Section A1 Applicant

Annex Point IIA, I 1

1.1	**Applicant**	Company name:	Syngenta Ltd
		Contact name:	[redacted]
		Address:	Surrey Research Park Guildford Surrey GU2 7YH, UK
		Telephone:	[redacted]
		Fax:	[redacted]
		E-Mail:	[redacted]
1.2	**Manufacturer of Active Substance** (if different)	Manufacturer:	[redacted]
		Contact person:	as Applicant
1.3	**Manufacturer of Product(s) (if different)**	Company name:	[redacted]
		Contact name:	[redacted]
		Address:	[redacted]
		Telephone:	[redacted]
		Fax:	[redacted]
		E-Mail:	[redacted]

Section A1 Applicant

Annex Point IIA, I 1

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	
Materials and methods	
Conclusion	
Reliability	
Acceptability	*acceptable*
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant´s summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A2 Identity of impurities and additives (active substance)

Subsection A2.8

Annex Point IIA, II 2.8

Subsection			Official use only
2.8.1.1	**Common name**	The identity of impurities and additives in the active substance as manufactured is confidential. This information is provided separately in the confidential part of the dossier (A2_conf.doc and A2_8_01_conf.doc to A2_8_10_conf.doc).	
2.8.1.2	**Function**		
2.8.2	**IUPAC name**		
2.8.3	**CAS-No**		
2.8.4	**EC-No**		
2.8.5	**Other**		
	CIPAC		
2.8.6	**Molecular formula**		
2.8.7	**Structural formula**		
2.8.8	**Molecular mass**		
2.8.9	**Concentration of the impurity or additive** *typical and range of concentrations*		

Section A2 Identity of impurities and additives (active substance)
Subsection A2.8
Annex Point IIA, II 2.8

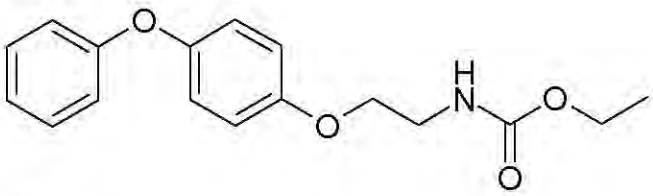
	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2006/03/31
Materials and methods	
Conclusion	[redacted]
Reliability	
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant´s summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A2 **Subsection A2.8** **Annex Point IIA, II 2.8**	**Identity of Active Substance** 2.8.5 OTHER NUMBERS	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [ ]** **Other justification [X]**	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]	–	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	2006/03/31	
Evaluation of applicant's justification	[redacted]	
Conclusion		
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A2 **Subsection A2.9** **Annex Point IIA, II 2.9**	**Identity of Active Substance** THE ORIGIN OF THE NATURAL ACTIVE SUBSTANCE OR THE PRECURSOR(S) OF THE ACTIVE SUBSTANCE	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure** [ ]	**Technically not feasible** [ ] **Scientifically unjustified** [ ] **Other justification [X]**	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]	–	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	2006/03/31	
Evaluation of applicant's justification	[redacted]	
Conclusion		
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A2 Identity of Active Substance

Annex point IIA, II 2

Subsection (Annex Point)			Official use only
2.1	**Common name (IIA, II)**	Fenoxycarb (ISO draft)	
2.2	**Chemical name (IIA, II 2.2)**	**IUPAC nomenclature:** [2-(4-phenoxy-phenoxy)-ethyl]-carbamic acid ethyl ester **CA nomenclature:** [2-(4-phenoxyphenoxy)ethyl]-carbamic acid ethyl ester	x
2.3	**Manufacturer´s development code number(s) (IIA, II 2.3)**	CGA 114597 Ro 13-5223	
2.4	**CAS No and EC numbers (IIA, II 2.4)**		
2.4.1	**CAS-No**	72490-01-8	
	Isomer 1	Not relevant	
	Isomer n	Not relevant	
2.4.2	**EC-No**	276-696-7	
	Isomer 1	Not relevant	
	Isomer n	Not relevant	
2.4.3	**Other**	CIPAC No.: 425	
2.5	**Molecular and structural formula, molecular mass (IIA, II 2.5)**		
2.5.1	**Molecular formula**	$C_{17}H_{19}NO_4$	
2.5.2	**Structural formula**		
2.5.3	**Molecular mass**	301.4 g/mol	
2.6	**Method of manufacture of the active substance (IIA, II 2.6)**	The method of manufacture of the active substance is confidential. This information is provided separately in the confidential part of the dossier (A2_conf.doc).	
2.7	**Specification of the purity of the active substance, as appropriate (IIA, II 2.7)**	The specification of the purity of the active substance is confidential. This information is provided separately in the confidential part of the dossier (A2_conf.doc).	

Section A2 Identity of Active Substance

Annex point IIA, II 2

2.8	**Identity of impurities and additives, as appropriate (IIA, II 2.8)**	The identity of impurities and additives is confidential. This information is provided separately in the confidential part of the dossier (A2_conf.doc and A2_8_01_conf.doc to A2_8_10_conf.doc)).
2.8.1	**Isomeric composition**	Information about isomeric composition is confidential. This information is provided separately in the confidential part of the dossier (A2_conf.doc).
2.9	**The origin of the natural active substance or the precursor(s) of the active substance (IIA, II 2.9)**	Not applicable as the active substance fenoxycarb has no natural origin.

Evaluation by Competent Authorities

Use separate "evaluation boxes" to provide transparency as to the comments and views submitted

EVALUATION BY RAPPORTEUR MEMBER STATE

Date	2007/02/05
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	
Acceptability	[redacted]
Remarks	

COMMENTS FROM...

Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A2.10

Annex Point IIA2.10

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

Subsection		Official use only
2.10.1 Human exposure towards active substance		
2.10.1.1 Production of the formulation		
i) Description of process	The formulation is produced [redacted].	
ii) Workplace description	The formulation is produced [redacted]. The active substances and the formulation are only handled by professionals with adequate training and protective equipment (gloves, boots coveralls and face protection).	
iii) Inhalation exposure	The formulation is produced [redacted]; therefore no releases into air occur during production.	
iv) Dermal exposure	Direct dermal contact with fenoxycarb is not foreseen. An incidental contact is possible during transfer of the substance to the mixing vessel. Protective equipment for the mixing process; see workplace description.	
2.10.1.2 Intended use(s)		
1. Professional Users		
i) Description of application process	Tank dipping, see Doc. II-B	
ii) Workplace description	PPE: new suitable protective gloves at start of each daily dipping session, protective footwear, impermeable coverall, plus goggles for mixing/loading phase	
iii) Inhalation exposure	4.43×10^{-7} mg/kg bw/day	
iv) Dermal exposure	4.11×10^{-4} mg/kg bw/day	
2. Non-professional Users including the general public	Product is only for sale to industrial/professional users	
2.10.2 Environmental exposure towards active substance		
2.10.2.1 Production of the formulation		
(i) Releases into water	The formulation is produced [redacted]; therefore no releases into water occur during production.	
(ii) Releases into air	The formulation is produced [redacted]; therefore no releases into air occur during production.	
(iii) Waste disposal	No waste materials are produced during the production process. After	

Section A2.10 Annex Point IIA2.10	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
	production of the formulation [redacted]
2.10.2.2 Intended use(s)	see Doc. II-B
Affected compartment(s):	see Doc. II-B
water	see Doc. II-B
sediment	see Doc. II-B
air	see Doc. II-B
soil	see Doc. II-B
Predicted concentration in the affected compartment(s)	see Doc. II-B
water	see Doc. II-B
sediment	see Doc. II-B
air	see Doc. II-B
soil	see Doc. II-B

Section A2.10
Annex Point IIA2.10

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

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2006-09-29
Materials and methods	acceptable
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A3 Physical and Chemical Properties of Active Substance

Annex point IIA, III 3

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 (IIA, III 3.1)								
3.1.1 Melting point	OECD 102 (DSC)	Purity: 99.5% (pure substance) Specification: as given in Section 2 of dossier.	54.6°C	–	Y	1	Geoffroy, 2007	
3.1.2 Boiling point	OECD 103 (DSC)	Purity: 99.5% (pure substance) Specification: as given in Section 2 of dossier.	An evaporation corresponding to decomposition begins at 180 °C, i.e. before the boiling point at 101.3 kPa is reached: the boiling point of fenoxycarb at 101.3 kPa cannot be determined and is > 180 °C.	–	Y	1	Geoffroy, 2007	
3.1.3 Bulk density/ relative density	OECD 109	Purity: 99.2% (pure substance) Specification: as given in Section 2 of dossier.	$1.23 \cdot 10^3$ kg / m^3 at 20°C corresponding to a relative density of 1.23.	–	Y	1	Füldner, 1992	x

Section A3 Physical and Chemical Properties of Active Substance

Annex point IIA, III 3

Subsection (Annex point)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.2 Vapour pressure and Henry`s Law Constant (IIA, III 3.2)								
Vapour pressure	EC A.4	Purity: 99.2% (pure substance) Specification: as given in Section 2 of dossier.	Vapour pressure curve in the solid state: $^{10}\log P\ [Pa] = 20.8030 - 8009.80 \cdot 1 / T\ [K]$ from fit of measurements between 75.5 and 155.6°C Vapour pressure at 25°C: $8.67 \cdot 10^{-7}$ Pa		Y	1	Rordorf, 1992	
Henry´s Law Constant	Calculation	Calculation	Result at 25 °C: $3.3 \cdot 10^{-5}$ Pa · m³ / mol	–	Y	1	Burkhard, 1998	

Section A3 Physical and Chemical Properties of Active Substance

Annex point IIA, III 3

Subsection (Annex point)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.3 Appearance (IIA, III 3.3)								
3.3.1 Physical state	Visual inspection	Purity: 99.5% (pure substance) Specification: as given in Section 2 of dossier.	Pure active substance: solid (flakes)	–	Y	1	Das, 1999	
	Visual inspection	Purity: 97.6% (technical substance) Specification: as given in Section 2 of dossier.	Technical grade active substance: solidified melt	–	Y	1	Rodler, 1992a	
3.3.2 Colour	Visual inspection	Purity: 99.5% (pure substance) Specification: as given in Section 2 of dossier.	Pure active substance: white	–	Y	1	Das, 1999	
	Visual inspection	Purity: 97.6% (technical substance) Specification: as given in Section 2 of dossier.	Technical grade active substance: colourless to white	–	Y	1	Rodler, 1992a	

Section A3 Physical and Chemical Properties of Active Substance

Annex point IIA, III 3

Subsection (Annex point)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.3.3 Odour	Organoleptic inspection	Purity: 99.5% (pure substance) Specification: as given in Section 2 of dossier.	Pure active substance: odourless	–	Y	1	Das, 1999	
	Organoleptic inspection	Purity: 97.6% (technical substance) Specification: as given in Section 2 of dossier.	Technical grade active substance: odourless	–	Y	1	Rodler, 1992a	
3.4 Absorption spectra (IIA, III 3.4)								

