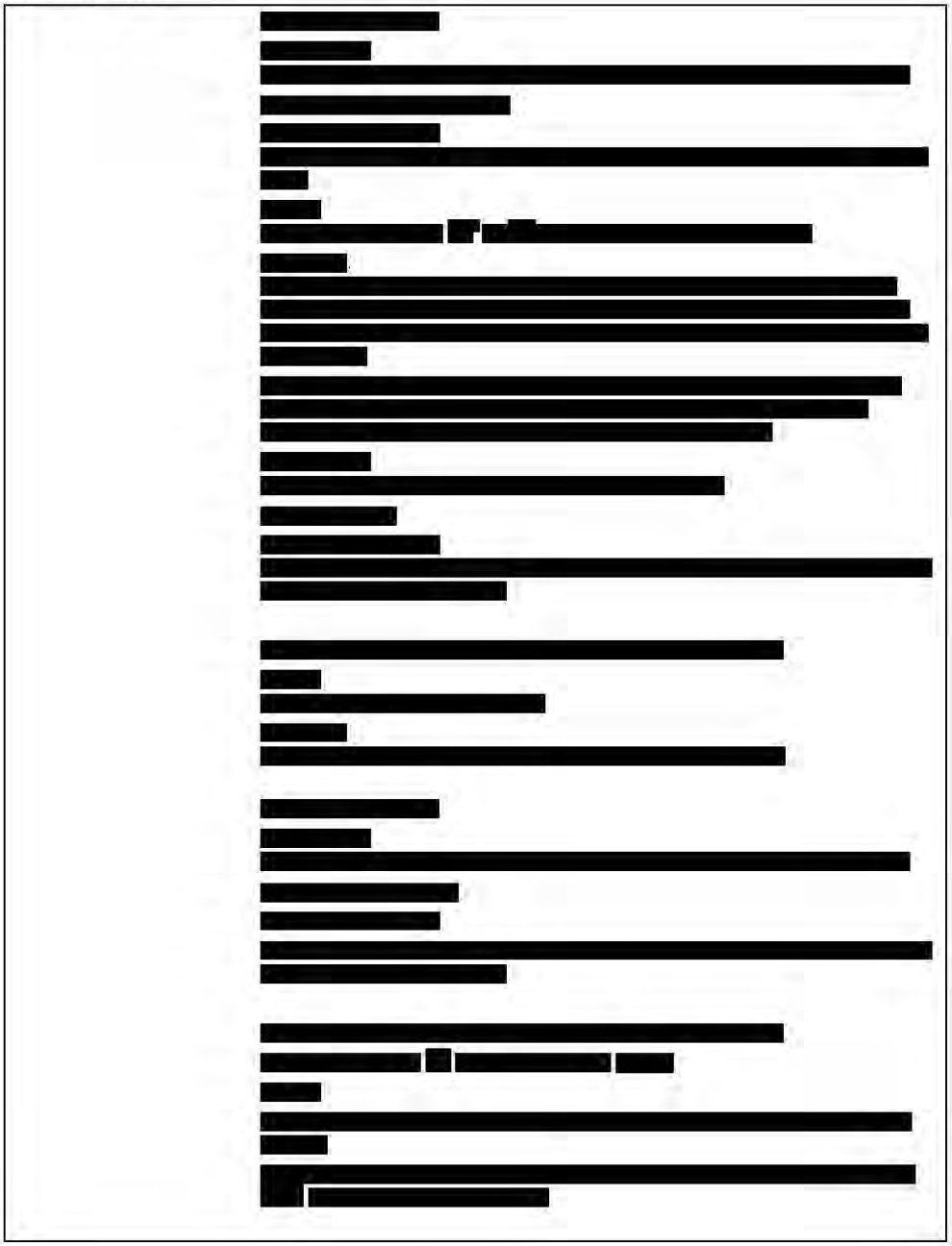
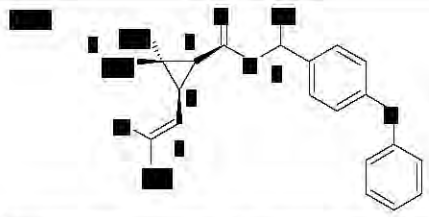
Section A3 **Physical and Chemical Properties of Active Substance**

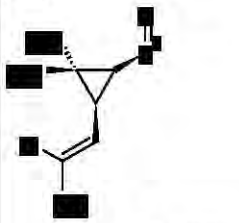
Annex Points IIA, III.3.1.1 to 3.13, Annex Points IIIA, III.1 to 2 and TnsG Chapter 3, Part A, Point 3.6 and Point 3.14

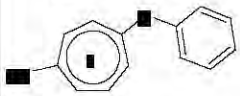


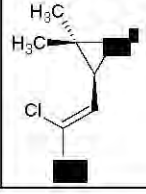
Section A3 Physical and Chemical Properties of Active Substance

Annex Points IIA, III.3.1.1 to 3.13, Annex Points IIIA, III.1 to 2 and TnsG Chapter 3, Part A, Point 3.6 and Point 3.14









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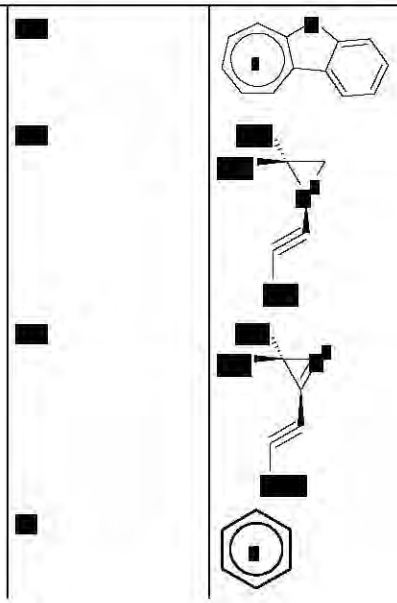
Section A3 Physical and Chemical Properties of Active Substance

Annex Points IIA, III.3.1.1 to 3.13, Annex Points IIIA, III.1 to 2 and TnsG Chapter 3, Part A, Point 3.6 and Point 3.14



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

Annex Points IIA, III.3.1.1 to 3.13, Annex Points IIIA, III.1 to 2 and TnsG Chapter 3, Part A, Point 3.6 and Point 3.14

[redacted]

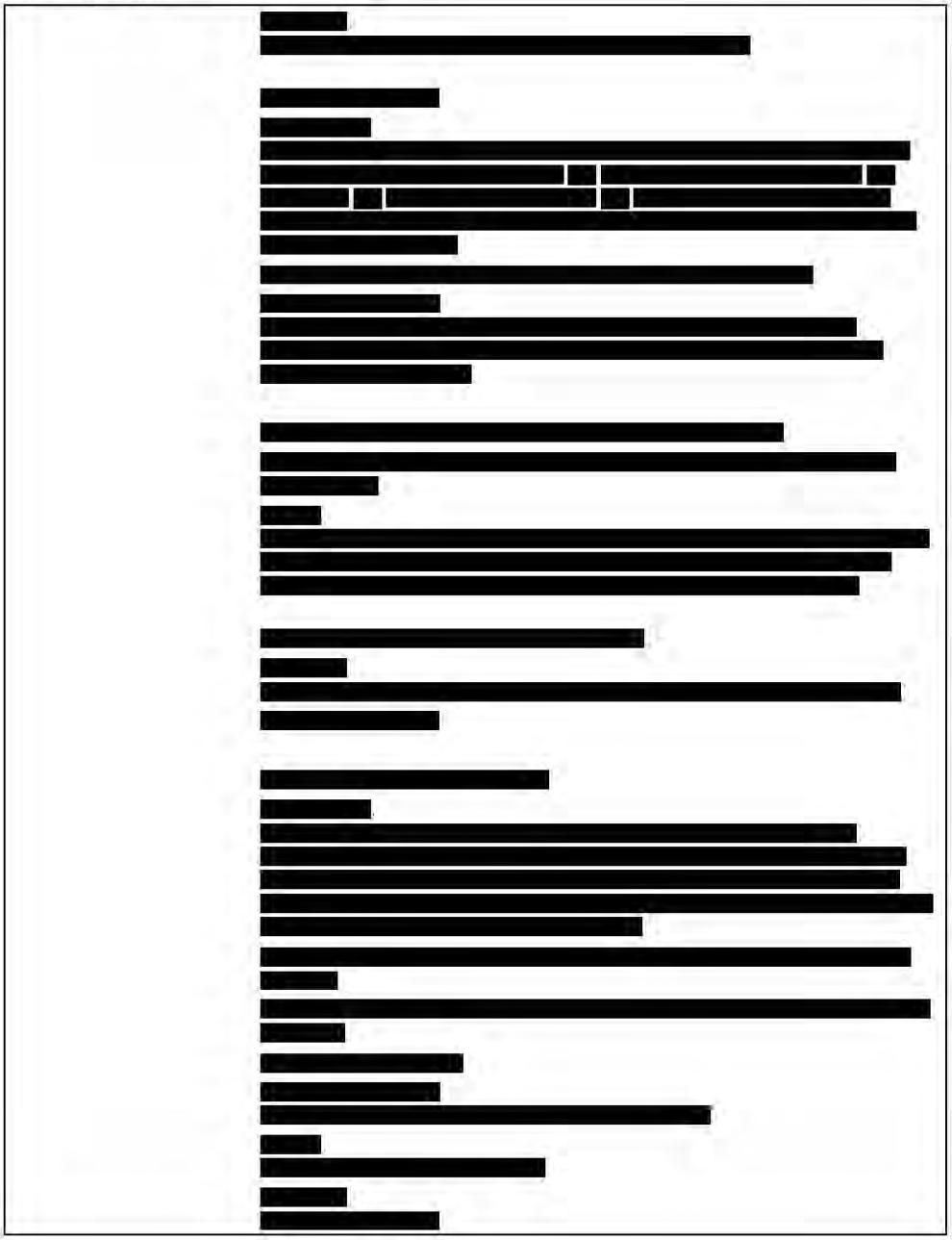
rted but the measurement is assumed to have been done with deionised water.