Section A3 Physical and Chemical Properties of Active Substance

Annex point IIA, III 3

Subsection (Annex point)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
UV/VIS	UV spectrum	Purity: 99.2% (pure substance) Specification: as given in Section 2 of dossier.	Fenoxycarb was identified by UVspectrum; methanol was used as solvent. The molar extinction coefficients were determined to be: Neutral solution: 228 nm 15219 l / mol · cm 278 nm 2453 l / mol · cm 300 nm 745 l / mol · cm Acidic solution: 228 nm 15062 l / mol · cm 278 nm 2357 l / mol · cm 300 nm 643 l / mol · cm Basic solution: 228 nm 11540 l / mol · cm 278 nm 2374 l / mol · cm 300 nm 664 l / mol · cm No absorption maximum between 310 nm and 750 nm was observed.		Y	1	Oggenfuss, 1999	x
IR	IR spectrum	Purity: 99.2% (pure substance) Specification: as given in Section 2 of dossier.	Fenoxycarb was identified by IR spectrum using a KBr pellet.	–	Y	1	Oggenfuss, 1999	x
NMR	^{13}C-NMR spectrum (75 MHz,) ^{1}H-NMR spectrum (300 MHz)	Purity: 99.2% (pure substance) Specification: as given in Section 2 of dossier.	Fenoxycarb was identified by ^{1}H-NMR spectrum using $CDCl_3$ as solvent and ^{13}C-NMR spectrum using DMSO as solvent.	–	Y	1	Oggenfuss, 1999	x

Section A3 Physical and Chemical Properties of Active Substance

Annex point IIA, III 3

Subsection (Annex point)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
MS	MS spectrum (EI)	Purity: 99.2% (pure substance) Specification: as given in Section 2 of dossier.	Fenoxycarb was identified by mass spectrometry.	–	Y	1	Oggenfuss, 1999	X
3.5 Solubility in water (IIA, III 3.5)	EC A.6 (shake flask method)	Purity: 99.2% (pure substance) Specification: as given in Section 2 of dossier.	7.9 mg/L at 25 °C	Fenoxycarb is a neutral molecule having no dissociation constant in an accessible pH range. This means the pH has no effect to the water solubility of the compound in the pH range 4 to 10.	Y	2	Stulz, 1993	X

Section A3 Physical and Chemical Properties of Active Substance

Annex point IIA, III 3

Subsection (Annex point)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
	Not applicable (statement based on experience)	Not applicable (statement)	The shake flask method can also be applied with good and reliable results to substances with water solubilities below 10 mg/L if the following conditions are met: equilibrium is obtained and no influence of adsorption to surfaces is given. This is not in contrast to OECD 105 which recommends to use the column elution method below 10 mg/L. There is no indication that below the trigger value it is not possible to obtain reliable results. The octanol/water partition coefficient allows a good estimation whether the determined water solubility value is reliable. The log Pow can be calculated using the solubility in octanol (110 g/L) and the water solubility (7.9 mg/L). The calculated value of log Pow (4.14) is in a very good agreement to the experimentally determined value (4.07) and thus confirms that the water solubility determination was correct.		N	2	Stulz, 2007	
3.6 Dissociation constant (-)	OECD 112	Purity: 99.2% (pure substance) Specification: as given in Section 2 of dossier.	Fenoxycarb has no dissociation constant in an accessible pH-range.	–	Y	1	Jäkel, 1992	

Section A3 Physical and Chemical Properties of Active Substance

Annex point IIA, III 3

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 (IIIA, III 1)	CIPAC MT 157.3	Purity: 97.6% (technical substance) Specification: as given in Section 2 of dossier.	Results at 25 °C: Acetone > 500 g / L Dichloromethane > 500 g / L Ethyl acetate > 500 g / L Hexane 4.6 g / L Methanol > 500 g / L Octanol 110 g / L Toluene > 500 g / L		Y	2	Kettner, 2000	
3.8 Stability in organic solvents used in b.p. and identity of relevant breakdown products (IIIA, III 2)	–	–	–	[redacted]	–	–	–	
3.9 Partition coefficient n-octanol/water (IIA, III 3.6)	OECD 107	Purity: 99.2% (pure substance) Specification: as given in Section 2 of dossier.	The octanol / water partition coefficient (P_{ow}) and its logarithm to base 10 ($\log P_{ow}$) at 25 °C were determined to be: P_{ow}: 11600 ± (131) $\log P_{ow}$: 4.07 ± (0.005) (As fenoxycarb does not dissociate in water it is assumed that the values for the partition coefficient are independent of pH within the range 5-9.)		Y	2	Rodler, 1992b	

Section A3 Physical and Chemical Properties of Active Substance

Annex point IIA, III 3

Subsection (Annex point)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.10 Thermal stability, identity of relevant breakdown products (IIA, III 3.7)	OECD 103 (DSC)	Purity: 99.5% (pure substance) Specification: as given in Section 2 of dossier.	An evaporation corresponding to a decomposition begins at 180 °C.	–	Y	1	Geoffroy, 2007	
3.11 Flammability, including auto-flammability and identity of combustion products (IIA, III 3.8)								x
Flammability	EC A.10	Purity: 97.6% (technical substance) Specification: as given in Section 2 of dossier.	Fenoxycarb is not considered highly flammable.	–	Y	1	Schürch, 1992a	x
Auto-flammability	EC A.16	Purity: 97.6% (technical substance) Specification: as given in Section 2 of dossier.	Fenoxycarb shows no self-ignition.	–	Y	1	Schürch, 1992b	x
3.12 Flash-point (IIA, III 3.9)	–	–	–	[redacted]	–	–	–	

Section A3 Physical and Chemical Properties of Active Substance

Annex point IIA, III 3

Subsection (Annex point)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.13 Surface tension (IIA, III 3.10)	OECD 115	Purity: 97.6% (technical substance) Specification: as given in Section 2 of dossier.	62.7 mN/m at 20 °C Fenoxycarb is not surface active.	The test was performed at 90% of the saturation concentration of fenoxycarb in water.	Y	1	Martin-Keusch, 2007	
3.14 Viscosity (-)	–	–	–	[redacted].	–	–	–	
3.15 Explosive properties (IIA, III 3.11)	EC A.14	Purity: 97.6% (technical substance) Specification: as given in Section 2 of dossier.	Fenoxycarb is not considered to be explosive in accordance with EC method A.14.	–	Y	1	Schürch, 1992c	
3.16 Oxidizing properties (IIA, III 3.12)	EC A.17	Purity: 97.6% (technical substance) Specification: as given in Section 2 of dossier.	Fenoxycarb is not considered to have oxidising properties.	–	Y	1	Schürch, 1992d	
3.17 Reactivity towards container material (IIA, III 3.13)	Not applicable (statement)	Purity and Specification: as given in Section 2 of dossier.	Fenoxycarb is not corrosive against tin plate, iron steel ST 37 and stainless steel DIN 1.4541.	–	N	2	Meyer, 1991	

Section A3 **Physical and Chemical Properties of Active Substance**
Annex point IIA, III 3

Section A3 Physical and Chemical Properties of Active Substance

Annex point IIA, III 3

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2008/06/30
3.1.1 Melting point (IIA, III 3.1)	
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
Date	2006/04/03
3.1.2 Boiling point (IIA, III 3.1)	
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
Date	2008/07/25
3.1.3 Bulk density/ relative density (IIA, III 3.1)	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]
Date	2008/07/25
3.2 Vapour pressure (IIA, III 3.2)	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
Date	2008/07/25
3.2 Henry´s law constant (IIA, III 3.2)	[redacted]
Reliability	[redacted]
Acceptability	[redacted]

Section A3 Physical and Chemical Properties of Active Substance
Annex point IIA, III 3

Remarks	
Date	2006/04/03
3.3 Appearance (IIA, III 3.3)	
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
Date	2008/07/25
3.4 Absorption spectra (IIA, III 3.4)	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
Date	2008/07/28
3.5 Solubility in water (IIA, III 3.5)	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	

Section A3 Physical and Chemical Properties of Active Substance
Annex point IIA, III 3

Date	2006/04/03
3.6 Dissociation constant	
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
Date	2006/04/03
3.7 Solubility in organic solvents, including the effect of temperature on solubility (IIIA, III 1)	
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
Date	2006-04-03
3.8 Stability in organic solvents (IIIA, III 2)	
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
Date	2006/04/03
3.9 Stability in organic solvents (IIIA, III 2)	
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
Date	2006/04/03
3.10 Thermal stability, identity of relevant breakdown products (IIA, III 3.7)	
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
Date	2007/06/29
3.11 Flammability, including auto-flammability (IIA, III 3.8)	

Section A3 Physical and Chemical Properties of Active Substance
Annex point IIA, III 3

Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]
Date	2007/06/29
3.12 Flash-point (IIA, III 3.9)	
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
Date	2008/07/25
3.13 Surface tension (IIA, III 3.10)	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
Date	2008/07/25
3.14 Viscosity	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
Date	2007/06/29
3.15 Explosive properties (IIA, III 3.11)	
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
Date	2007/06/29
3.16 Oxidizing properties (IIA, III 3.12)	

Section A3 Physical and Chemical Properties of Active Substance
Annex point IIA, III 3

Reliability	[redacted]
Acceptability	[redacted]
Remarks	
Date	2007/06/29
3.17 Reactivity towards container material (IIA, III 3.13)	
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A3 **Subsection A3.8** **Annex Point IIIA, III 2**	**Physical and chemical properties of the active substance** STABILITY IN ORGANIC SOLVENTS	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [ ]** **Other justification [X]**	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]	–	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	2006/03/31	
Evaluation of applicant's justification	[redacted]	
Conclusion		
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A3 **Subsection A3.14** **Annex Point (-)**	**Physical and chemical properties of the active substance** VISCOSITY	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [ ]** **Other justification [X]**	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]	–	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	2006/03/31	
Evaluation of applicant's justification	[redacted]	
Conclusion		
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A3 **Subsection A3.12** **Annex Point IIA, III 3.9**	**Physical and chemical properties of the active substance** FLASH POINT	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [ ]** **Other justification [X]**	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]	–	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	2006/03/31	
Evaluation of applicant's justification	[redacted]	
Conclusion		
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A4.1 Analytical Methods for Detection and Identification

Annex Point IIA, IV 4.1 ANALYTICAL METHOD FOR THE DETERMINATION OF PURE ACTIVE SUBSTANCE IN THE ACTIVE SUBSTANCE AS MANUFACTURED

Official use only

		1 REFERENCE
1.1	**Reference**	Rodler, M. (1992c), Analytical Method for CGA 114597. Ciba-Geigy Ltd., Basel, Switzerland, Report No. AW-164/1 (unpublished). Rodler, M. (1991), Method Validation for technical active substances. Ciba-Geigy Ltd., Basel, Switzerland, Report No. AW-164/1 (unpublished).
1.2	**Data protection**	Yes
1.2.1	Data owner	Syngenta
1.2.2	Companies with letter of access	[redacted]
1.2.3	Criteria for data protection	[redacted]
		2 GUIDELINES AND QUALITY ASSURANCE
2.1	**Guideline study**	None stated
2.2	**GLP**	No
2.3	**Deviations**	No
		3 MATERIALS AND METHODS
3.1	**Preliminary treatment**	
3.1.1	Enrichment	195.0-205.0 mg of the test sample is weighed into a 100 mL volumetric flask. After dissolving with 20 mL acetonitrile the flask is made up to the mark with acetonitrile. 5.0 mL of this solution and 10.0 mL of internal standard solution are pipetted into a 100 mL volumetric flask and made up to the mark with acetonitrile. An aliquot of the sample solution is filtered through a 45 µm membrane filter prior to injection.
3.1.2	Cleanup	
3.2	**Detection**	
3.2.1	Separation method	Liquid chromatography on a reversed phase C-18 column using isocratic elution.
3.2.2	Detector	UV detection at 275 nm.
3.2.3	Standard(s)	Internal standard dibutyl phthalate
3.2.4	Interfering substance(s)	Substances of the sample matrix may interfere.
3.3	**Linearity**	
3.3.1	Calibration range	The linearity was tested using 5 weights of fenoxycarb in the range of 50%, 75%, 100%, 125% and 150% of the target weight.
3.3.2	Number of measurements	Each concentration was measured twice.
3.3.3	Linearity	The determined concentrations of fenoxycarb are in linear correlation to the actual concentration. The coefficient of variation is 0.99995

Section A4.1 Analytical Methods for Detection and Identification

Annex Point IIA, IV 4.1 ANALYTICAL METHOD FOR THE DETERMINATION OF PURE ACTIVE SUBSTANCE IN THE ACTIVE SUBSTANCE AS MANUFACTURED

3.4	**Specificity: interfering substances**	The specificity of the analytical method was demonstrated, no interference was observed. The HPLC method is able to separate the active substance fenoxycarb from its by-products and the solvent.
3.5	**Recovery rates at different levels**	The accuracy of the method is established based on the findings for specificity, precision and linearity.
3.5.1	Relative standard deviation	The accuracy of the method is established based on the findings for specificity, precision and linearity.
3.6	**Limit of determination**	As fenoxycarb is the main component of the active substance as manufactured and the analytical method is used to check if its specification is met no limit of determination is required.
3.7	**Precision**	
3.7.1	Repeatability	The repeatability was determined with 5 individual subsamples of the same batch of fenoxycarb. The relative standard deviation was found to be: $s_{rel} = 0.13\%$
3.7.2	Independent laboratory validation	No independent laboratory validation available.
		4 APPLICANT'S SUMMARY AND CONCLUSION
4.1	**Materials and methods**	The determination of the active substance, fenoxycarb, was carried out with liquid chromatography on a reversed phase C-18 column using isocratic elution and UV detection at 275 nm. Quantification was done by comparison of peak area ratios (internal standard method).
4.2	**Conclusion**	The accuracy of the method is established based on the findings for specificity, recovery and linearity. The precision of the method is established based on the findings for repeatability and ruggedness of the method. The HPLC method is able to separate the active substance fenoxycarb from its by-products and the solvent.
4.2.1	Reliability	2
4.2.2	Deficiencies	No

Section A4.1 Analytical Methods for Detection and Identification

Annex Point IIA, IV 4.1 ANALYTICAL METHOD FOR THE DETERMINATION OF PURE ACTIVE SUBSTANCE IN THE ACTIVE SUBSTANCE AS MANUFACTURED

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2006/03/31
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A4.1 Analytical Methods for Detection and Identification

Annex Point IIA, IV 4.1

ANALYTICAL METHOD FOR THE DETERMINATION OF IMPURITIES IN THE ACTIVE SUBSTANCE AS MANUFACTURED

Official use only

	1 REFERENCE
1.1 Reference	The analytical methods for the determination of impurities in the active substance as manufactured are confidential. This information is provided separately in the confidential part of the dossier (A4_1_01_conf.doc to A4_1_02_conf.doc).
1.2 Data protection	
1.2.1 Data owner	
1.2.2 Companies with letter of access	
1.2.3 Criteria for data protection	
	2 GUIDELINES AND QUALITY ASSURANCE
2.1 Guideline study	
2.2 GLP	
2.3 Deviations	
	3 MATERIALS AND METHODS
3.1 Preliminary treatment	
3.1.1 Enrichment	
3.1.2 Cleanup	
3.2 Detection	
3.2.1 Separation method	
3.2.2 Detector	
3.2.3 Standard(s)	
3.2.4 Interfering substance(s)	
3.3 Linearity	
3.3.1 Calibration range	
3.3.2 Number of measurements	
3.3.3 Linearity	
3.4 Specificity: interfering substances	
3.5 Recovery rates at different levels	
3.5.1 Relative standard deviation	
3.6 Limit of determination	
3.7 Precision	

Section A4.1	Analytical Methods for Detection and Identification
Annex Point IIA, IV 4.1	ANALYTICAL METHOD FOR THE DETERMINATION OF IMPURITIES IN THE ACTIVE SUBSTANCE AS MANUFACTURED

3.7.1 Repeatability

3.7.2 Independent laboratory validation

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1 Materials and methods

4.2 Conclusion

4.2.1 Reliability

4.2.2 Deficiencies

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2006/03/31
Materials and methods	
Conclusion	[redacted]
Reliability	
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A4.2 Analytical Methods for Detection and Identification

Annex Point IIA, IV 4.2 ANALYTICAL METHOD FOR THE DETERMINATION OF ACTIVE SUBSTANCE RESIDUES IN SOIL

Official use only

1 REFERENCE

1.1	**Reference**	Robinson, N.J. (2004), Residue analytical method for the determination of residues of fenoxycarb in soil (RAM 406/01). Syngenta Crop Protection, Jealott's Hill International Research Centre, Bracknell, Berkshire, UK, issue date: February 2004 (unpublished report). Emburey, S.N. (2004). Validation of a residue analytical method for the determination of residues in soil. Syngenta Crop Protection, Jealott's Hill International Research Centre, Bracknell, Berkshire, UK, Report No. TMJ4912B, issue date: January 2004 (unpublished).
1.2	**Data protection**	Yes
1.2.1	Data owner	Syngenta
1.2.2	Companies with letter of access	[redacted]
1.2.3	Criteria for data protection	[redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	None stated
2.2	**GLP**	Yes
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Preliminary treatment**	
3.1.1	Enrichment	To 20 g of soil 20 mL 1% (v/v) H_3PO_4 solution is added. The samples are swirled and allowed to stand for 30 minutes. After adding 200 mL of acetone, the samples are homogenized for 30 minutes and afterwards centrifuged. The soil extracts are diluted with water.
3.1.2	Cleanup	
3.2	**Detection**	
3.2.1	Separation method	High performance liquid chromatography
3.2.2	Detector	Mass spectrometry detection (selected reaction monitoring (SRM), parent ion: m/z 302, product ion: m/z 116).
3.2.3	Standard(s)	External standard fenoxycarb (purity: 99.5%)
3.2.4	Interfering substance(s)	Substances of the sample matrix may interfere.
3.3	**Linearity**	
3.3.1	Calibration range	Linearity of detector response was demonstrated over the range of 0.25 ng/mL to 50 ng/mL (equivalent to 2.5 pg to 500 pg injected on column when using a 10 µL injection volume).
3.3.2	Number of measurements	Each of five standard concentrations was analysed in triplicate.
3.3.3	Linearity	$R^2 = 0.9997$

Section A4.2 Analytical Methods for Detection and Identification

Annex Point IIA, IV 4.2 ANALYTICAL METHOD FOR THE DETERMINATION OF ACTIVE SUBSTANCE RESIDUES IN SOIL

3.4	**Specificity: interfering substances**	LC-MS/MS is a highly specific method. No additional confirmatory method is necessary.
3.5	**Recovery rates at different levels**	Samples of two different untreated soil types were each fortified with 0.01, 0.1 and 0.5 mg/kg fenoxycarb. Each fortification level was analysed five times. The mean recoveries obtained at the three fortification levels for both soil types ranged from 100% to 110% with individual recoveries ranging from 94% to 115%. Results are shown in Table 4_2-1.
3.5.1	Relative standard deviation	Relative standard deviations at the three fortification levels ranged from 1.4% to 5.7%. Results are shown in Table 4_2-1.
3.6	**Limit of determination**	The limit of quantification has been set at 0.01 mg/kg.
3.7	**Precision**	
3.7.1	Repeatability	The precision of the method is established based on the findings for recovery rates which were performed under repeatability conditions.
3.7.2	Independent laboratory validation	No independent laboratory validation available.

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1	**Materials and methods**	Specific analytical method RAM 406/01 is used to determine and quantify fenoxycarb residues in soil by LC-MS/MS.
4.2	**Conclusion**	The LC-MS/MS method is able to determine the active substance fenoxycarb in soil. It can be used in normal routine analysis and for monitoring purposes.
4.2.1	Reliability	1
4.2.2	Deficiencies	No

Section A4.2 Analytical Methods for Detection and Identification

Annex Point IIA, IV 4.2 ANALYTICAL METHOD FOR THE DETERMINATION OF ACTIVE SUBSTANCE RESIDUES IN SOIL

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2006-11-09
Materials and methods	[redacted] s. [redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant´s summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 4_2-1: Fenoxycarb recovery data

Soil	Fenoxycarb			SD (%)	CV (%)	n
	Fortification (mg/kg)	Recovery (%)				
		individual values	mean			
Pappelacker (sandy loam)	0.01	105, 111, 98, 109, 111	107	5.5	5.1	5
	0.1	105, 113, 108, 105, 110	108	3.4	3.2	5
	0.5	103, 105, 101, 103, 103	103	1.4	1.4	5
Scheueracker (silty clay loam)	0.01	108, 106, 108, 115, 112	110	3.6	3.3	5
	0.1	109, 99, 106, 108, 100	105	4.6	4.4	5
	0.5	97, 109, 94, 102, 99	100	5.7	5.7	5
Overall		94 - 115	105	5.1	4.9	30

Section A4.2 Analytical Methods for Detection and Identification

Annex Point IIA, IV 4.2 ANALYTICAL METHOD FOR THE DETERMINATION OF ACTIVE SUBSTANCE RESIDUES IN AIR

Official use only

1 REFERENCE

1.1	**Reference**	Hargreaves, S.L. (2003a), Residue analytical method for the determination of fenoxycarb residues in air (RAM 409/01). Syngenta Crop Protection, Jealott's Hill International Research Centre, Bracknell, Berkshire, UK, Report No. TMJ4834, issue date: April 2003 (unpublished). Hargreaves, S.L. (2003b). Fenoxycarb: Validation of an analytical method for the determination of residues in air (RAM 409/01). Syngenta Crop Protection, Jealott's Hill International Research Centre, Bracknell, Berkshire, UK, Report No. TMJ4834, issue date: April 2003 (unpublished).
1.2	**Data protection**	Yes
1.2.1	Data owner	Syngenta
1.2.2	Companies with letter of access	[redacted]
1.2.3	Criteria for data protection	[redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	None stated
2.2	**GLP**	Yes
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Preliminary treatment**	
3.1.1	Enrichment	Air is drawn through sampling tubes containing two layers of XAD-2 adsorbent at a rate of 0.5 L min^{-1} for a period of six hours, using pre-calibrated motorised pumps. After this period the XAD-2 adsorbent is removed from the tubes and residues of fenoxycarb are desorbed by ultrasonication in methanol. Aliquots are diluted further with methanol as required and then with ultra pure water.
3.1.2	Cleanup	
3.2	**Detection**	
3.2.1	Separation method	High performance liquid chromatography
3.2.2	Detector	Triple quadrupole mass spectrometry detection (selected reaction monitoring (SRM), parent ion: m/z 302, product ion: m/z 116).
3.2.3	Standard(s)	External standard
3.2.4	Interfering substance(s)	Substances of the sample matrix may interfere.
3.3	**Linearity**	
3.3.1	Calibration range	The detector response was shown to be linear over a standard concentration range of 2.5 pg to 500 pg injected on column (equivalent to 0.25 ng/mL to 50 ng/mL standards when using a 10 µL injection

		volume).
3.3.2	Number of measurements	Each standard concentration was analysed in triplicate.
3.3.3	Linearity	$R^2 = 0.9999$
3.4	**Specificity: interfering substances**	LC-MS/MS is a highly specific method. No additional confirmatory method is necessary.
3.5	**Recovery rates at different levels**	XAD-2/glass filter tubes were fortified with a fenoxycarb solution at 2.8 µg/m^3 and 28 µg/m^3, equivalent to 0.5 µg and 5 µg, respectively. Each fortification level was analysed five times under two environmental settings, 20°C at 45 % relative humidity and 35°C at 80 % relative humidity. The mean recoveries obtained at the two fortification levels under both sets of environmental conditions ranged from 91% to 102% with individual recoveries ranging from 86% to 109%. Results are shown in Table 4_2-1.
3.5.1	Relative standard deviation	Relative standard deviations at the two fortification levels under both sets of environmental conditions ranged from 4.3% to 8.2%. Results are shown in Table 4_2-1.
3.6	**Limit of determination**	The limit of quantification has been set at 2.8 ng/L (i.e. 2.8 µg/m^3), equivalent to 0.5 µg fortified onto the XAD-2 tubes.
3.7	**Precision**	
3.7.1	Repeatability	The precision of the method is established based on the findings for recovery rates which were performed under repeatability conditions.
3.7.2	Independent laboratory validation	No independent laboratory validation available.