Borttaget: September

Borttaget: 0

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

Annex Points IIA, III.3.1.1 to 3.13, Annex Points IIIA, III.1 to 2 and TnsG Chapter 3, Part A, Point 3.6 and Point 3.14

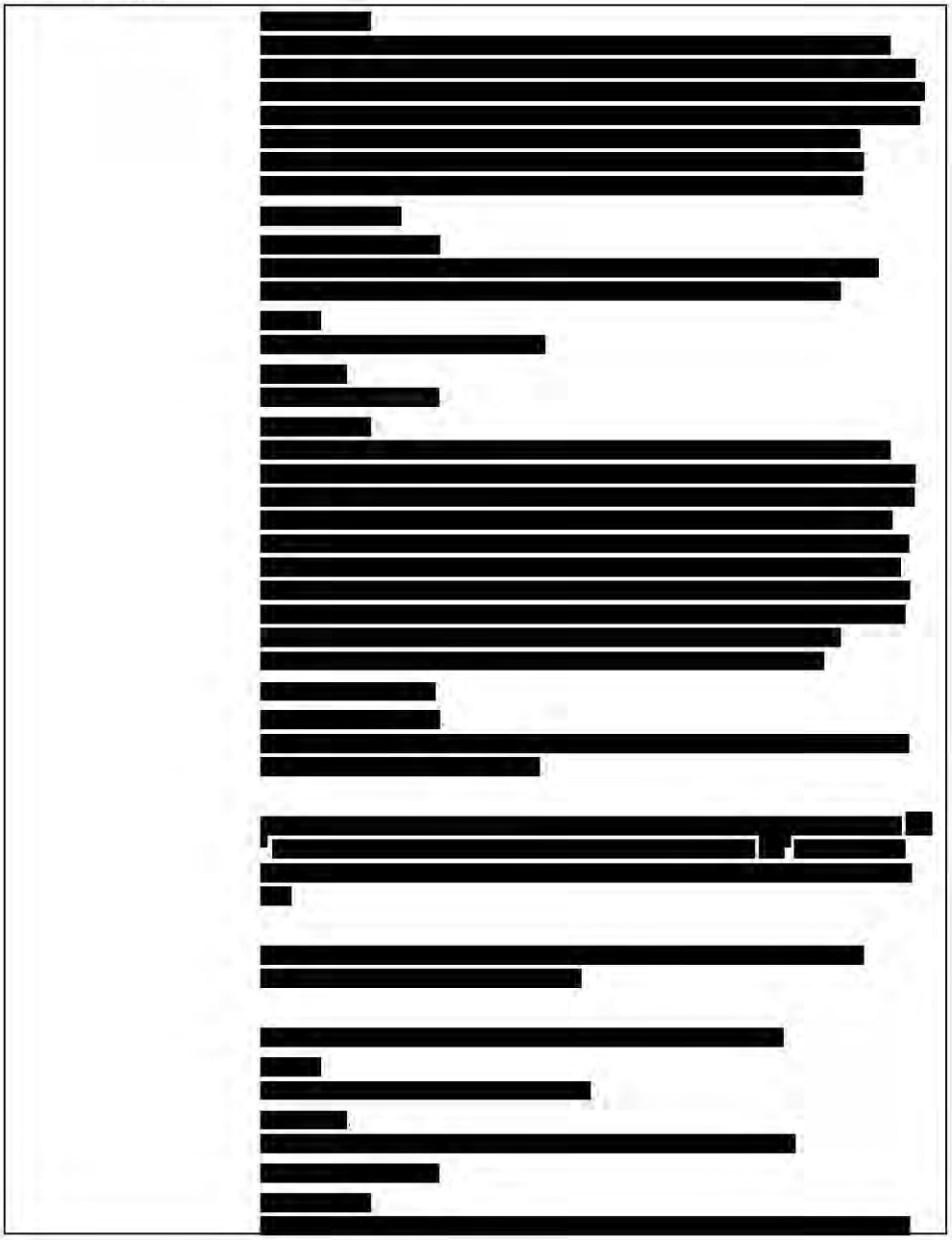


Borttaget: September

Borttaget: 0

Section A3 Physical and Chemical Properties of Active Substance

Annex Points IIA, III.3.1.1 to 3.13, Annex Points IIIA, III.1 to 2 and TnsG Chapter 3, Part A, Point 3.6 and Point 3.14



Borttaget: September

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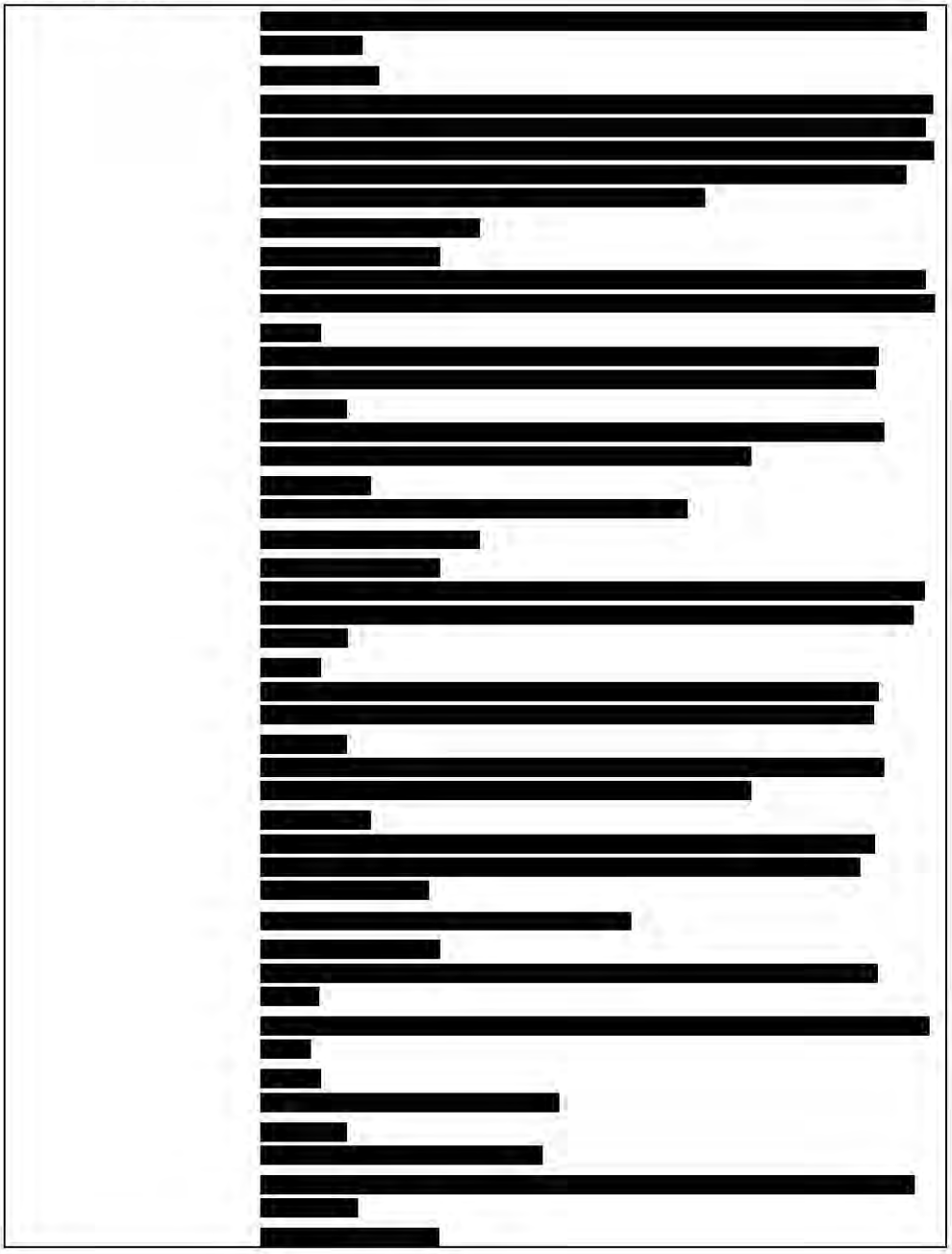
Section A3 **Physical and Chemical Properties of Active Substance**

Annex Points IIA, III.3.1.1 to 3.13, Annex Points IIIA, III.1 to 2 and TnsG Chapter 3, Part A, Point 3.6 and Point 3.14



Borttaget: September

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Section A3 Physical and Chemical Properties of Active Substance

Annex Points IIA, III.3.1.1 to 3.13, Annex Points IIIA, III.1 to 2 and TnsG Chapter 3, Part A, Point 3.6 and Point 3.14

[redacted]

Borttaget: September

Borttaget: 0

Reference list of studies submitted (by Section No.)

Section No. / Reference No.	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes / No)	Owner
IIIA 3.1.1(01)	Wollerton C.	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
IIIA 3.1.2(01)	Wollerton C.	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
IIIA 3.1.3(01)	Jackson W A	1994	Determination of Some Physico-Chemical Properties of *Lambda*-cyhalothrin TGAI. Zeneca Fine Chemicals Report number HT 94/140. R1C0719 28/9/1994 GLP, Not Published	Y	SYN
IIIA 3.2(01)	Wollerton C.	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
IIIA 3.3.1(01)	Wollerton C.	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
IIIA 3.3.2(01)	Wollerton C.	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
IIIA 3.3.3(01)	Wollerton C.	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
IIIA 3.4(01)	Wollerton C.	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN

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Borttaget: 0

Section No. / Reference No.	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes / No)	Owner
IIIA 3.5(01)	Wollerton C.	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
IIIA 3.6(01)	Wollerton C.	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
IIIA 3.7(01)	Wollerton C.	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
IIIA 3.9(01)	Wollerton C.	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
IIIA 3.10(01)	Wollerton C.	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
IIIA 3.10(02)	Jackson W A	1994	Determination of Some Physico-Chemical Properties of *Lambda*-cyhalothrin TGAI. Zeneca Fine Chemicals Report number HT 94/140. R1C0719 28/9/1994 GLP, Not Published	Y	SYN
IIIA 3.11(01)	Jackson W A	1994	Determination of Some Physico-Chemical Properties of *Lambda*-cyhalothrin TGAI. Zeneca Fine Chemicals Report number HT 94/140. R1C0719 28/9/1994 GLP, Not Published	Y	SYN
IIIA 3.12(01)	Jackson W A	1994	Determination of Some Physico-Chemical Properties of *Lambda*-cyhalothrin TGAI. Zeneca Fine Chemicals Report number HT 94/140. R1C0719 28/9/1994 GLP, Not Published	Y	SYN

Borttaget: September

Borttaget: 0

Section No. / Reference No.	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes / No)	Owner
IIIA 3.13(01)	Wollerton C.	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
IIIA 3.15(01)	Jackson W A	1994	Determination of Some Physico-Chemical Properties of *Lambda*-cyhalothrin TGAI. Zeneca Fine Chemicals Report number HT 94/140. R1C0719 28/9/1994 GLP, Not Published	Y	SYN
IIIA 3.16(01)	Jackson W A	1994	Determination of Some Physico-Chemical Properties of *Lambda*-cyhalothrin TGAI. Zeneca Fine Chemicals Report number HT 94/140. R1C0719 28/9/1994 GLP, Not Published	Y	SYN