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1	**Materials and methods**	Analytical method RAM 409/01 is used to determine and quantify fenoxycarb residues in air by LC-MS/MS using an external standardisation procedure.
4.2	**Conclusion**	The LC-MS/MS method is able to determine the active substance fenoxycarb in air. It can be used in normal routine analysis and for monitoring purposes.
4.2.1	Reliability	1
4.2.2	Deficiencies	No

Section A4.2 Analytical Methods for Detection and Identification

Annex Point IIA, IV 4.2 ANALYTICAL METHOD FOR THE DETERMINATION OF ACTIVE SUBSTANCE RESIDUES IN AIR

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2006-11-09
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 4_2-1: Fenoxycarb recovery data

Conditions	Fortification Level (µg)	Individual Values (%)	Mean (%)	SD (%)	CV (%)	n
20°C at 45 % relative humidity	0.5	106, 100, 109, 92, 105	102	6.7	6.5	5
	5.0	95, 95, 90, 89, 86	91	3.9	4.3	5
	Overall	86 - 109	97	7.9	8.2	10
35°C at 80 % relative humidity	0.5	102, 93, 90, 104, 87	95	7.5	7.8	5
	5.0	101, 96, 107, 91, 93	98	6.5	6.6	5
	Overall	87 - 107	96	6.7	7.0	10

Section A4.2 Analytical Methods for Detection and Identification

Annex Point IIA, IV 4.2 ANALYTICAL METHOD FOR THE DETERMINATION OF ACTIVE SUBSTANCE RESIDUES IN WATER

Official use only

		1 REFERENCE
1.1	**Reference**	Greulich, K., Alder, L. (2006), Fast multi residue screening of 300 pesticides in drinking water. Federal Institute for Risk Assessment, Berlin, Germany, Report No. BFR-IX-2005, issue date: May 2006 (published in: http://www.bfr.bund.de/cd/5832).
1.2	**Data protection**	No
1.2.1	Data owner	Federal Institute for Risk Assessment (BfR)
1.2.2	Companies with letter of access	
1.2.3	Criteria for data protection	
		2 GUIDELINES AND QUALITY ASSURANCE
2.1	**Guideline study**	None stated
2.2	**GLP**	Yes
2.3	**Deviations**	No
		3 MATERIALS AND METHODS
3.1	**Preliminary treatment**	
3.1.1	Enrichment	After addition of 15 µL methanol to the 1 mL sample of water it is injected directly into the liquid chromatograph without any extraction and/or cleanup of the sample.
3.1.2	Cleanup	
3.2	**Detection**	
3.2.1	Separation method	High performance liquid chromatography
3.2.2	Detector	Triple quadrupole mass spectrometry detection (selected reaction monitoring (SRM), first transition: parent ion: m/z 302, product ion: m/z 88; second transition: parent ion: m/z 302, product ion: m/z 116).
3.2.3	Standard(s)	External standard fenoxycarb (purity: 99.5%)
3.2.4	Interfering substance(s)	Other analytes included in the multi-residue method may interfere.
3.3	**Linearity**	
3.3.1	Calibration range	The linearity of the detector response was shown over a standard concentration range of 0.03 ng/mL to 5 ng/mL (equivalent to 3 – 500 pg injected on column when using a 100 µL injection volume).
3.3.2	Number of measurements	The seven standard concentrations were analysed in single determinations.
3.3.3	Linearity	$R^2 = 0.9993$

Section A4.2 Analytical Methods for Detection and Identification

Annex Point IIA, IV 4.2 ANALYTICAL METHOD FOR THE DETERMINATION OF ACTIVE SUBSTANCE RESIDUES IN WATER

3.4	**Specificity: interfering substances**	LC-MS/MS with two validated transitions is a highly specific method.
3.5	**Recovery rates at different levels**	Drinking water were fortified at 0.1 µg/L and 1.0 µg/L with a fenoxycarb standard solution. Each fortification level was analysed five times. The mean recoveries obtained at fortification levels from 0.1 µg/L and 1.0 µg/L ranged from 101 % to 114 % with individual recoveries ranging from 98 % to 125%. Results are shown in Table 4_2-2.
3.5.1	Relative standard deviation	Relative standard deviations at fortification levels from 0.1 µg/L and 1.0 µg/L ranged from 2 % to 6 %. Results are shown in Table 4_2-2.
3.6	**Limit of determination**	The limit of quantification is set to 0.1 µg/L.
3.7	**Precision**	
3.7.1	Repeatability	The precision of the method is established based on the findings for recovery rates which were performed under repeatability conditions.
3.7.2	Independent laboratory validation	No independent laboratory validation available.

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1	**Materials and methods**	
4.2	**Conclusion**	
4.2.1	Reliability	
4.2.2	Deficiencies	

Section A4.2 Analytical Methods for Detection and Identification

Annex Point IIA, IV 4.2 ANALYTICAL METHOD FOR THE DETERMINATION OF ACTIVE SUBSTANCE RESIDUES IN WATER

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2006-11-09
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant´s summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 4_2-1: Fenoxycarb recovery data

Water Type	Fortification Level (µg/L)	Individual Values (%)	Mean (%)	SD (%)	CV (%)	n
Drinking Water	0.1	125, 11, 112, 106, 118	114	6.5	5.7	5
First transition	1.0	104, 102, 99, 98, 102	101	2.2	2.2	5
302 → 88 amu	Overall	98 – 125	108	8.3	7.7	10
Drinking Water	0.1	111, 110, 104, 117, 106	110	4.5	4.1	5
Second transition	1.0	100, 98, 104, 103, 105	102	2.6	2.6	5
302 → 116 amu	Overall	98 – 117	106	5.3	5.0	10

Section A4.2 Analytical Methods for Detection and Identification

Annex Point IIA, IV 4.2 ANALYTICAL METHOD FOR THE DETERMINATION OF ACTIVE SUBSTANCE RESIDUES IN WATER

Official use only

1 REFERENCE

1.1	**Reference**	Hargreaves, S.L. (2003c), Residue analytical method for the determination of residues of fenoxycarb in water (RAM 408/01). Syngenta Crop Protection, Jealott's Hill International Research Centre, Bracknell, Berkshire, UK, Report No. RJ3391B, issue date: June 2003 (unpublished). Hargreaves, S.L. (2003d). Fenoxycarb: Validation of a residue analytical method for the determination of residues of fenoxycarb in surface water (RAM 408/01). Syngenta Crop Protection, Jealott's Hill International Research Centre, Bracknell, Berkshire, UK, Report No. RJ3391B, issue date: June 2003 (unpublished).
1.2	**Data protection**	Yes
1.2.1	Data owner	Syngenta
1.2.2	Companies with letter of access	[redacted]
1.2.3	Criteria for data protection	[redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	None stated
2.2	**GLP**	Yes
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Preliminary treatment**	
3.1.1	Enrichment	A 10 mL sample of water is loaded onto an Oasis HLB solid phase extraction (SPE) cartridge on which residues of fenoxycarb are retained. Fenoxycarb is eluted from the SPE column with methanol. The column eluate is diluted with ultra pure water.
3.1.2	Cleanup	
3.2	**Detection**	
3.2.1	Separation method	High performance liquid chromatography
3.2.2	Detector	Triple quadrupole mass spectrometry detection (selected reaction monitoring (SRM), parent ion: m/z 302, product ion: m/z 116).
3.2.3	Standard(s)	External standard fenoxycarb (purity: 99.5%)
3.2.4	Interfering substance(s)	Substances of the sample matrix may interfere.
3.3	**Linearity**	
3.3.1	Calibration range	The linearity of the detector response was shown over a standard concentration range of 0.20 ng/mL to 20 ng/mL (equivalent to 2 – 200 pg injected on column when using a 10 µL injection volume).
3.3.2	Number of measurements	Each of five standard concentrations was analysed in triplicate.

Section A4.2 Analytical Methods for Detection and Identification

Annex Point IIA, IV 4.2 ANALYTICAL METHOD FOR THE DETERMINATION OF ACTIVE SUBSTANCE RESIDUES IN WATER

3.3.3	Linearity	$R^2 = 0.9998$
3.4	**Specificity: interfering substances**	LC-MS/MS is a highly specific method. No additional confirmatory method is necessary.
3.5	**Recovery rates at different levels**	Surface water, groundwater and drinking water were fortified at 0.1 µg/L and 1.0 µg/L with a fenoxycarb standard solution. Each fortification level was analysed five times. The mean recoveries obtained at fortification levels from 0.1 µg/L and 1.0 µg/L ranged from 77% to 84% with individual recoveries ranging from 72% to 87%. Results are shown in Table 4_2-1.
3.5.1	Relative standard deviation	Relative standard deviations at fortification levels from 0.1 µg/L and 1.0 µg/L ranged from 1.6% to 5.9%. Results are shown in Table 4_2-1.
3.6	**Limit of determination**	The limit of quantification is set to 0.1 µg/L.
3.7	**Precision**	
3.7.1	Repeatability	The precision of the method is established based on the findings for recovery rates which were performed under repeatability conditions.
3.7.2	Independent laboratory validation	No independent laboratory validation available.