Borttaget: September

Borttaget: 0

Reference list of studies submitted (by Author)

Author(s)	Section No. / Reference No.	Year	Title Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes / No)	Owner
Jackson W A	IIIA 3.1.3(01)	1994	Determination of Some Physico-Chemical Properties of *Lambda*-cyhalothrin TGAI. Zeneca Fine Chemicals Report number HT 94/140. R1C0719 28/9/1994 GLP, Not Published	Y	SYN
Jackson W A	IIIA 3.10(02)	1994	Determination of Some Physico-Chemical Properties of *Lambda*-cyhalothrin TGAI. Zeneca Fine Chemicals Report number HT 94/140. R1C0719 28/9/1994 GLP, Not Published	Y	SYN
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Jackson W A	IIIA 3.12(01)	1994	Determination of Some Physico-Chemical Properties of *Lambda*-cyhalothrin TGAI. Zeneca Fine Chemicals Report number HT 94/140. R1C0719 28/9/1994 GLP, Not Published	Y	SYN
Jackson W A	IIIA 3.15(01)	1994	Determination of Some Physico-Chemical Properties of *Lambda*-cyhalothrin TGAI. Zeneca Fine Chemicals Report number HT 94/140. R1C0719 28/9/1994 GLP, Not Published	Y	SYN
Jackson W A	IIIA 3.16(01)	1994	Determination of Some Physico-Chemical Properties of *Lambda*-cyhalothrin TGAI. Zeneca Fine Chemicals Report number HT 94/140. R1C0719 28/9/1994 GLP, Not Published	Y	SYN
Wollerton C.	IIIA 3.1.1(01)	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN

Borttaget: September

Borttaget: 0

Author(s)	Section No. / Reference No.	Year	Title Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes / No)	Owner
Wollerton C.	IIIA 3.1.2(01)	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
Wollerton C.	IIIA 3.2(01)	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
Wollerton C.	IIIA 3.3.1(01)	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
Wollerton C.	IIIA 3.3.2(01)	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
Wollerton C.	IIIA 3.3.3(01)	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
Wollerton C.	IIIA 3.4(01)	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
Wollerton C.	IIIA 3.5(01)	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
Wollerton C.	IIIA 3.6(01)	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN

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Author(s)	Section No. / Reference No.	Year	Title Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes / No)	Owner
Wollerton C.	IIIA 3.7(01)	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
Wollerton C.	IIIA 3.9(01)	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
Wollerton C.	IIIA 3.10(01)	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN
Wollerton C.	IIIA 3.13(01)	1984	PP321: Physico-Chemical Data File. ICI plant protection division Report No. RJ0366B, 18/07/1984 GLP, Not Published	Y	SYN

Competent Authority Report

According to Directive 98/8/EC

lambda-Cyhalothrin

CAS 91465-08-6

Active substance in Biocidal Products, Product Type 18 (Insecticide)

Notifier: Syngenta European Center

DOCUMENT III-A

Section 5: Effectiveness against target organisms and intended uses

Rapporteur Member State: Sweden

Final CAR, May 2011

Borttaget: Draft f

Borttaget: September

Borttaget: 2010

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

For official use only

5.1 Function

Lambda-cyhalothrin is a synthetic pyrethroid acting as an insecticide.

5.2 Organism(s) to be controlled and products, organisms or objects to be protected

5.2.1 Organism(s) to be controlled

Musca domestica L (house fly)

Blatta Orientalis (Oriental cockroach)

*Blatta Germanica (*German cockroach)

Ants

Dermanyssus gallinae, (poultry mite)

Mosquitoes

General nuisance pest

5.2.2 Products, objects or organisms to be protected

Lambda-cyhalothrin is used in or around animal premises for the protection of animals, as well as in and around factories, hospitals, homes to protect man.

5.3 Effects on target organisms, and likely concentration at which the active substance will be used

5.3.1 Effects on target organisms

The principal effect of pyrethroids is to delay sodium channel closure on nerve axons, this in turn delays membrane repolarisation following an action potential. This leads to spontaneous repetitive nerve firing and convulsions.
The visible symptoms of pyrethroid poisoning are typically a lack of co-ordination of movements and normal behaviour (often termed the "knockdown or kd effect"), the appearance of convulsive activity, regurgitation of alimentary canal contents, and ultimately paralysis and death. Symptoms which inhibit feeding and movement occur within minutes of dosing, but death due to dehydration and other secondary effects may take up to 24 hours.

As a residual application, *Lambda*-cyhalothrin can give complete control of *Musca domestica* for at least 16-17 weeks.

The threshold concentration of *lambda*-cyhalothrin required to effect a range of pest species has been determined through a number of studies. The results of dose response assays have demonstrated *lambda*-cyhalothrin to be highly potent insecticide. These results are summarised below: X1

Pest species	Test type	LC_{50} (ppm)	LC_{90} (ppm)	Reference
Musca domestica	Topical	8.7	16.56	IIIA 5.3(01)

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(house fly)	application			
Blatta Germanica (German cockroach)	Topical application	6.24	14.89	IIIA 5.3(02)
Aedes aegypti (yellow fever mosquito)	Topical application	0.086[1] 0.109[2]	1.19[1] 1.345[2]	IIIA 5.3(03)

[1] = assessed 1 day after treatment.
[2] = assessed 2 days after treatment.

5.3.2 Likely concentrations at which the active substance will be used

Target	Amount of product per 5 liters water (ml)	Area treated (m2)	Concentration (mg a.i./m2)
Flies	50	200	25
Other insects and poultry mites	50	As crack and crevice treatment	25

X

The use of residual surface applications of insecticide is one of the most effective and versatile means of controlling insect pests. The surfaces on which insecticides are applied vary greatly, but are typically porous which can adversely affect the biological availability of insecticides. Other surfaces may, in addition, be chemically reactive and denature the active substance compromising its persistence. For this reason, the application rate required to achieve high levels of residual control over a number of months is often greater than the amount required to kill the target pest.

Despite the highly potent nature of *lambda*-cyhalothrin, a rate of 25 mg a.s./m^2 is required to achieve 4 months residual control of *Aedes aegypti* when applied to a porous surface (see results of study summarised in IIIB1 5.10.2(12)/IIIB2 5.10.2(11)). When applied at the lower rates the length of residual control is reduced.

5.4 Mode of action (including time delay)

5.4.1 Mode of action

Oxyfly/Demand/Icon® CS is a formulation containing microcapsules of *lambda*-cyhalothrin suspended in water. The slow release of the active ingredient provides long-lasting residual control up to 4 months depending on substrate and dose rate. Oxyfly/Demand/Icon® CS (capsule suspension) is a modern, high-technology insecticide developed for the most demanding pest controllers.

Oxyfly/Demand/Icon® CS formulations contains 100 g/L *lambda*-cyhalothrin to control a broad range of insect pests, both indoors and outdoors. These unique water-based formulations avoid the use of organic solvents and are among the most powerful insecticides available for the control of public health pests; such as mosquitoes, flies and other flying insects, and cockroaches, ants and other crawling insects and poultry mites.

X2

XX

Oxyfly/Demand/Icon® CS uses state-of-the-art microcapsule technology to give a product that combines the ease of use of an emulsifiable concentrate with the long-lasting residual strength of a wettable powder. Tiny droplets of *lambda*-cyhalothrin are contained within microcapsules in a creamy white suspension. In use, the products are diluted in water and applied to surfaces using conventional compression sprayer equipment. After spraying, the water evaporates to leave the microcapsules on treated surfaces. The active ingredient remains isolated from the environment within the microcapsules and this protection provides extended duration of effect, especially on challenging surfaces such as cement. Insects moving over treated surfaces pick up microcapsules on their bodies. Once attached to the insects, the active ingredient rapidly moves out of the capsule and into the insect, providing a

rapid knockdown effect followed by quick kill. X3

5.4.2 Time delay

Depending on the applied surface and concentration, from 60 minutes up to 24 hours.

5.5 Field of use envisaged

Insecticide (PT 18), residential use.

Details of the intended fields of use, method of application, rates and timings for products containing *lambda*-cyhalothrin are given in IIIB1 5.1 to 5.4 (OXYFLY 10CS) and IIIB2 5.1 to 5.4 (Demand/ICON 10CS).

5.6 User: industrial, professional, general public (non-professional)

Lambda-cyhalothrin containing products are used :

- for insecticidal uses in and around animal premises by professional applicators, e.g. farmers.
- for indoor (*in situ*) uses against general nuisance pests in hotels, hospitals, etc. by professional applicators.
- for indoor and outdoor perimeter (*in situ*) uses against general nuisance pests in home by general public. X4

5.7 Information on the occurrence or possible occurrence of the development of resistance and appropriate management

5.7.1 Development of resistance

One of several known causes of resistance to pyrethroids is genetic mutation leading to altered structure or expression of sodium channels. Molecular biologists have recently linked pyrethroid resistance to a sodium channel gene locus in the housefly, fruit fly and tobacco budworm. [References: (1) Huang J.; Kristensen M.; Qiao C-l.; Jespersen J.B. (2004). Frequency of *kdr* Gene in House Fly Field Populations: Correlation of Pyrethroid Resistance and *kdr* Frequency. *Journal of Economic Entomology*, Volume 97, Number 3, June 2004, pp. 1036-1041(6). (2) Liu Z, Tan J, Valles SM, Dong K (2003). Synergistic interaction between two cockroach sodium channel mutations and a tobacco budworm sodium channel mutation in reducing channel sensitivity to a pyrethroid insecticide. *Insect Biochem Mol Biol.* 2002 Apr;32(4):397-404. (3) Vector resistance to pesticides. 15th report of the WHO expert committee on vector biology and control, p.35ff, Geneva 1992.]

Resistance to pyrethroid insecticides has occurred in a number of insects around the world. In many cases, key species such as house flies and cockroaches, at least somewhere within their range, developed resistance to representatives of all the chemical classes that have been used for their control (Keiding, 1999; Scott *et al.*, 1990). This does not imply widespread failure of these product groups throughout a region. *Lambda*-cyhalothrin remains highly effective for control of a wide range of pests in almost all areas. The most effective means to prevent resistance is to adopt a pro-active approach that seeks to prevent over-use or mis-use. Where resistance problems do arise it is essential to implement a management programme

that reduces selection pressure and allows continued use of favoured products such as *lambda*-cyhalothrin even though resistance may have occurred. The strategies outlined below are designed to prevent or delay the development of resistance and to restore susceptibility should resistance occur. [References: (1) Keiding, J. (1999). Review of the global status and recent development of insecticide resistance in field populations of the housefly, *Musca domestica* (Diptera:Muscidae). *Bull. Ent. Res. 89 (1) S7-S67.* (2) Scott J.G., Cochran D.G. and Siegfried B.D. (1990). Insecticide toxicity, synergism, and resistance in the German Cockroach (Dictyoptera: Blattellidae). *J. Econ. Entomol. 83: 1698-1703.*]

5.7.2 Management strategies

In areas where the presence of tolerance strains is confirmed, it may be necessary to implement an Insecticide Resistance Management (IRM) strategy within an Integrated Pest Management (IPM) programme. Effective programmes of this type incorporate and combine the use of pyrethroids with other effective insecticidal compounds from alternative mode of action groups as recommended by the Insecticide Resistance Action Committee (IRAC).

An effective and sustainable IRM strategy consists of a combination of the tactics outlined below. The overriding principle is to reduce selection pressure and to adopt a preventative and pro-active, integrated approach to insect control.

- Consult a local agricultural advisor in the area for up-to-date recommendations and advice on IPM and IRM programmes.
- Include effective cultural and biological control practices that work in harmony with effective IRM programmes. Adopt all non-chemical techniques known to control or suppress pest populations, including good hygiene and sanitation.
- Where possible select insecticides and other pest management tools which preserve beneficial insects.
- Use products at their full recommended doses. Reduced (sub-lethal) doses quickly select populations with average levels of tolerance, whilst dose that are too high impose excessive selection pressures.
- Appropriate, well-maintained equipment should be used to apply insecticides. Recommended water volumes, spray pressures and optimal temperatures should be used to obtain optimal coverage.
- Follow label recommendations or local expert advice for use of alternations or sequences of different classes of insecticide with differing modes of action as part of an IRM strategy.
- Where there are multiple applications per year, alternate products of different classes.
- In the event of a control failure, do not reapply the same insecticide but change the class of insecticides to one having a different mode of action and to which there is no [locally] known cross-resistance.
- Mixtures may offer a short-term solution to resistance problems, but it is essential to ensure that each component of a mixture belongs to a different insecticide class, and each is used at an effective dose.

• Consideration should be given to monitoring for the incidence of resistance in the most commercially important situations and gauge levels of control obtained. • Withholding use of a product to which resistance has developed until susceptibility returns may be a valid tactic if sufficient alternatives chemical classes remain to provide effective control. **5.8 Likely tonnage to be placed on the market per year**	X5

	Evaluation by Competent Authorities
98/8 Doc IIIA section No. 5.1-5.8	**Effectiveness Against Target Organisms And Intended Uses**
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	May 2007
Discussion	[redacted]
Conclusion	[redacted]

Borttaget: September
Borttaget: 2010

Reliability	[redacted]
Acceptability	

Table A 5.3-1: Summary table of experimental data on the effectiveness of the active substance against target organisms at different fields of use envisaged, where applicable

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference[#]
Insecticide	PT18	*Lambda*-cyhalothrin active substance as given in section 2.	House fly *Musca domestica*	1 µL test substance was applied to the pronotum of each insect (3 replicates; 10 female adult insects/replicate). Mortality was assessed 2 days after treatment. LC_{50} and LC_{90} values were estimated using Logit analysis.	Not stated.	LC_{50} = 8.7 ppm LC_{90} = 16.56 ppm	Weeks et al. (2002a). IIIA 5.3(01)
Insecticide	PT18	*Lambda*-cyhalothrin active substance as given in section 2.	German cockroach *Blatella germanica;* American cockroach Periplaneta *americana*	1 µL test substance was applied to each insect (adult males). Mortality was assessed 2 days after treatment. LC_{50} and LC_{90} values were estimated using Logit analysis.	Not stated.	German cockroach: LC_{50} = 6.24 ppm LC_{90} = 14.89 ppm American cockroach: LC_{50} = 20-30 ppm LC_{90} = 30-40 ppm	Weeks et al. (2002b). IIIA 5.3(02)

<table>
<tr><th>Function</th><th>Field of use envisaged</th><th>Test substance</th><th>Test organism(s)</th><th>Test method</th><th>Test conditions</th><th>Test results: effects, mode of action, resistance</th><th>Reference#</th></tr>
<tr><td>Insecticide</td><td>PT18</td><td>Lambda-cyhalothrin active substance as given in section 2.</td><td>Yellow fever mosquito Aedes aegypti</td><td>Topical application

1 µL test substance was applied to the pronotum of each insect (non-blood fed adult females).

Mortality was assessed 1 and 2 days after treatment.

Residual assay

Insects (non-blood fed adult females) were exposed to treated surfaces (glazed ceramic tile, non-glazed ceramic tile and filter paper) treated at 0.3, 3 and 30 mg/m^2 for 60 minutes.

Knockdown was assessed after 1 hour and mortality was assessed after 24 hours.</td><td>Not stated.</td><td>Topical application

1 DAT:
LC_{50} = 0.086 ppm
LC_{90} = 1.19 ppm

2 DAT:
LC_{50} = 0.109 ppm
LC_{90} = 1.345 ppm

Residual assay
<table>
<tr><th>Surface</th><th colspan="3">% Mortality* 1 hour knockdown</th><th colspan="3">% Mortality* 24 hour mortality</th></tr>
<tr><th>Dose (mg/m^2):</th><th>0.3</th><th>3</th><th>30</th><th>0.3</th><th>3</th><th>30</th></tr>
<tr><td>Glazed tile (non-porous)</td><td>55</td><td>100</td><td>100</td><td>90</td><td>100</td><td>100</td></tr>
<tr><td>Non-glazed tile (porous)</td><td>5</td><td>70</td><td>100</td><td>30</td><td>100</td><td>100</td></tr>
<tr><td>Filter paper</td><td>0</td><td>90</td><td>100</td><td>5</td><td>60</td><td>100</td></tr>
</table>
*Values are presented graphically in the report and so the numerical values presented are approximate.</td><td>Weeks et al. (2002c). IIIA 5.3(03)</td></tr>
</table>

References: Refer to main reference list for full details.

Competent Authority Report

According to Directive 98/8/EC

lambda-Cyhalothrin

CAS 91465-08-6

Active substance in Biocidal Products, Product Type 18 (Insecticide)

Notifier: Syngenta European Center

DOCUMENT III-A

Section 6: Toxicological and metabolic studies

Addendum: Studies submitted January -February 2008 and January 2010

Rapporteur Member State: Sweden

Final CAR, September 2010

Borttaget: Draft f

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

1. NEUROTOXICITY

98/8 Doc IIIA section No. 6.9	Neurotoxicity studies	Official use only

Title:	**Second Preliminary Developmental Neurotoxicity Study in Rats**	
Lab Report Number:	[redacted]/RR0812/Regulatory/Report	
Authors:	[redacted]	
Test Substance:	*Lambda*-cyhalothrin (otherwise known as PP321) Purity [redacted]% w/w	X1
Species:	Rat	
Method:	Not applicable	X2
Date of Report:	2001	
Published:	No	
GLP:	Yes	

Material and Methods:	Groups of 10 time-mated female Alpk: APfSD (Wistar-derived) rats were fed diet containing 0 (control), 25, 60 or 150ppm *lambda*-cyhalothrin. The dosing period commenced on gestation day 7 and finished on lactation day 22. The dams were allowed to rear the ensuing litters to lactation day 22. Satellite groups of 6 time-mated female rats were also fed diet containing 25, 60 or 150ppm *lambda*-cyhalothrin. The following endpoints were evaluated for maternal animals: clinical condition, bodyweight and food consumption throughout gestation and lactation. The following endpoints were measured for the offspring: clinical condition, bodyweight, number and sex. Blood samples were collected from the maternal animals and pups in the satellite groups during the study and plasma levels of *lambda*-cyhalothrin were determined.	X3 X4
Results:	Maternal animals in the 150ppm group had significantly lower (6%) bodyweights during gestation and food consumption was also lower during this phase. On *post partum* day 1, bodyweights of male and female pups were significantly lower in the 150ppm group, but the growth of these pups thereafter was not different from control animals. All other endpoints evaluated during the in-life	

	phase were unaffected by treatment (e.g. clinical condition, bodyweights and food consumption during lactation, pup survival and clinical condition, litter size, and sex distribution). *Lambda*-cyhalothrin was detected in the plasma of maternal animals and pups at all time points evaluated. In general, plasma levels increased in both pups and dams with increasing dietary concentration of *lambda*-cyhalothrin.	X5 X6
Conclusion:	Dose levels of 0, 25, 60 and 150ppm *lambda*-cyhalothrin in the diet are considered to be acceptable for the main developmental neurotoxicity study in the rat.	

Reliability Indicator	1	
Data Protection Claim	Yes	

	Evaluation by Competent Authorities
98/8 Doc IIIA section No. 6.9/ 03	**Preliminary Developmental Neurotoxicity Study in Rats**
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	March 2008
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]y)
Acceptability	[redacted]
Remarks	[redacted]

2. GENOTOXICITY

98/8 Doc IIIA section No. 6.1.1 / 02	Official use only

Title:	**Induction of micronuclei by lambda-cyhalothrin in Wistar rat bone marrow and gut epithelial cells**	
Lab Report Number:	not known	
Authors:	[redacted]	
Test Substance:	Unspecified KARATE formulation, source [redacted], containing 2.5% lambda-cyhalothrin w/w formulated in aqueous propylene glycol	
Species:	Wistar rats	
Method:	Bone marrow and gut epithelial cell micronucleus assay	
Date of Report:	Accepted for publication 8 February 2005	
Published:	Mutagenesis vol. 20 no. 2 pp. 125--129, 2005	
GLP:	not known	