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1	**Materials and methods**	Specific analytical method RAM 408/01 is used to determine and quantify fenoxycarb residues in surface water, ground water and drinking water by LC-MS/MS.
4.2	**Conclusion**	The LC-MS/MS method is able to determine the active substance fenoxycarb in surface water, ground water and drinking water. It can be used in normal routine analysis and for monitoring purposes.
4.2.1	Reliability	1
4.2.2	Deficiencies	No

Section A4.2 Analytical Methods for Detection and Identification

Annex Point IIA, IV 4.2 ANALYTICAL METHOD FOR THE DETERMINATION OF ACTIVE SUBSTANCE RESIDUES IN WATER

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2007-01-19
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table 4_2-1: Fenoxycarb recovery data

Water Type	Fortification Level (µg/L)	Individual Values (%)	Mean (%)	SD (%)	CV (%)	n
River Water	0.1	87, 85, 80, 75, 79	81	4.8	5.9	5
	1.0	78, 82, 79, 80, 77	79	1.9	2.4	5
	Overall	75 – 87	80	3.6	4.5	10
Ground Water	0.1	77, 79, 78, 78, 72	77	2.8	3.6	5
	1.0	78, 79, 76, 79, 79	78	1.3	1.7	5
	Overall	72 – 79	78	2.2	2.8	10
Drinking Water	0.1	81, 83, 79, 83, 87	83	3.0	3.6	5
	1.0	83, 85, 86, 85, 83	84	1.3	1.6	5
	Overall	79 – 87	84	2.4	2.8	10

Section A4.2 **Annex Point IIA, IV 4.2**	**Analytical Methods for Detection and Identification** ANALYTICAL METHOD FOR THE DETERMINATION OF ACTIVE SUBSTANCE RESIDUES IN ANIMAL AND HUMAN BODY FLUIDS AND TISSUES	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [ ]** **Other justification [X]**	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]	–	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	2006-11-09	
Evaluation of applicant's justification	[redacted]	
Conclusion	[redacted]	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A4.3	Analytical Methods for Detection and Identification	
Annex Point IIIA, IV 1	ANALYTICAL METHOD FOR THE DETERMINATION OF ACTIVE SUBSTANCE RESIDUES IN/ON FOOD OR FEEDSTUFFS	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	**Technically not feasible** [ ] **Scientifically unjustified** [ ]	
Limited exposure [ ]	**Other justification** [X]	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]	–	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	2006-11-09	
Evaluation of applicant's justification	[redacted]	
Conclusion	[redacted]	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A5 Effectiveness against target organisms and intended uses

Subsection (Annex Point)			Official use only
5.1	**Function (IIA5.1)**	Generally fenoxycarb formulations have been examined for efficacy against insects in a range of applications from agriculture use to incorporation in wood preservatives (biocidal use). In wood preservation (product type 8 of the EU Biocidal Product Directive), fenoxycarb is used for the protective or remedial treatment of wood against wood-destroying insects.	
5.2	**Organism(s) to be controlled and products, organisms or objects to be protected (IIA5.2)**	--	
5.2.1	**Organism(s) to be controlled (IIA5.2)**	Fenoxycarb is applied against species of insects which attack (they bore) wood products. Fenoxycarb is particularly effective against House Longhorn Beetle (*Hylotropes bajulus*), Brown Powderpost Beetle (*Lyctus brunneus*) and Furniture Beetle (*Anobium punctatum*). Detailed data on efficacy are summarised in Table A5.1.	X
5.2.2	**Products, organisms or objects to be protected (IIA5.2)**	Protection of wooden articles and structures.	
5.3	**Effects on target organisms, and likely concentration at which the active substance will be used (IIA5.3)**	--	
5.3.1	**Effects on target organisms (IIA5.3)**	Fenoxycarb has an ovicidal effect on eggs of wood-destroying insects. Furthermore, growth of the larvae of wood-destroying insects - such as larvae of *Hylotrupes bajulus (L)* is prevented. Fenoxycarb also provides substantial eradicant efficacy against the wood-destroying action of the Brown Powderpost Beetle *(Lyctus brunneus)* and the Furniture Beetle *(Anobium punctatum).* See attached Summary Table A5.1 for detailed efficacy data. For more detailed information confer the separated study summaries for section 5.3.1 (Effects on target organisms). See also Study Summaries in section 5.10 of Document III-B of dossier (Effects of formulated product on target organisms).	X
5.3.2	**Likely concentrations at which the A.S. will be used (IIA5.3)**		
	PT8	Final concentration of active ingredient in biocidal product: Approximately 0.015% to 0.025% fenoxycarb in water based formulated wood preservatives.	

Section A5 Effectiveness against target organisms and intended uses

	PTn	--
5.4	**Mode of action (including time delay) (IIA5.4)**	--
5.4.1	**Mode of action**	Fenoxycarb is a non-neurotoxic insect growth regulator (IGR) with contact and stomach action. It exhibits a strong juvenile hormone activity, inhibiting metamorphosis to the adult stage and interfering with the moulting of early instar larvae.
5.4.2	**Time delay**	Not relevant for this kind of application (wood preservation)
5.5	**Field of use envisaged (IIA5.5)**	
	MG01: Disinfectants, general biocidal products	
	MG02: Preservatives MG03: Pest control	Product type PT08: Wood preservatives
	MG04: Other biocidal products Further specification	
5.6	**User (IIA5.6)**	
	Industrial	Industrial dipping. For details about use-conditions refer to Document II-B of dossier.
	i) Open system ii) Closed system	
	Professional	Professional dipping For details about use-conditions refer to Document II-B of dossier.
	i) Open system ii) Closed system	
	General public	Not intended
5.7	**Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies (IIA5.7)**	--
5.7.1	**Development of resistance**	A development of resistance is neither to be expected nor has been ever observed. During several years when fenoxycarb-based wood preservatives are in the market no resistance of the target organisms has been observed. No resistances were noted up to now, after a usage of Fenoxycarb in

Section A5		Effectiveness against target organisms and intended uses
		the impregnation of wood for several years in Europe..
5.7.2	**Management strategies**	Not relevant
5.8	**Likely tonnage to be placed on the market per year (IIA5.8)**	See entries in IUCLID database

Table A5.1: Summary Table: Data available on the effectiveness of fenoxycarb against wood-destroying insects

Test substance	Test organism(s)	Test system / concentrations applied / exposure time	Test results: lowest non-preventive concentration	Reference
FAROX (= fenoxycarb); solved in methanol	Larvae of *Hylotrupes bajulus (L)* (House Longhorn Beetle)	Preventive efficacy against larvae of wood destroying House Longhorn Beetle according to EN 46 (04/90) -Wood species: *Pinus sylvestris* - Concentrations applied: 0.1, 0.5, 1.0 and 5.0 mg/m²	Fenoxycarb provided substantial protection against the wood-destroying action of the house longhorn beetle *Hylotrupes bajulus (L).* At the lowest test concentration of 0.1 mg fenoxycarb/m² a mortality of 97 % was achieved for the House Longhorn Beetle *Hylotrupes bajulus*. At higher test concentrations the mortality rate of target organisms was 100 %. The test meets the criteria of EN 46.	Grube & Rudolph (1998): Abschlussbericht zur Wirksamkeit von FAROX (Fenoxycarb) gegen *Hylotrupes bajulus*. Report, BAM, FG IV.1, Berlin, Germany; unpublished
Fenoxycarb	Brown Powderpost Beetle *(Lyctus brunneus)* and Furniture Beetle *(Anobium punctatum).*	Eradicant efficacy on *Lyctus* and *Anobium* was evaluated in a Sandwich Test according to Pallaske (1997): Wood species: Pine sapwood (*Amobium*), oak sapwood (*Lyctus*). The *Lyctus* samples were first impregnated with a nutrient solution according to EN 20.1. After this treatment samples were dried. Two cavities, 2.0 and 2.5 mm in diameter were drilled into each slat. Controls were carried out in intervals of 4 weeks. At the end of the experiment, wood loss through consumption, the weight of the bore dust and the number of skins shed were evaluated.	Fenoxycarb applied by brushing, provided substantial eradicant efficacy against the wood-destroying action of the Brown Powderpost Beetle (*Lyctus brunneus*) and the Furniture Beetle (*Anobium punctatum*). Fenoxycarb led to a 100% mortality rate for *Lyctus brunneus* after 12 weeks and for *Anobium punctatum* after 48 weeks at a dosage of 1250 mg a.i./m².	Graf, E., Barkhoff, M., Hamberg, R., Büttner, H. and Pallaske, M. (2002): The use of insect hormones as non-neurotoxic insecticides in wood preservatives. The International Research Group on Wood Preservation. Report No. IRG/WP 02-30277, published.

Section A5 Effectiveness against target organisms and intended uses

	Evaluation by Competent Authorities
5.2.1	Organism(s) to be controlled
5.3.1	Effects on target organisms
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	27.06.2008
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant´s summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A5.3
Annex Point IIA5.3

Efficacy Data (1)

Efficacy of fenoxycarb on wood against the House Longhorn Beetle *Hylotrupes bajulus (L).*

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		1 REFERENCE
1.1	**Reference**	Grube & Rudolph (1998): Abschlußbericht zur Wirksamkeit von FAROX (Fenoxycarb) gegen *Hylotrupes bajulus*. Report, BAM, FG IV.1, Berlin, Germany; unpublished, dated: 1998-07-22.
1.2	**Data protection**	Yes
1.2.1	Data owner	Syngenta
1.2.2	Companies with letter of access	[redacted]
1.2.3	Criteria for data protection	[redacted]
1.3	**Guideline study**	Yes; EN 46 (04/90): Wood preservatives – Determination of the preventive action against recently hatched larvae of *Hylotrupes bajulus*.
1.4	**Deviations**	No
		2 METHOD
2.1	**Test Substance (Biocidal Product)**	
2.1.1	Trade name/ proposed trade name	FAROX (fenoxycarb)
2.1.2	Composition of Product tested	Fenoxycarb was only solved in methanol
2.1.3	Physical state and nature	Fenoxycarb was only solved in methanol
2.1.4	Monitoring of active substance concentration	No
2.1.5	Method of analysis	-
2.2	**Reference substance**	None
2.2.1	Method of analysis for reference substance	Not applicable
2.3	**Testing procedure**	-
2.3.1	Test population / inoculum / test organism	Test organism: Eggs and larvae of house longhorn beetle *Hylotrupes bajulus (L);* Number of eggs and larvae exposed to test substance: See Table A5_3-1
2.3.2	Test system	Areas of Scots pine sapwood (*Pinus sylvestris*) were treated with a defined amount of the product (0.1, 0.5, 1.0 and 5.0 mg/m²). The evaluation of the test was done according to EN 46. Dimensions of test specimens: according to EN 46.

Section A5.3
Annex Point IIA5.3

Efficacy Data (1)

Efficacy of fenoxycarb on wood against the House Longhorn Beetle *Hylotrupes bajulus (L).*

		Test variants: See Tables A5_3-1 and A5_3-2.
		Test was performed without ageing procedure according to EN 84.
2.3.3	Application of TS	Volume of treatment solution: 150 ml/m²
2.3.4	Test conditions	The test substance was solved in methanol and then applied to the samples.
		Conditions in the culturing chamber (temperature, r.h., air circulation): according to EN 46.
		Conditions in the conditioning chamber (temperature, r.h., air circulation): according to EN 46.
		Conditions in the testing chamber (temperature, r.h., air circulation): according to EN 46.
		Concentrations tested: 0.1, 0.5, 1.0 and 5.0 mg/m².
2.3.5	Duration of the test / Exposure time	Test duration: according to EN 46
		Exposure time: Single application
2.3.6	Number of replicates performed	See Tables A5_3-1 and A5_3-2.
2.3.7	Controls	Negative control: The damaging activity of the insects is verified by exposure untreated wood to the insects.
2.4	**Examination**	
2.4.1	Effect investigated	Prevention of hatching and mortality of recently hatched larvae was determined for the test concentrations.
2.4.2	Method for recording / scoring of the effect	The number of surviving larvae and number of dead gnawing larvae are registered
2.4.3	Intervals of examination	Test wood samples were assessed at the 4th week after incubation
2.4.4	Statistics	The arithmetic mean was calculated from all wood samples per treatment concentration.
2.4.5	Post monitoring of the test organism	No
		3 RESULTS
3.1	**Efficacy**	
3.1.1	Dose/Efficacy curve	No
3.1.2	Begin and duration of effects	At the lowest test concentration of 0.1 mg fenoxycarb/m² a mortality of 97 % was achieved for the House Longhorn Beetle *Hylotrupes bajulus*. At higher test concentrations the mortality rate of target organisms was 100 %.

Section A5.3
Annex Point IIA5.3

Efficacy Data (1)
Efficacy of fenoxycarb on wood against the House Longhorn Beetle *Hylotrupes bajulus (L).*

3.2	**Effects against organisms or objects to be protected**	In negative control samples that did not receive a protective coating, 83-88% of the larvae survived.
3.3	**Other effects**	None
3.4	**Efficacy of the reference substance**	Not applicable
3.5	**Tabular and/or graphical presentation of the summarised results**	See attached Tables A5_3-1 and A5_3-2.
3.6	**Efficacy limiting factors**	None
3.6.1	Occurrences of resistances	–
3.6.2	Other limiting factors	–
	4 RELEVANCE OF THE RESULTS COMPARED TO FIELD CONDITIONS	
4.1	**Reasons for laboratory testing**	Testing according to EN 46 is a standard procedure for efficacy assessment for wood preservatives.
4.2	**Intended actual scale of biocide application**	The applied amount of wood preservative and active substance is comparable with the intended scale of product to be applied in practice.
4.3	**Relevance compared to field conditions**	-
4.3.1	Application method	-
4.3.2	Test organism	Yes, the test organisms are among the intended target organisms.
4.3.3	Observed effect	Yes, the protective effect was significant.
4.4	**Relevance for read-across**	Yes
	5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	The protective effectiveness of the active substance fenoxycarb against house longhorn beetle *Hylotrupes bajulus (L)* in service was assessed according to DIN EN 46 (04/90). The substrate was Scots pine (*Pinus sylvestris*). The test formulation was applied at different concentrations (0.1, 0.5, 1.0 and 5.0 mg/m²); the test blocks were inoculated with the longhorn beetle and incubated for 4 weeks. The test blocks were scored for gnawing and surviving larvae were counted.
5.2	**Reliability**	1

Section A5.3
Annex Point IIA5.3

Efficacy Data (1)

Efficacy of fenoxycarb on wood against the House Longhorn Beetle *Hylotrupes bajulus (L).*

5.3	**Assessment of efficacy, data analysis and interpretation**	Fenoxycarb provided substantial protection against the wood-destroying action of the House Longhorn Beetle *Hylotrupes bajulus (L).* At the lowest test concentration of 0.1 mg fenoxycarb/m² a mortality of 97 % was achieved for the House Longhorn . At higher test concentrations the mortality rate of target organisms was 100 %. The test meets the criteria of EN 46.
5.4	**Conclusion**	The test is valid.
5.5	**Proposed efficacy specification**	Fenoxycarb provided substantial protection against the wood-destroying action of the house longhorn beetle *Hylotrupes bajulus (L).*

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	27.06.2008
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A5_3-1 Efficacy of fenoxycarb against eggs of House Longhorn Beetles (*Hylotrupes bajulus L.*) according to the EN 46 without ageing procedure

FAROX dose (mg/m²)	Total number of eggs	Number of test replicates	Mortality of eggs		Effect on larvae development/hatching		
			(total number)	(%)	Larvae developed, not hatched	Larvae hatched, dead	No development of larvae
Control	565	n = 7	64	11.3	27	16	21
0.1	545	n = 10	198	36.3	122	21	55
0.5	572	n = 10	363	63.5	222	41	100
1.0	1140	n = 10	1102	96.7	906	15	181
5.0	426	n = 10	397	93.2	285	8	104

Table A5_3-2 Cummulative preventive efficacy of fenoxycarb against eggs and recently hatched larvae of House Longhorn Beetles (*Hylotrupes bajulus L.*) according to the EN 46 without ageing procedure

FAROX dose (mg/m²)	Total number of eggs	Number of samples	Number and condition of recovered larvae			Number of larvae not founded	Mortality (%)
			Dead		Alive		
			Not gnawed into wood	Gnawed into wood	Gnawed into wood		
Control	53	5	0	9	42	2	**17**
0.1	347	15	298	37	12	0	**97**
0.5	209	10	209	0	0	0	**100**
1.0	38	4	33	5	0	0	**100**
5.0	29	3	29	0	0	0	**100**

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Annex Point IIA5.3

Efficacy Data (2)

Efficacy of fenoxycarb on wood against the Brown Powderpost Beetle *(Lyctus brunneus)* and Furniture Beetle *(Anobium punctatum).*

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		1 REFERENCE
1.1	**Reference**	Graf, E., Barkhoff, M., Hamberg, R., Büttner, H. and Pallaske, M. (2002): The use of insect hormones as non-neurotoxic insecticides in wood preservatives. The International Research Group on Wood Preservation. Report No. IRG/WP 02-30277. Sponsored by the "Deutsche Bundesstiftung Umwelt", Project No. DBSU 08176.
1.2	**Data protection**	No
1.2.1	Data owner	Published
1.2.2	Companies with letter of access	[redacted]
1.2.3	Criteria for data protection	[redacted]
1.3	**Guideline study**	Yes; Eradicant efficacy on *Lyctus* and *Anobium*: Sandwich Test according to Pallaske; *Reference for test method:* Pallaske, M. (1997): Insect Growth Regulators – mode of action and mode of action-dependent peculiarities in the evaluation of the efficacy for their use in wood preservation. Report, IRG/WP 97-30155; 17 p
1.4	**Deviations**	No
		2 METHOD
2.1	**Test Substance (Biocidal Product)**	
2.1.1	Trade name/ proposed trade name	Fenoxycarb
2.1.2	Composition of Product tested	Fenoxycarb was only diluted
2.1.3	Physical state and nature	Solution miscible in water
2.1.4	Monitoring of active substance concentration	No
2.1.5	Method of analysis	-
2.2	**Reference substance**	The efficacy of fenoxycarb was compared to two ecdyson analogues (tebufenozid and halofenozid) and a juvenile hormone analogue (pyriproxyfen).
2.2.1	Method of analysis for reference substance	Standard HPLC procedures were applied for the measurements of the other active substances.

Section A5.3
Annex Point IIA5.3

Efficacy Data (2)

Efficacy of fenoxycarb on wood against the Brown Powderpost Beetle *(Lyctus brunneus)* and Furniture Beetle *(Anobium punctatum).*

2.3	**Testing procedure**	-
2.3.1	Test population / inoculum / test organism	Test organism: The Brown Powderpost Beetle (*Lyctus brunneus*) and Furniture Beetle (*Anobium punctatum*).
2.3.2	Test system	Eradicant efficacy on *Lyctus* and *Anobium*: Sandwich Test according to Pallaske (1997): Pine sapwood slats were used for the *Amobium* and oak sapwood slats for *Lyctus*, both approx. 76 x 26 x 2.5 mm in size. The *Lyctus* samples were first impregnated with a nutrient solution according to EN 20.1. After this treatment samples were dried at 20°C/65% r.h.. Two cavities, 2.0 and 2.5 mm in diameter were drilled into each slat. The *Anobium* larvae that were placed into the cavities weighted between 2.6 and 3.5 mg, the *Lyctus* between 2 and 4 mg. The slats were fixed between two slides with TESA fabric tape and incubated in a standard conditioning environment until beetles hatched or the larvae died. Controls were carried out in intervals of 4 weeks. At the end of the experiment, mortality of target beetles, wood loss through consumption, the weight of the bore dust and the number of skins shed were evaluated. For each series in this experiment (active substance, concentration) two larvae were placed in each of the 13 samples.
2.3.3	Application of TS	The diluted test substance was brushed to the wood slats by brushing to evaluate the eradicative efficacy of fenoxycarb against the mentioned wood-destroying insects.
2.3.4	Test conditions	See Point 2.3.2 for details
2.3.5	Duration of the test / Exposure time	Duration of whole test: 80 weeks. Exposure times: Fenoxycarb: 12 weeks (*Lyctus brunneus*) or 48 weeks (*Anobium punctatum*). Tebufenozid: 24 weeks (*Lyctus brunneus*) or 80 weeks (*Anobium punctatum*). Halofenozid: 12-20 weeks (*Lyctus brunneus*) or 56-80 weeks (*Anobium punctatum*).
2.3.6	Number of replicates performed	Sandwich Test according to Pallaske (1997): For each series in this experiment (active substance, concentration) two larvae were placed in each of the 13 samples.
2.3.7	Controls	Controls were carried out in intervals of 4 weeks.
2.4	**Examination**	
2.4.1	Effect investigated	At the end of the experiment, wood loss through consumption, the weight of the bore dust and the number of skins shed were evaluated.
2.4.2	Method for recording / scoring of the effect	See Point 2.3.2 for details
2.4.3	Intervals of examination	See Point 2.3.2 for details
2.4.4	Statistics	The arithmetic mean was calculated from all replications of each test series.

Section A5.3
Annex Point IIA5.3

Efficacy Data (2)

Efficacy of fenoxycarb on wood against the Brown Powderpost Beetle *(Lyctus brunneus)* and Furniture Beetle *(Anobium punctatum).*

2.4.5	Post monitoring of the test organism	No
		3 RESULTS
3.1	**Efficacy**	
3.1.1	Dose/Efficacy curve	No
3.1.2	Begin and duration of effects	In a test according the Sandwich Method (Pallaske 1997), the juvenile hormone analogue substance fenoxycarb led to a 100% mortality rate for *Lyctus brunneus* after 12 weeks and for *Anobium punctatum* after 48 weeks at a dosage of 1250 mg a.i./m².
3.2	**Effects against organisms or objects to be protected**	In negative control samples all test wood articles were strongly bored at the time of testing.
3.3	**Other effects**	Distribution of fenoxycarb in the different matrices: Amount of a.i. taken up by the larvae which becomes metabolised: Fenoxycarb: 75.7% (Reference substances: Tebufenozid: 66.6%, Halofenozid: 70.4%, Pyriproxyfen: 81.8%). The amount of test substance remaining is almost quantitatively exceted. The bio-available share is very low: Fenoxycarb: <0.05% (Reference substances: Tebufenozid: 0.1%, Halofenozid: 0.25%, Pyriproxyfen: 0.03%).
3.4	**Efficacy of the reference substance**	Halofenozid: At a dosage of 1250 mg a.i./m² 100% effect on *Lyctus brunneus* after 12 weeks and for *Anobium punctatum* after 56 weeks. Tebufenozid: At a dosage of 1250 mg a.i./m² 80.8% effect on *Lyctus brunneus* after 24 weeks and for *Anobium punctatum* 7.7% after 80 weeks. Tebufenozid was considerably less effective against these two wood destroying insects. See attached Table A5_3-1 for details.
3.5	**Tabular and/or graphical presentation of the summarised results**	See attached Table A5_3-1
3.6	**Efficacy limiting factors**	None
3.6.1	Occurrences of resistances	–
3.6.2	Other limiting factors	–

Section A5.3
Annex Point IIA5.3

Efficacy Data (2)

Efficacy of fenoxycarb on wood against the Brown Powderpost Beetle *(Lyctus brunneus)* and Furniture Beetle *(Anobium punctatum).*