Material and Methods:	Female Swiss albino rats (Wistar rats) [age 6-8 weeks, 180-200 g] four animals/dose level were used in this study. The highest dose was set at 6.12 mg/kg body wt i.e. 1% of the LD50 dose, the lowest dose was determined to be 0.8 mg/kg. KARATE was diluted with isotonic saline as required and was administered by gavage at doses of 0.8, 3.06 and 6.12 mg/kg body wt (0.02, 0.077 and 0.153 mg/kg of LCT, respectively), one dose per 48 h given for 13 days (total 7 doses/animal). Mitomycin C (MMC) (2 mg/ kg), as a single i.p. dose, was used as a positive control. The positive control and untreated control rats were treated identically with equal volumes of normal saline. In vivo gut MN test Animals were killed by cervical dislocation and colons excised and flushed free of faeces with phosphate-buffered saline (PBS). The colon was averted on a glass rod and placed in trypsin-EDTA solution at 30°C for 15 min. The crypts were isolated from the colon by vibrating the glass rod for 5 min then dispersed into single cells by pipetting with Pasteur pipettes. The cells were collected by centrifugation at 84 ×g for 10 min, re-suspended in a small amount of PBS, and then fixed in methanol : acetic acid (3:1, v/v) (Carnoy's fixative). Cells were re-suspended in a small amount of fresh fixative, dropped onto clean slides,	X1

	allowed to dry and stained with May-Grunwald and Giemsa protocol. Slides were scored at a magnification of 1000× using a light microscope. At least 1000 intact cells were analyzed per animal for the presence or absence of MN. To determine the cytotoxicity of Karate on the gut epithelial cells, binucleated cells were counted in 1000 cells within the crypt of colon. *In vivo* bone marrow MN test Rats were killed by cervical dislocation 30 h after the last treatment. The frequency of micronucleated erythrocytes in femoral bone marrow was evaluated. Bone marrow was flushed out from both femora using 1 ml of foetal calf serum and centrifuged at 336 ×g for 10 min. Evenly spread bone marrow smears were stained using the May-Grunwald and Giemsa protocol. Slides were scored at a magnification of 1000× using a light microscope. For the analysis of MN, 2000 polychromatic erythrocytes (PCEs) per animal were scored to calculate the MN frequencies, and 200 erythrocytes (immature and mature erythrocytes) were examined to determine the ratio of PCE to normochromatic erythrocytes (NCEs). The arc-sin square root transformation was applied to all the data. Statistical analyses were performed by the repeated measure test. Multiple comparisons were analyzed using the least significant difference (LSD) test. $P < 0.05$ was considered as the level of significance, the Pearson correlation test was used.	
Results:	Karate treatment caused significant dose-related increases in the MN formation in bone marrow and colonic crypt epithelial cells ($P < 0.001$). 0.8 mg/kg dose of Karate similarly affected both the bone marrow (3.50±0.28 MN (‰±SE)) and gut epithelial cells 4.25±0.25). 3.06 and 6.12 mg/kg doses of Karate caused a larger increase in MN frequency in gut epithelial cells (6.75±0.25 and 8.25±0.47) than in bone marrow (4.00±0.40 and 6.00±0.40). While there was a significant difference among all doses in gut epithelial cells, there was no difference between the 0.8 and 3.06 mg/kg doses in bone marrow cells. The cytotoxic effect of Karate in both bone marrow and gut epithelial cells was tested. Karate caused a decrease in the proportion of PCEs (in PCEs 1 NCEs) in bone marrow. The decrease in the number of PCEs was dose-dependent (correlation coefficient: $r = -0.87$). To determine the cytotoxic effects of Karate on gut epithelial cells, mitotic index values were calculated in 1000 gut epithelial cells. LCT induced a statistically significant decrease in the values of mitotic index compared with negative controls ($P < 0.001$). There was a significant difference between Karate doses	X2

	and negative controls for binucleated cell frequency. Statistical analyses showed that there was a correlation between Karate doses and the frequency of binucleated cells (correlation coefficient: r = 0.81). Nuclear changes (karyorrhexis KR, karyolysis KL and binucleated cells) were scored in 1000 epithelial cells in the gut, there was a statistically significant dose-dependent increase in nuclear changes. The frequency of KR increased with dose of Karate (P = 0.05), except at the doses of 0.8 and 3.06 mg/kg (Table III). The frequency of KL increased with dose (P = 0.05), except at 0.8 mg/kg. The study implies that oral administration of Karate has an inhibiting potential on erythropoiesis in bone marrow but also a clastogenic effect in both bone marrow and gut epithelial cells.	
Conclusion:	This study used an unusual dosing regimen, & had some deficiencies in study design and conduct. In particular, the group size is smaller than the recommended 5 for studies of this type, and only one sex has been tested, with no justification for choice of that sex. The stain used is also not generally recommended for rat studies, as it can stain mast cell granules which are then falsely counted as micronuclei; thus the MN data should be viewed as unreliable. It is also not known if the study was conducted to GLP. The data appear to show genotoxic and cytotoxic effects of Karate in both bone marrow and gut epithelial cells. Karate appeared to elevate the MN frequency in both tissues, and induced a decrease in the number of PCEs in bone marrow in a dose dependent manner indicating it to be an inhibitor of mitosis. In addition to binucleus formation, Karate induced not only a decrease in mitotic index but also apoptosis, measured by an increase in the frequency of KR and KL in gut. Karate had similar cytotoxic effects in both bone marrow and gut epithelial tissue. Overall, these data indicate that Karate may have cytotoxic and genotoxic effects and also antimitotic and apoptotic effects on gut epithelial cells.	X3

Reliability Indicator	4?	
Data Protection Claim	No	

	Evaluation by Competent Authorities
98/8 Doc IIIA section No. 6.6.5(01)/ 98/8 Doc IIIB section No. 6.7	**Second in vivo mutagenicity study/Further Health related studies**
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	April 2007
Materials and Methods	[redacted]

Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

3. DERMAL ABSORPTION

98/8 Doc IIIA section No. 6.1.2 / 01	Metabolism - Human	Official use only

Title:	**The Metabolism and Pharmacokinetics of *Lambda*-Cyhalothrin in Man**	
Lab Report Number:	Laboratory Report No. [redacted]/P/4208	
Authors:	[redacted]	
Test Substance:	*Lambda*-cyhalothrin (otherwise known as PP321) Purity [redacted]%	
Species:	Humans	
Method:	OPPTS 870.7485; OECD 417, 12 Nohsan No 8147 (2000).	
Date of Report:	1994	
Published:	No	
GLP:	Yes	

Material and Methods:	The purpose of the study was to assess the oral and dermal metabolism of *lambda*-cyhalothrin in humans. The study design involved a dermal tolerance test to screen out any individuals who might be particularly susceptible to a skin reaction (paraesthesia) which is elicited by pyrethroids (phase I). Six male volunteers (healthy, males aged between 23-42 years old) then received an oral dose of *lambda*-cyhalothrin (phase II) and of these 5 subsequently received a dermal dose (phase III) (1 volunteer was withdrawn from the study). Prior to oral and dermal dosing in phases II and III volunteers fasted overnight and refrained from alcohol for a minimum period of 24 hours. Urine was collected the day before dosing. During phase II and III, food and drink intake was standardised. In the dermal tolerance test, a 50 cm^2 area of the central top half of the back was marked out. The dosing solution (0.25 mL containing 1.25 mg *lambda*-cyhalothrin) was applied as a series of drops which were spread evenly over the area. After the application site had dried volunteers put on a cotton T-shirt and the application site was inspected	

	after 1, 3, 7 and 24 hours and any subjective sensations recorded. For oral dosing, volunteers were asked to swallow the capsule with 150 mL water. A light breakfast was provided 1 hour after dosing. Dermal dosing was done as described for the tolerance test, except that a grid of 16 rectangles, each 50 cm^2, was marked on the back using a plastic template. A nominal 0.25 mL containing 1.25 mg of *lambda*-cyhalothrin was applied to each rectangle. Air blown from a hair drier was used to prevent run-off at the edges of the application site. Eight hours after dosing each rectangle was washed individually with a cotton wool swab moistened with 2 mL of 3% Teepol in water. The swabs were pooled and analysed for *lambda*-cyhalothrin. Following the washing procedure, each volunteer was given a loose fitting cotton T-shirt to wear continuously until 24 hours after dosing. The T-shirts were extracted and analysed for *lambda*-cyhalothrin. 10 mL blood samples were collected pre-dose and at 0.5, 1, 2, 3, 4, 5, 6, 8, 10, 12, 24, 31 and 48 hours post-dosing. Plasma and red blood cells were prepared from each sample by centrifugation then stored frozen. Complete urine collections were made for the periods 0-2, 2-4, 4-6, 6-8, 8-10, 10-12, 12-14, 14-24 and then for 12 hour intervals up to 120 hours. Urine volume and pH were recorded and aliquots taken and stored deep frozen until analysis for *lambda*-cyhalothrin and its metabolites. Faeces samples were collected for the periods 0-1, 1-2 and 2-3 days following oral dosing.	
Results:	No clinical signs or symptoms of toxicity were observed in any of the volunteers. Following dermal administration of 20 mg to an area of 800 cm^2 on the back, varying degrees of paraesthesia were experienced by all the volunteers, typically, mild tingling/warm feeling over the middle to the whole of the back, and/or itchiness over the whole back. The paraesthesia effect was amplified when the application area was increased from 50 cm^2 to 800 cm^2 despite the dose per unit area remaining constant. Following dermal administration of *lambda*-cyhalothrin in formulation	

	WF1303 a substantial proportion of the dose (mean 50%, range 38-60%) was recovered from the skin using a mild detergent wash after 8 hours. An average of a further 24% and 4% were recovered in T-shirts worn between 8-24 and 24-48 hours respectively. Overall, an average of 78% of the dose was recovered by these procedures demonstrating that *lambda*-cyhalothrin is quite readily removed from the skin. Of the remaining 22% only a small fraction was absorbed and excreted in urine as the metabolites measured during the study. Urine samples from the dermal phases were not analysed for unchanged *lambda*-cyhalothrin as none had been found in the oral phases of the study. Insufficient absorption took place to enable estimation of urinary elimination half-lives of metabolites following dermal administration. Whilst *lambda*-cyhalothrin and its metabolite TFMCVA are detectable in blood following an oral dose they are very unlikely to be detectable in blood following dermal exposure. Following oral dosing approximately equal amounts of TFMCVA and PBA (3PBA + 40H3PBA) metabolites were excreted with peak excretion rates occurring between 2 and 14 hours after dosing. Based on TFMCVA measurements in urine the average amount of *lambda*-cyhalothrin absorbed was estimated to be 59% (range 50-64%). Unabsorbed *lambda*-cyhalothrin and TFMCVA were detected in faeces but with the exception of one subject these accounted for less than 1.5% of the dose. Trace amounts of *lambda*-cyhalothrin and TFMCVA were detected in plasma. Analysis of the faecal samples indicated that, in the majority of cases minimal amounts of *lambda*-cyhalothrin or its metabolites are excreted by this route. It was not possible to estimate the other metabolites in faecal extracts due to matrix interference.	
Conclusion:	Following dermal dosing of *lambda*-cyhalothrin, concentrations of metabolites were extremely low. Based on TFMCVA excretion in urine the mean amount of *lambda*-cyhalothrin absorbed was estimated to be 0.12% (range 0.04-0.19%).	