4 RELEVANCE OF THE RESULTS COMPARED TO FIELD CONDITIONS

4.1	**Reasons for laboratory testing**	Tests according to the mentioned methods are standard procedures for efficacy assessment for wood preservatives.
4.2	**Intended actual scale of biocide application**	The applied amount of wood preservative and active substance is comparable with the intended scale of product to be applied in practice.
4.3	**Relevance compared to field conditions**	-
4.3.1	Application method	--
4.3.2	Test organism	Yes, the test organisms are among the intended target organisms.
4.3.3	Observed effect	Yes, the eradicant efficacy was significant.
4.4	**Relevance for read-across**	Yes

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	Eradicant efficacy on *Lyctus* and *Anobium*: Sandwich Test according to Pallaske (1997): Pine sapwood slats were used for the *Amobium* and oak sapwood slats for *Lyctus*, both approx. 76 x 26 x 2.5 mm in size. The *Lyctus* samples were first impregnated with a nutrient solution according to EN 20.1. After this treatment samples were dried at 20°C/65% r.h.. Two cavities, 2.0 and 2.5 mm in diameter were drilled into each slat. The *Anobium* larvae that were placed into the cavities weighted between 2.6 and 3.5 mg., the *Lyctus* between 2 and 4 mg. The slats were fixed between two slides with TESA fabric tape and incubated in a standard conditioning environment until beetles hatched or the larvae died. Controls were carried out in intervals of 4 weeks. At the end of the experiment, mortality of target beetles, wood loss through consumption, the weight of the bore dust and the number of skins shed were evaluated. For each series in this experiment (active substance, concentration) two larvae were placed in each of the 13 samples.
5.2	**Reliability**	2
5.3	**Assessment of efficacy, data analysis and interpretation**	Fenoxycarb applied by brushing, provided substantial eradicant efficacy against the wood-destroying action of the Brown Powderpost Beetle *(Lyctus brunneus)* and the Furniture Beetle *(Anobium punctatum).*
5.4	**Conclusion**	The test is valid.
5.5	**Proposed efficacy specification**	Fenoxycarb applied by brushing, provided substantial eradicant efficacy against the wood-destroying action of the test beetles.

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	27.06.2008
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant´s summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A5_3-1 Eradicant efficacy of fenoxycarb against the the Brown Powderpost Beetle *(Lyctus brunneus)* and Furniture Beetle *(Anobium punctatum)* in a test according to Sandwich Method (Pallaske, 1997)

0Active substance		Mortality (%)	
		Lyctus brunneus (24 weeks)	*Anobium punctatum* (80 weeks)
Tebufenozid	1250	80.8	7.7
	125	65.4	23.1
	12.5	23.1	7.7
Halofenozid	1250	100 (12 weeks)	100 (56 weeks)
	125	92.3 (20 weeks)	34.6
	12.5	65.4 (20 weeks)	15.4
Fenoxycarb	1250	100 (12 weeks)	100 (48 weeks)

Section A6.1.1 Acute Toxicity

Annex Point IIA VI.6.1.1 6.1.1 Acute oral toxicity in rats (LD_{50} test)

			Official use only
		1 REFERENCE	
1.1	**Reference**	[redacted] (1982), Acute Oral LD50 In Rats On Ro 13-5223/000. [redacted], Report No. 007402, 25 May 1982 (unpublished).	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Syngenta	
1.2.2	Companies with letter of access	[redacted]	
1.2.3	Criteria for data protection	[redacted]	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	No 92/69/EEC B.1(1992) ≅ OECD 401 (1987) ≅ FIFRA § 81-1 The study was performed prior to the above guidelines but has been checked for compliance with the above.	
2.2	**GLP**	Yes	
2.3	**Deviations**	None	
		3 MATERIALS AND METHODS	
3.1	**Test material**	Fenoxycarb technical (Ro 13-5223/000)	
3.1.1	Lot/Batch number	[redacted]	
3.1.2	Specification		
3.1.2.1	Description	not reported	
3.1.2.2	Purity	[redacted]	
3.1.2.3	Stability	not reported	
3.2	**Test Animals**		
3.2.1	Species	Rat	
3.2.2	Strain	[redacted]	
3.2.3	Source	not reported	X
3.2.4	Sex	Males & Females	
3.2.5	Age/weight at study initiation	not reported	X
3.2.6	Number of animals per group	Five per sex	
3.2.7	Control animals	No	
3.3	**Administration/ Exposure**	Oral	
3.3.1	Postexposure period	14 days	
3.3.2	Type	Gavage	
3.3.3	Concentration	3000, 5000, 8000 or 10,000 mg fenoxycarb/kg bw	
3.3.4	Vehicle	Polyethylene glycol (PEG) 400	

Section A6.1.1 Acute Toxicity

Annex Point IIA VI.6.1.1 6.1.1 Acute oral toxicity in rats (LD_{50} test)

3.3.5	Concentration in vehicle	not reported	
3.3.6	Total volume applied	not reported	
3.3.7	Control	–	
3.4	**Examinations**	Clinical observations, gross necropsy, body weights	
3.5	**Method of determination of LD_{50}**	not reported	X
3.6	**Further remarks**	None	

4 RESULTS AND DISCUSSION

4.1	**Clinical signs**	Two of the females dosed at 10000 mg/kg died on day 2. There were no other mortalities. Clinical signs were seen in animals from all groups but were more pronounced in the higher dose groups. Common signs recorded included sedation, dyspnoea, ventral, latero-abdominal or curved body position, diarrhoea, ruffled fur, spasms and tremor. All surviving animals had recovered within 7 to 9 days of dosing. The mean bodyweights for each group increased during the study.
4.2	**Pathology**	In the two females dosed at 10000 mg/kg that died, slight to moderate unicellular and multicellular necrosis was noted in the liver. A gastric ulcer was noted in one male dosed at 10000 mg/kg and splenic haematopoiesis was noted in most animals of all groups. Other lesions recorded are commonly seen in rats of this age and strain and were considered not to be treatment-related.
4.3	**Other**	–
4.4	**LD_{50}**	LD_{50} > 10, 000 mg/kg bw (males and females)

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	Groups of five male and five female [redacted] rats received a single oral dose of 3000, 5000, 8000 or 10,000 mg fenoxycarb/kg bw in polyethylene glycol (PEG) 400. The animals were assessed daily for the following 14 days for any signs of systemic toxicity and their bodyweights were recorded at intervals throughout the study. Animals in extremis and those surviving to the end of the study were killed and subjected to a macroscopic examination post mortem. Heart, lung, liver, kidney and spleen were examined histopathologically.

Section A6.1.1 Acute Toxicity

Annex Point IIA VI.6.1.1 6.1.1 Acute oral toxicity in rats (LD_{50} test)

5.2	**Results and discussion**	**General observations:** Two of the females dosed at 10000 mg/kg died on day 2. There were no other mortalities. Clinical signs were seen in animals from all groups but were more pronounced in the higher dose groups. Common signs recorded included sedation, dyspnoea, ventral, latero-abdominal or curved body position, diarrhoea, ruffled fur, spasms and tremor. All surviving animals had recovered within 7 to 9 days of dosing. The mean bodyweights for each group increased during the study. **Gross pathology, histopathology:** In the two females dosed at 10000 mg/kg that died, slight to moderate unicellular and multicellular necrosis was noted in the liver. A gastric ulcer was noted in one male dosed at 10000 mg/kg and splenic haematopoiesis was noted in most animals of all groups. Other lesions recorded are commonly seen in rats of this age and strain and were considered not to be treatment-related.
5.3	**Conclusion**	**The acute oral LD_{50} for fenoxycarb was in excess of 10,000 mg/kg bw. According to Commission Directive 2001/59/EC, a classification for acute oral toxicity is not required.**
5.3.1	Reliability	1
5.3.2	Deficiencies	None

Section A6.1.1 Acute Toxicity

Annex Point IIA VI.6.1.1 6.1.1 Acute oral toxicity in rats (LD_{50} test)

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2006/08/02
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A6.1.2 Acute Toxicity

Annex Point IIA VI.6.1.2 6.1.2 Acute dermal toxicity in rats (Limit Test)

			Official use only
		1 REFERENCE	
1.1	**Reference**	[redacted] (1981), Acute Percutaneous Toxicity to Rats of Ro 13-5223/000. [redacted], Report No. 80648D/HLR85/AC, 20 February 1981 (unpublished).	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Syngenta	
1.2.2	Companies with letter of access	[redacted]	
1.2.3	Criteria for data protection	[redacted]	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	No 92/69/EEC B.3 (1992) ≅ OECD 402 (1987) ≅ FIFRA § 81-2 The study was performed prior to the above guidelines but has been checked for compliance with the above	
2.2	**GLP**	Yes	
2.3	**Deviations**	None	
		3 MATERIALS AND METHODS	
3.1	**Test material**	Fenoxycarb (Ro 13-5223/000)	
3.1.1	Lot/Batch number	[redacted]	
3.1.2	Specification	Not reported	
3.2	**Test Animals**		
3.2.1	Species	Rat	
3.2.2	Strain	CD (Sprague-Dawley derived)	
3.2.3	Source	Not reported	X
3.2.4	Sex	Males and females	
3.2.5	Age/weight at study initiation	Young adult	X
3.2.6	Number of animals per group	5 per sex	X
3.2.7	Control animals	Yes	X
3.3	**Administration/ Exposure**	Dermal	
3.3.1	Postexposure period	14 days	
3.3.2	Vehicle	Corn oil	
3.3.3	Total volume applied	Max. 5 mL/kg bw	
3.3.4	Duration of exposure	24 h	
3.3.5	Controls	Vehicle	

Section A6.1.2 Acute Toxicity

Annex Point IIA VI.6.1.2 6.1.2 Acute dermal toxicity in rats (Limit Test)

3.4	**Examinations**	Clinical observations, body weights, gross necropsy	
3.5	**Method of determination of LD_{50}**	Not applicable; no mortalities occurred.	
3.6	**Further remarks**	–	
		4 RESULTS AND DISCUSSION	
4.1	**Clinical signs**	There were no mortalities or clinical observations related to administration of fenoxycarb. There was no observable dermal irritation at the site of application in either treated or control animals.	X
4.2	**Pathology**	There were no treatment related findings at macroscopic examination *post mortem.*	
4.3	**Other**	All animals gained bodyweight throughout the study.	
4.4	**LD_{50}**	LD_{50} > 2000 mg/kg bw	
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	A group of five male and five female, young adult, CD (Sprague-Dawley derived) rats received a single dermal application 2000 mg fenoxycarb/kg bw as a 40% w/v suspension in corn oil and dosed at a volume not exceeding 5 mL/kg. A vehicle control group of 5 rats per sex was treated with corn oil at the same dose volume as the test group. The animals were assessed daily for the following 14 days for any signs of systemic toxicity and their bodyweights were recorded at intervals throughout the study. At the end of the study the animals were killed and subjected to a macroscopic examination *post mortem.*	
5.2	**Results and discussion**	**General observations:** There were no mortalities or clinical observations related to administration of fenoxycarb. There was no observable dermal irritation at the site of application in either treated or control animals. All animals gained bodyweight throughout the study. **Gross pathology:** There were no treatment related findings at macroscopic examination *post mortem.*	
5.3	**Conclusion**	**The acute dermal LD_{50} for fenoxycarb in male and female rats was in excess of 2000 mg/kg.** **According to Commission Directive 2001/59/EC a classification for acute dermal toxicity is not required.**	
5.3.1	Reliability	2	
5.3.2	Deficiencies	Yes The test substance is poorly characterised. This does not impair the overall validity of the study since there were no critical effects observed in this study.	