Reliability Indicator	1	
Data Protection Claim	Yes	

Evaluation by Competent Authorities	
98/8 Doc IIIA	**Metabolism - Human**

section No. 6.2	
Date	EVALUATION BY RAPPORTEUR MEMBER STATE March 2008
Remarks	[redacted]

98/8 Doc IIIA section No.	6.1.3 / 01	Acute toxicity – Inhalation	Official use only

Title:	***Lambda*-cyhalothrin 100g/L CS Formulation: In Vitro Absorption of *Lambda*-cyhalothrin Through Human Epidermis**	
Lab Report Number:	[redacted]/P/5695	
Authors:	[redacted]	
Test Substance:	*Lambda*-cyhalothrin 100 g/L CS Formulation (freeze protected formulation for agricultural use) (9.7%)	X1
Species:	Human	
Method:	OECD Guideline 428 "Dermal Absorption (human skin)"	
Date of Report:	1997	
Published:	No	
GLP:	Yes	

Material and Methods:	The purpose of the study was to assess the absorption and distribution of *lambda*-cyhalothrin from a nominal 100g/L CS Formulation measured *in vitro* through human epidermis. Epidermal membranes were prepared from human whole skin by heat separation (by immersion in water at 60°C for 40-45 seconds). The integrity of the membranes was checked by measurement of the electrical resistance across the skin. Only those membranes with an acceptable resistance, thereby showing that they were intact, were used on the study. Absorption was measured using glass diffusion cells in which the epidermal sheet forms a horizontal membrane, with 50% ethanol in water as a receptor fluid. Throughout the experiment the receptor fluid was stirred and maintained at 30°C by use of a water bath.	X2

	Both the concentrate and the spray dilution were applied at a dose rate of 10 µL/cm^2 and left unoccluded for the duration of the exposure period (48h). The formulation was applied to the skin membranes as the concentrate and as 0.4g *lambda*-cyhalothrin/L aqueous spray strength dilution. The skin was exposed to the test preparations for 24 hours during which time samples of receptor fluid were taken at recorded intervals to allow adequate characterisation of the absorption profile. Results of the analysis of the samples of receptor fluid collected in the study were expressed as amounts of *lambda*-cyhalothrin in the receptor solution. The absorbed (systemically available) dose is considered to be the test material detected in the receptor fluid.	X3 X4
Results:	The mean absorption rate for *lambda*-cyhalothrin from the concentrate formulation during the first 10h of exposure was 0.018 µg/cm^2/h. This increased to give an essentially unchanging mean rate of 0.036 µg/cm^2/h between 12-48h. In terms of amount of *lambda*-cyhalothrin absorbed during working day periods, a mean of 0.062 µg/cm^2 (0.006% of applied dose) was absorbed by 6h and 0.142 µg/cm^2 (0.013%) by 10h, with 0.613 µg/cm^2 (0.059%) being absorbed over a 24h period. From the spray dilution, no *lambda*-cyhalothrin was detected to have been absorbed during the first 10h of exposure (<0.009 µg/cm^2 ≡ 0.218% of applied dose). After 12h, absorption was just detectable and maintained a rate of 0.001 µg/cm^2/h up to the end of the exposure period (48h), with 0.013 µg/cm^2 (0.315%) being absorbed by 24h. When compared with the absorption rates of other penetrants measured using this *in vitro* technique ([redacted]), the results obtained in this study indicate that *lambda*-cyhalothrin is absorbed very slowly from the CS concentrate formulation and extremely slowly from the 0.4g/L spray dilution through human epidermis. For such a slow penetrant, the relatively high percentage of the dose absorbed from the spray strength dilution (up to 0.315% at 24h) reflects the fact that only a very low dose (4.12 µg *lambda*-cyhalothrin/cm^2) was applied.	
Conclusion:	These data predict that the human dermal absorption of *lambda*-cyhalothrin from normal field exposure to this formulation would be minimal.	X5

Reliability Indicator	1	
Data Protection Claim	Yes	

	Evaluation by Competent Authorities
98/8 Doc IIIB1/B2 section No. 6.2 / 03	**Information on dermal absorption**
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	March 2008
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

4. SHORT-TERM INHALATION TOXICITY

In January 2010, the RMS became aware of a repeated dose inhalation toxicity study that was not included in the dossier submitted for *lambda*-cyhalothrin.
Upon request, this study was submitted and summarised by the applicant.

Section A6.3 / 6.4 / 6.5 **Repeated dose toxicity**

Annex Point IIA6.3 / 6.4 / 6.5

Section 6.3.3 Repeat Dose Inhalation, 21 Days sub-acute inhalation toxicity study in the rat

Official use only

1. REFERENCE

A. Reference

[redacted] 1990, Lambda-cyhalothrin production material: 21 Days sub-acute inhalation toxicity study in the rat, January 1990

B. Data protection

Yes
(indicate if data protection is claimed)

1. Data owner

Syngenta Crop Protection AG

2.

3. Criteria for data

[redacted]

Section A6.3 / 6.4 / 6.5 **Repeated dose toxicity**

Annex Point IIA6.3 / 6.4 / 6.5 *Section 6.3.3 Repeat Dose Inhalation, 21 Days sub-acute inhalation toxicity study in the rat*

protection

2. GUIDELINES AND QUALITY ASSURANCE

A.	**Guideline study**	No. Methods used comparable to OECD 412.	X1
B.	**GLP**	Yes	
C.	**Deviations**	No	X2

3. MATERIALS AND METHODS

A.	**Test material**	Lambda-cyhalothrin production material
1.	**Lot/Batch number**	Batch 367
2.	**Specification**	See section 3.1.2.2
a)	**Description**	Dark brown viscous liquid
b)	**Purity**	Total pyrethroid content: [redacted]% Cis B content: [redacted]%
c)	**Stability**	Not stated
B.	**Test Animals**	
1.	**Species**	Rat
2.	**Strain**	Alpk:APfSD
3.	**Source**	[redacted]
4.	**Sex**	Male & females
5.	**Age/weight at study initiation**	Approximately 8 weeks old at the start of the study. The body weight ranges on day 1 (prior to exposure) of 238 - 297 g for males and 195 - 241 g for females.
6.	**Number of animals per group**	10/sex/dose
7.	**Control animals**	Yes

Section A6.3 / 6.4 / 6.5	**Repeated dose toxicity**
Annex Point IIA6.3 / 6.4 / 6.5	*Section 6.3.3 Repeat Dose Inhalation, 21 Days sub-acute inhalation toxicity study in the rat*

C.	**Administration/ Exposure**	Inhalation
1.	**Duration of treatment**	Other (21 Days)
2.	**Frequency of exposure**	6h/day, 5 days per week for 21 consecutive days (15 exposures)
3.	**Postexposure period**	Other (terminated the day after the last exposure period)
4.	Oral	
a)	**Type**	
b)	**Concentration**	
c)	**Vehicle**	
d)	**Concentration in vehicle**	
e)	**Total volume applied**	
f)	**Controls**	
5.	Inhalation	

Section A6.3 / 6.4 / 6.5		**Repeated dose toxicity**
Annex Point IIA6.3 / 6.4 / 6.5		*Section 6.3.3 Repeat Dose Inhalation, 21 Days sub-acute inhalation toxicity study in the rat*
a)	**Concentrations**	Nominal concentration : 0, 0.3, 3.3, 16.7 µg/L Analytical concentration : 0, 0.21, 2.64, 12.80 µg/L
b)	**Particle size**	MMAD (mass median aerodynamic diameter) [µm] (± GSD (geometric standard deviation) [µm] 0.25 µg/L: 1.91 µm ± 2.24 GSD 2.5 µg/L: 1.48 µm ± 1.82 GSD 15.0 µg/L: 1.47 µm ± 1.68 GSD
c)	**Type or preparation of particles**	Glass concentric jet atomiser with a size-selective cyclone
d)	**Type of exposure**	Nose only
e)	**Vehicle**	
f)	**Concentration in vehicle**	
g)	**Duration of exposure**	Other (6h/day)
h)	**Controls**	Sham exposed
6.	Dermal	
a)	**Area covered**	
b)	**Occlusion**	
c)	**Vehicle**	
d)	**Concentration in vehicle**	
e)	**Total volume applied**	
f)	**Duration of exposure**	
g)	**Removal of test substance**	
h)	**Controls**	
7.	Intraperitoneal/ Intravenous/ Intratracheal instillation	

Section A6.3 / 6.4 / 6.5	**Repeated dose toxicity**	
Annex Point IIA6.3 / 6.4 / 6.5	*Section 6.3.3 Repeat Dose Inhalation, 21 Days sub-acute inhalation toxicity study in the rat*	
a)	**Vehicle**	
b)	**Concentration in vehicle**	
c)	**Total volume applied**	
d)	**Controls**	
D.	**Examinations**	
1.	**Observations**	
a)	**Clinical signs**	yes (approximately every 30 minutes during exposure and following each exposure and also daily on non-exposure days) X3
b)	**Mortality**	yes (daily)
2.	**Body weight**	yes (prior to exposure on day 1, 2 and 3 (males), 1, 2 and 5(females) and on days 7 and 15. Also weighed on non-exposure days 11 and 18 and prior to post mortem on day 22)
3.	**Food consumption**	yes (weekly)
4.	**Water consumption**	no
5.	**Ophthalmoscopic examination**	yes (Following exposure on day 21) X4
6.	**Haematology**	yes, number of animals: all animals time points: At post-mortem examination Parameters: Haemoglobin, red blood cell count, haematocrit, mean cell volume, mean cell haemoglobin, mean cell haemoglobin concentration, white cell count, platelet count, kaolin-cephalin and prothrombin times
7.	**Clinical Chemisty**	yes, number of animals: all animals time points: At post-mortem examination Parameters: plasma urea, creatinine, glucose, albumin, total protein, cholesterol, calcium, phosphorus, bilirubin, plasm alkaline phosphatise (ALP), alanine transaminase (ALT), aspartate transaminase (AST), creatine kinase (CK), triglycerides, plasma sodium and plasma potassium.
8.	**Urinalysis**	yes, number of animals: 5/sex/group time points: After exposure on day 20 Parameters: volume, specific gravity, pH, glucose, blood, ketones, urobilinogen, protein and sediment.

Section A6.3 / 6.4 / 6.5 **Repeated dose toxicity**

Annex Point IIA6.3 / 6.4 / 6.5

Section 6.3.3 Repeat Dose Inhalation, 21 Days sub-acute inhalation toxicity study in the rat

E. Sacrifice and pathology

1. Organ Weights

yes
organs: Lungs (with trachea attached but larynx removed), liver, kidneys, testes, adrenal glands, heart and brain. Paired organs were weighed together.

2. Gross and histopathology

yes
Tissues removed from all animals were adrenal gland, aorta, urinary bladder, femur (bone and bone marrow), brain, caecum, cervix, colon, duodenum, heart, ileum, jejunum, kidney, larynx, liver, lung, lymph node (axillary, cervical and mesenteric), nasal cavity, sciatic nerve, oesophagus, ovary, pancreas, pituitary gland, prostate gland, rectum, salivary gland, seminal vesicle, spinal cord, spleen, sternum, stomach, thymus, thyroid gland, parathyroid gland, trachea, uterus, voluntary muscle and any abnormal tissue, testis, epididymus, skin, mammary gland (females only), eye, harderian gland.

3. Other examinations

4. Statistics

Bodyweight gain from the start of the study to each day of measurement, final bodyweight and food consumption were considered by analysis of variance, separately for males and females.

Biochemical blood and urine and haematological data were considered by analysis of variance. With the exception of urine protein, for which there were markedly differing variances between the sexes, male and female data were analysed together and the results examined to determine whether any differences between control and treated groups were consistent between sexes. Monocyte counts were not analysed statistically as only a small number of non-zero counts were observed.

Organ weights were considered by analysis of variance and analysis of covariance on final bodyweight, separately for males and females.

Each treatment group mean was compared with the control group mean using a two-sided Student's t-test, based on the error mean square in the analysis.

All data were checked for unusual values and where such values were detected the analyses were repeated omitting these values to determine their influence on the conclusions.

F. Further remarks

Section A6.3 / 6.4 / 6.5 **Repeated dose toxicity**

Annex Point IIA6.3 / 6.4 / 6.5

Section 6.3.3 Repeat Dose Inhalation, 21 Days sub-acute inhalation toxicity study in the rat

4. RESULTS AND DISCUSSION

A. Observations

1. Clinical signs

Abnormalities generally associated with restraint (stains around the snout, wet fur, chromodacryorrhea, hunched posture and piloerection) were seen in test and control animals throughout the study.

Observation During Exposure: Salivation and lachrymation were present during exposure in some animals exposed to 3.3 and 16.7µg/L.

Observations Immediately Following Exposure: The major treatment-related effects seen in animals exposed to 3.3 and 16. 7µg/L were either neurological in nature (eg paw flicking and tail erections) or indicative of irritancy (e.g. lachrymation , salivation). Animals exposed to 16.7µg/L were more severely affected and displayed a greater range of clinical effects.

Observation on Non-Exposure Days: The only significant effects were tail erections and tiptoe gaite in some animals exposed to 16.7µg/L lambda-cyhalothrin production material.

2. Mortality

No mortalities at any dose level.

B. Body weight gain

Bodyweight gain was reduced throughout the study in both sexes at 16. 7µg/L lambda-cyhalothrin production material compared with controls, final weights being 15% and 12% below controls in males and females respectively. These effects on bodyweight gain in females appeared to be dependent on whether bodyweights were recorded on an exposure or non-exposure day since there appeared to be some recovery in bodyweight gain in this sex on non-exposure days. Males showed a steady but reduced bodyweight gain over the duration of the study but the overall pattern in the females was an approximate maintenance of the starting weight. Effects of a similar nature although smaller in magnitude were seen throughout the study at 3.3 µg/L lambda-cyhalothrin production material.

X5

C. Food consumption and compound intake

Males and females exposed to 16.7 µg/L lambda-cyhalothrin production material had statistically significantly reduced food consumption up to day 18, and slight reduction between days 18 to 22. Reduced food consumption was also seen in males exposed to 3.3µg/L during the first week of the study. These effects were consistent with the bodyweight effects.

D. Ophtalmoscopic examination

There was a dose-related increase in the incidence of punctuate foci on the cornea in males and females exposed to 3.3and 16.7 µg/L lambda-cyhalothrin production material. There were no other treatment-related ocular changes. No effects were seen at 0.3 µg/L or on histological examination of the eyes

Section A6.3 / 6.4 / 6.5 **Repeated dose toxicity**

Annex Point IIA6.3 / 6.4 / 6.5

Section 6.3.3 Repeat Dose Inhalation, 21 Days sub-acute inhalation toxicity study in the rat

E. Blood analysis

1. Haematology

The platelet count was reduced in all females treated groups and the prothrombin time was slightly raised in top dose females. There were changes in other haematological parameters although these, together with the changes in the platelet count of females, are considered to be of no toxicological significance.

See Table A6_3-2

2. Clinical chemistry

Plasma urea levels were lower in females exposed to 16.7 µg/L lambda-cyhalothrin production material. There were slight reductions in the plasma albumin and total protein levels in females exposed to 3.3 and 16.7 µg/L and minimal reductions in males exposed to 3.3 µg/L.

There were slight increases in the plasma aspartate transaminase and alkaline phosphatise activities of females exposed to 16.7 µg/L. Small reductions were seen in the plasma cholesterol levels of females at 3.3 and 16.7 µg/L and in the plasma triglyceride levels of males exposed to 16.7 µg/L lambda-cuhalothrin production materials. Other statistically significant changes between test and control groups were small and/or not dose-related and were considered to be of no toxicological significance.

See Table A6_3-1

3. Urinalysis

Urine volume was reduced and specific gravity slightly raised in both sexes exposed to 3.3 and 16.7 µg/L lambda-cyhalothrin production material. An apparent reduction in volume was also seen in males exposed to 0.3 µg/L lambda-cyhalothrin production material. This is considered to reflect a few extreme control value giving rise to a high control mean and is not considered to be of any toxicological significance.

There were reductions in protein levels of males exposed to 3.3 and 16.7 µg/L and of females exposed to 16.7 µg/L.

There were no significant effects on urine sediment parameters.

See Table A6_3-3

F. Sacrifice and pathology

1. Organ weights

There were small, statistically significant differences in liver weights adjusted for bodyweight in males and absolute liver weights in females exposed to 3.3 and 16.7 µg/L lambda-cyhalothrin production material. There were no toxicologically significant effects on absolute organ weights or organ weights adjusted for

Section A6.3 / 6.4 / 6.5 **Repeated dose toxicity**

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bodyweights for the remaining organs.

2. Gross and histopathology

There was a slight increase in the incidence of alveolitis in females exposed to 16.7 µg/L lambda-cyhalothrin production material when compared with controls.

One male exposed to 16.7 µg/L had a benign meningioma in the brain. This is a rare tumour, especially in a young rat, but it is considered highly unlikely that this tumour was caused by exposure to lambda-cyhalothrin production material.

All changes in other tissues were considered to be incidental to treatment.

G. Other

5. APPLICANT'S SUMMARY AND CONCLUSION

A. Materials and methods

Rats (Alpk:APfSD) (10/sex/dose) were exposed nose only to lambda-cyhalothrin production material at actual concentrations of 0, 0.21, 2.64 and 12.80 µg/L for 6 h/day, 5 days/week over a 21 day period (total of 15 exposures). The MMAD of the particles ranged from 1.47 to 1.91 µm. Clinical signs were recorded daily. Detailed clinical examination was performed weekly. Body weights and food consumption were recorded weekly. Ophthalmoscopy was performed prior to treatment and following exposure on day 21. Urinalysis was performed on samples taking during the last day of treatement. The day after the last exposure the animals were killed and macroscopically examined, and blood was collected for haematology and clinical chemistry. A selection of organs was weighed. An extensive range of organs and tissues of the control and high dose animals, and any abnormal tissue of the low- and mid-dose animals was microscopically examined.

B. Results and discussion

No major problem occurred in the conduct of this study. The atmospheres of lambda-cyhalothrin production material generated were close to target and demonstrated acceptable stability. The particle size data demonstrated that the test aerosols were highly respirable and therefore capable of penetrating to the alveolar regions of the respiratory tract.

The major clinical effects seen following exposure to 16.7 µg/L and to a lesser extent 3.3 µg/L lambda cyhalothrin production material, were either neurological in nature or indicated irritancy. This is consistent with the known effects of synthetic pyrethroids. On non-exposure days throughout the study, the majority of the abnormalities had disappeared, again consistent with the effects of synthetic pyrethroids.

The bodyweight and food consumption effects are consistent with the severity of the treatment-related clinical effects.

The small increases in liver weight adjusted for bodyweight in male rats exposed to 3.3 and 16.7 µg/L lambda-cyhalothrin production material, in the absence of any

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histopathological findings, are considered to be an adaptive response to exposure to the test material and of no toxicological significance.

The changes seen in some clinical chemistry and haematological parameters in both sexes suggest a minimal effect on liver metabolism and together with the other changes in the urine profile and plasma urea, probably reflect the general toxicity of lambda-cyhalothrin production material to rats in the two higher exposure groups.

The presence of an increased incidence of punctuate foci on the cornea in males and females exposure to 3.3 and 16.7 µg/L lambda-cyhalothrin production material indicates a dose response to treatment. In view of the clinical observation of excess lachrymation during exposure, the absence of histopathological change and the nature of the opathalmoscopic effect, it is considered likely that this treatment-related increase represented an abnormal pre-corneal film due to excessive lachyrmation. As such, it is of no toxicological significance.

The slight increase in the incidence of alveolitis in top dose females was possibly due to an irritant effect of the test material depositing in the lungs.

C. Conclusion

1.	**LO(A)EL**	3.3 µg/L
2.	**NO(A)EL**	0.3 µg/L
3.	**Other**	
4.	**Reliability**	2
5.	**Deficiencies**	No

Section A6.3 / 6.4 / 6.5 **Repeated dose toxicity**

Annex Point IIA6.3 / 6.4 / 6.5

Section 6.3.3 Repeat Dose Inhalation, 21 Days sub-acute inhalation toxicity study in the rat

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	June 2010
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

Table A6_3-1. Results of Clinical Chemistry

Parameter Changed	Unit	Control (0 µg/L)	Low Dose (0.3 µg/L)	Medium Dose (3.3 µg/L)	High Dose (16.7 µg/L)
Males					
Plasma Triglycerides	mg/100 mL	129	133	129	105(↓)*
Females					
Plasma Urea	mg/100 mL	54.7	51.5	50.5	42.8(↓)**
Plasma Albumin	g/100 mL	4.44	4.32	4.20(↓)**	4.05(↓)**
Plasma Total Protein	g/100 mL	6.48	6.44	6.11(↓)**	5.92(↓)**
Plasma Aspartate Transaminase	mU/mL	69.4	73.2	78.6	82.6(↑)*
Plasma Alkaline Phosphatase	mU/mL	151	169	165	184(↑)*
Plasma Cholesterol	mg/100 mL	74.5	78.9	62.5(↓)*	59.5(↓)*

Table A6_3-2. Results of Haematology

Parameter Changed	Unit	Control (0 µg/L)	Low Dose (0.3 µg/L)	Medium Dose (3.3 µg/L)	High Dose (16.7 µg/L)
Males					
None					
Females					
Prothrombin Time	seconds	19.3	19.8	20.0	20.6(↑)**

Table A6_3-3. Results of Urinalysis

Parameter Changed	Unit	Control (0 µg/L)	Low Dose (0.3 µg/L)	Medium Dose (3.3 µg/L)	High Dose (16.7 µg/L)
Males					
Urine Volume	mL	7.50	5.08(↓)*	3.02(↓)**	2.72(↓)**
Specific Gravity	-	1.041	1.048	1.061(↓)**	1.064(↓)**
Urine Protein	mg/TPV	13.78	10.36	7.80(↓)**	6.01(↓)**
Females					
Urine Volume	mL	5.34	4.48	3.32	2.28(↓)**
Specific Gravity	-	1.045	1.047	1.053(↓)*	1.060(↓)**

Table A6_3-4. Results 21 Days sub-acute inhalation toxicity study in the rat) of repeated dose toxicity study

Parameter	Control (0 µg/L)		Low Dose (0.3 µg/L)		Medium Dose (3.3 µg/L)		High Dose (16.7 µg/L)		Dose-response +/-	
	m[a]	f[a]	m[a]	f[a]	m[a]	f[a]	m[a]	f[a]	m	f
number of animals examined	40	40	40	40	40	40	40	40	40	40
Mortality	No Mortalities									
clinical signs	-	-	-	-	↑	↑	↑	↑	+	+
body weight	-	-	-	-	↓	↓	↓	↓	+	+
food consumption	-	-	-	-	↓	↓	↓	↓	+	+
organ weight	No Toxicological Significance									
gross pathology	-	-	-	-	-	-	-	↑[a]	-	-
microscopic pathology	No Toxicological Significance									

[a] *The slight increase in the incidence of alveolitis in top dose females was possibly due to an irritant effect of the test material depositing in the lungs.*

Competent Authority Report

According to Directive 98/8/EC

lambda-Cyhalothrin

CAS 91465-08-6

Active substance in Biocidal Products, Product Type 18 (Insecticide)

Notifier: Syngenta European Center

DOCUMENT III-A

Section 6: Toxicological and metabolic studies

Rapporteur Member State: Sweden

Final CAR, May 2011

Borttaget: Draft

Borttaget: September

Borttaget: 2010

KEMI

Kemikalieinspektionen

Swedish Chemicals Agency

INFORMATION FROM THE RMS:

Format

Lambda-cyhalothrin has previously been evaluated as a plant protection product and was included in the annex I of the Council Directive of 15 July 1991 concerning placing of plant protection products on the market (91/414/EEC) in 2002. Syngenta has used the possibility to utilise the PPP dossier for the BP dossier preparation in agreement with the EU document "Guidance Document on How to utilize PPP Dossiers/Monographs and Existing Substances (ESR) Dossiers/Risk Assessments for the Preparation of BP dossiers/ CAs' reports" thus study summaries in this dossier does not follow the standard BPD format.

Read across from cyhalothrin

The human health effect assessment of *lambda*-cyhalothrin is based on data obtained for *lambda*-cyhalothrin or cyhalothrin. *Lambda*-cyhalothrin is the pure cis 1RαS and cis 1SαR enantiomeric pair whereas cyhalothrin is a 50/50 mixture of lambda-cyhalothrin and the R157836 (the cis 1RαR and cis 1SαS) enantiomeric pair. Read across between the two substances is considered justified based on the results from two 90 day studies performed in Alpk:APSD rats with identical dose levels of either *lambda*-cyhalothrin or cyhalothrin. Read across is further supported by a bridging study demonstrating that the absorption, tissue distribution, metabolism and excretion of *lambda*-cyhalothrin and cyhalothrin is quantitatively and qualitatively similar in rat. Results of existing studies on sub-chronic, long term and reproductive toxicity performed with cyhalothrin are therefore considered relevant for the toxicological evaluation of *lambda*-cyhalothrin.

However, when comparing the acute oral toxicity of *lambda*-cyhalothrin reported in this dossier to the acute oral toxicity of cyhalothrin reported in literature[1], *lambda*-cyhalothrin appears to be approximately three times more potent than cyhalothrin in both rats and mice. This needs to be taken into consideration in the risk assessment of *lambda*-cyhalothrin.

[1] The LD50 values reported for instance in IPCS, Health and Safety Guide No. 38 was 144-243 mg/kg in rats and 37-62mg/kg in mice respectively.

1. ACUTE TOXICITY

98/8 Doc IIIA section No.	6.1.1 / 01	Acute toxicity – Oral	Official use only
91/414 Annex Point addressed	II 5.2.1	Acute toxicity - oral	

Title:	„PP321: Acute Oral Toxicity Studies"	
Lab Report Number:	No. [redacted]/P/1102	
Authors:	[redacted]	
Test Substance:	Technical grade *lambda*-cyhalothrin (otherwise known as PP321). other TS: Two samples - purity [redacted]% and [redacted] w/w	X1
Species:	rat	
Method:	OECD Guideline 401 "Acute Oral Toxicity"	
Date of Report:	1985	
Published:	No	
GLP:	Yes	
Reliability:	1	

Material and Methods:	The purpose of the study was to assess the acute toxicity of the test substance following administration of a single oral (gavage) dose. The animals were young healthy specific pathogen free (SPF) adult rats of the [redacted] strain. At the beginning of the study the males weighed 151-235 g and the females weighed 122-178 g and were aged between 5 and 7 weeks. The animals were supplied by the [redacted] Groups of five male and/or five female rats were used. Each animal was fasted for 16-20 hours immediately prior to being given a single dose of test substance in corn oil. Five dose-levels were selected for sample 1 study. Dose levels of 29.7, 50.8, 75.3 mg/kg were administered to groups of male and female rats, a dose level of 62.5 mg/kg was administered to a group of male rats and a dose level of 94.1 mg/kg was administered to a group of female rats. Eight dose-levels were selected for sample 2 study. Dose	X2

	levels of 47, 102, 136, 137 and 216 mg/kg were administered to groups of male and female rats and dose levels of 11.3, 23 and 24 mg/kg were administered to groups of male rats. A standard volume of 10 ml/kg was dosed to each animal and differences in the dose-levels were achieved by altering the concentration of the dosed preparation. The volume of the dose was calculated for each animal according to its weight at the time of dosing. Animals were observed for signs of systemic toxicity between 30 and 100 minutes and between 3 and 6 hours after dosing. Subsequent observations were made daily up to day 15. The animals were weighed at intervals throughout the study. Most of the animals were given a post mortem examination for any macroscopic signs of abnormalities.	X3
Results:	Sample 1: None of the males died following doses of 29.7 or 50.8 mg/kg. All female animals died following a dose of 94.1 mg/kg. In all other groups a proportion of the animals died. Deaths occurred by day 3 of the study. Sample 2: None of the male animals died following a dose of 47 mg/kg. All males died following a dose of 137 or 216 mg/kg. None of the female animals died following a dose of 11.3 or 24 mg/kg. All females died following a dose of 137 or 216 mg/kg. In all other groups a proportion of the animals died. Deaths occurred by day 3 of the study. Signs of toxicity were seen in most of the surviving animals; the most common effects were decreased activity, ataxia, splayed gait, dehydration, upward curvature of the spine, urinary incontinence/signs of urinary incontinence, pilo-erection, salivation/signs of salivation and pinched sides. The clinical signs, especially those of abnormal motor function, are consistent with pyrethroid toxicity. Initially, all animals decreased in bodyweight (due to fasting prior to dosing). All surviving rats increased in bodyweight throughout the study and by day 8 all bodyweights were increased when compared to the initial bodyweight. No macroscopic signs of abnormalities were observed in any of the animals which were examined by necropsy.	X4
Conclusion:	The acute oral LD_{50} was 79 mg/kg in male rats (lower 95% confidence limit was estimated to be 51 mg/kg, representing the highest dose with zero mortality) and 56 mg/kg in female rats (95% confidence limits 40, 78 mg/kg).	X4 X5

Reliability Indicator	1	
Data Protection Claim	Yes	

	Evaluation by Competent Authorities
98/8 Doc IIIA section No. 6.1.1 / 01	Acute toxicity – Oral
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	August 2006
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

Table 6.1.1(01a): Acute oral toxicity (males)

Dose (mg/kg)	Cumulative Mortality	Time of death (day/total number of dead animals)	Test sample*
29.7	0/5		1
47	0/5		2
50.8	0/5		1
62.5	4/5	2/3, 3/4	1
75.3	5/5	2/2, 3/5	1
102	1/5	2/1**	2
136	3/5	1/4, 3/3	2
137	5/5	3/3	2
216	5/5	1/5	2

* Purity sample 1: 92.6%, purity sample 2: 96%
** Killed in extremis.

Table 6.1.1(01b): Acute oral toxicity (females)

Dose (mg/kg)	Cumulative Mortality	Time of death (day/total number of dead animals)	Test sample*
11.3	0/5		2
23	2/5	2/2	2
24	0/5		2
29.7	1/5	2/1	1
47	1/5	2/1	2
50.8	2/5	2/2	1
75.3	4/5	2/3, 3/4	1
94.1	5/5	2/5	1
102	3/5	2/3**	2
136	3/5	2/2***, 3/3**	2
137	5/5	1/5	2
216	5/5	1/5	2

* Purity sample 1: 92.6%, purity sample 2: 96%

** One animal killed in extremis.
***Two animals killed in extremis.

98/8 Doc IIIA section No.	**6.1.1 / 02**	**Acute toxicity – Oral**	**Official use only**
91/414 Annex Point addressed	**II 5.2.1**	**Acute toxicity - oral**	

Title:	„PP321: Acute Oral Toxicity Studies"	
Lab Report Number:	No. [redacted]/P/1066	
Authors:	[redacted]	
Test Substance:	Technical grade *lambda*-cyhalothrin (otherwise known as PP321). Purity [redacted] w/w. Other TS: [redacted] w/w	X1
Species:	Mouse	
Method:	OECD Guideline 401 "Acute Oral Toxicity"	
Date of Report:	1984	
Published:	No	
GLP:	Yes	
Reliability:	1	

Material and Methods:	The purpose of the study was to assess the acute toxicity of the test substance following administration of a single oral (gavage) dose.	