Section A6.1.2 Acute Toxicity

Annex Point IIA VI.6.1.2 6.1.2 Acute dermal toxicity in rats (Limit Test)

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2006/08/01
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A6.1.2 Acute Toxicity

Annex Point IIA VI.6.1.2 6.1.2 Acute dermal toxicity in rats (Limit Test)

Table A6_1-1. Table for acute dermal toxicity

Dose [mg/kg bw]	Toxicological result*	Duration of clinical signs	Observations
Males			
2000	0/5/5	Day 2- 10	Slight reddening at application site, with incrustation on day 5
Females			
2000	0/5/5	Day 2 - 14	Slight reddening at application site, with incrustation on day 5
LD_{50} value	> 2000 mg/kg bw (males and females)		

* 1st number = number of dead animals
2nd number = number of animals with clinical signs
3rd number = number of animals exposed

Section A6.1.3 Acute Toxicity

Annex Point IIA VI.6.1.3 6.1.3 Acute inhalation toxicity to the rat (Limit Test)

Official use only

		1 REFERENCE
1.1	**Reference**	[redacted]1992), CGA 114597: Acute Inhalation Toxicity in the Rat. CGA 114597 tech. [redacted], Report No. 911362, 22 January1992 (unpublished)
1.2	**Data protection**	Yes
1.2.1	Data owner	Syngenta
1.2.2	Companies with letter of access	[redacted]
1.2.3	Criteria for data protection	[redacted]
		2 GUIDELINES AND QUALITY ASSURANCE
2.1	**Guideline study**	Yes 92/69/EEC B.2 (1992) ≅ OECD 403 (1981) ≅ FIFRA § 81-3
2.2	**GLP**	Yes
2.3	**Deviations**	None
		3 MATERIALS AND METHODS
3.1	**Test material**	CGA 114597 technical (also known as fenoxycarb)
3.1.1	Lot/Batch number	Lot No. [redacted]
3.1.2	Specification	
3.1.2.1	Description	Not reported
3.1.2.2	Purity	[redacted]
3.1.2.3	Stability	Not reported
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain	Albino rats (Tif:RAIf(SPF); hybrids of RII/1xRII/2)
3.2.3	Sex	Males and females (1:1)
3.2.4	Age/weight at study initiation	Young adult
3.2.5	Number of animals per group	5 per sex
3.2.6	Control animals	Yes
3.3	**Administration/ Exposure**	Inhalation
3.3.1	Postexposure period	14 days
3.3.2	Concentrations	Nominal concentration: 6321 mg/m³ Exposure concentration (mean ± SD): 4434 ± 162 mg/m³ See Table A6_1-3.1.

Section A6.1.3 Acute Toxicity

Annex Point IIA VI.6.1.3 6.1.3 Acute inhalation toxicity to the rat (Limit Test)

3.3.3	Particle size	MMAD; GSD: 0.9 – 1.2 µm; 2.6 – 3.4
3.3.4	Type of exposure	Nose-only
3.3.5	Vehicle	Ethanol
3.3.6	Concentration in vehicle	Not applicable
3.3.7	Duration of exposure	4 h
3.3.8	Controls	Vehicle
3.4	**Examinations**	Clinical observations, body weight, gross necropsy.
3.5	**Method of determination of LC_{50}**	Not applicable, no mortalities occurred.
		4 RESULTS AND DISCUSSION
4.1	**Clinical signs**	Due to the physical characteristics of fenoxycarb, exposure concentrations higher than 4434 mg/m^3 could not be generated, therefore the achieved dose is considered to be a limit dose. There were no mortalities. Animals of both sexes exposed to fenoxycarb showed piloerection, hunched posture, dyspnoea and reduced locomotor activity to a similar extent, with recovery within 4 days.
4.2	**Pathology**	No treatment-related macroscopic findings were observed at examination *post mortem*.
4.3	**Other**	Animals of both sexes exposed to fenoxycarb showed significantly lower bodyweight gain in the first week of the study, with a compensatory increase in the second week, particularly in females. See Table A6_1-3.2.
4.4	**LC_{50}**	LC_{50} > 4400 mg/m^3 air for males and females.

Section A6.1.3 Acute Toxicity

Annex Point IIA VI.6.1.3 6.1.3 Acute inhalation toxicity to the rat (Limit Test)

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

A group of 5 male and 5 female young adult albino rats (Tif:RAIf(SPF); hybrids of RII/1xRII/2), was exposed nose-only for a single four-hour period to an aerosol fenoxycarb concentration of 4434 mg/m^3 in ethanol. A similar group of control animals was exposed to vehicle only. See Table A6_1-3.1.

Clinical observations and bodyweights were measured throughout the study. At the end of the 14-day observation period, the animals were killed and subjected to an examination *post mortem*.

5.2 Results and discussion

General observations: Due to the physical characteristics of fenoxycarb, exposure concentrations higher than 4434 mg/m^3 could not be generated, therefore the achieved dose is considered to be a limit dose. There were no mortalities.

Animals of both sexes exposed to fenoxycarb showed piloerection, hunched posture, dyspnoea and reduced locomotor activity to a similar extent, with recovery within 4 days.

Animals of both sexes exposed to fenoxycarb showed significantly lower bodyweight gain in the first week of the study, with a compensatory increase in the second week, particularly in females.

Gross pathology: No treatment-related macroscopic findings were observed at examination *post mortem*.

5.3 Conclusion

The LC_{50} of fenoxycarb to both male and female rats is considered to be greater than 4400 mg/m^3.

According to Commission Directive 2001/59/EC, a classification of fenoxycarb for acute inhalation toxicity is not required.

5.3.1 Reliability 1

5.3.2 Deficiencies No

Section A6.1.3 Acute Toxicity

Annex Point IIA VI.6.1.3 6.1.3 Acute inhalation toxicity to the rat (Limit Test)

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2006/08/02
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A6.1.3 Acute Toxicity

Annex Point IIA VI.6.1.3 6.1.3 Acute inhalation toxicity to the rat (Limit Test)

Table A6_1-3.1 Test atmosphere characteristics

Parameter	Control Group	Test Group
Nominal concentration	61879 mg/m^3 (ethanol)	6321 mg/m^3
Mean exposure concentration ± SD	-	4434 ± 162
Particle size MMAD; GSD	-	0.9 – 1.2 µm; 2.6 – 3.4
Particles ≤ 7 µm (% w/w)	-	93 – 97
Particles ≤ 3 µm (% w/w)	-	77 – 86
Flow rate (through chamber)	32 L/min	32 L/min
Flow rate (through generator)	19 L/min	20 L/min
Flow rate (individual tube)	2 L/min; 1.25 m/s	2 L/min; 1.25 m/s
Mean temperature	21.6 ± 0.2°C	22.5 ± 0.2°C
Mean humidity	55 % ± 1	50 % ± 1
Mean oxygen content	21.0 % ± 0.0	21.0 % ± 0.0

Table A6_1-3.2 Intergroup comparison of bodyweights (g)

	Experimental Group			
	Males		Females	
Study Day	Control	Test	Control	Test
0 (Immediately before exposure)	221	212	202	200
7	268	249*	221	207*
14	306	290	231	227*

* Statistically significant difference from control group mean, $p<0.05$

Section A6.1.4 Acute Dermal Irritation

Annex Point IIA VI.6.1.4 6.1.4 Acute dermal irritation

Official use only

		1 REFERENCE
1.1	**Reference**	[redacted] (1992a), Primary Dermal Irritation Study of Fenoxycarb Technical in Rabbits. [redacted], Report No. [redacted] 20800881, 11 November 1992 (unpublished)
1.2	**Data protection**	Yes
1.2.1	Data owner	Syngenta
1.2.2	Company with letter of access	[redacted]
1.2.3	Criteria for data protection	[redacted]
		2 GUIDELINES AND QUALITY ASSURANCE
2.1	**Guideline study**	Yes 92/69/EEC B.4 (1992) ≅ OECD 404 (1992) ≅ FIFRA § 81-5
2.2	**GLP**	Yes
2.3	**Deviations**	None
		3 MATERIALS AND METHODS
3.1	**Test material**	Fenoxycarb technical
3.1.1	Lot/Batch number	[redacted]
3.1.2	Specification	As given in Section 2 of dossier.
3.1.2.1	Description	Not reported
3.1.2.2	Purity	[redacted]
3.1.2.3	Stability	Not reported
3.2	**Test Animals**	
3.2.1	Species	Rabbit
3.2.2	Strain	New Zealand White (Hra:(NZW)SPF)
3.2.3	Sex	Males & females
3.2.4	Number of animals per group	3 per sex
3.2.5	Control animals	No
3.3	**Administration/ Exposure**	Dermal
3.3.1	Application	
3.3.1.1	Preparation of test substance	Moistened with 0.9% saline
3.3.1.2	Test site and preparation of test site	The dorsal skin was shorn.
3.3.2	Occlusion	Semi-occlusive
3.3.3	Vehicle	0.9% saline

Section A6.1.4 Acute Dermal Irritation

Annex Point IIA VI.6.1.4 6.1.4 Acute dermal irritation

3.3.4	Removal of test substance	Yes, with water
3.3.5	Duration of exposure	4 h
3.3.6	Postexposure period	72 h
3.3.7	Controls	None
3.4	**Examinations**	
3.4.1	Clinical signs	No
3.4.2	Dermal examination	Yes
3.4.2.1	Scoring system	According to Draize scoring system. Erythema 0-4: 0: No erythema, 1: very slight erythema (barely perceptible), 2: well-defined erythema, 3 moderate to severe erythema, 4: severe erythema (beet redness) to slight eschar formation (injuries in depth) Oedema 0-4: 0: No oedema, 1: very slight oedema (barely perceptible), 2: well-defined oedema (edges of area well-defined by definite raising), 3: moderate to severe oedema (raised approximately 1mm), 4: severe oedema (raised more than 1 mm extending beyond the area of exposure)
3.4.2.2	Examination time points	30 minutes, 24 h, 48 h, 72 h
3.4.3	Other examinations	None
3.5	**Further remarks**	None

4 RESULTS AND DISCUSSION

4.1	**Average score**	(see Table A6_1-4S-1)
4.1.1	Erythema	0.0
4.1.2	Oedema	0.0
4.2	**Reversibility**	Not applicable.
4.3	**Overall result**	Not irritating.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	A group of 3 male and 3 female New Zealand White (Hra:(NZW)SPF) albino rabbits received a single four-hour application of approximately 0.5 g of fenoxycarb (moistened with 0.9% saline) to the shorn back. The test substance was held in place with a semi-occlusive dressing. The application site was cleansed with water at the end of the 4-hour dosing period. The animals were assessed for up to 72 hours for any signs of skin irritation. The Draize scale was used to assess the degree of erythema and oedema at the application sites approximately 30 minutes, 1, 2 and 3 days after removal of the dressings. Mean erythema and oedema scores were calculated. Bodyweights were recorded at the start of the study.
5.2	**Results and discussion**	Application of fenoxycarb to the skin of rabbits under 4-hour semi-occluded conditions resulted in no dermal irritation.

Section A6.1.4 Acute Dermal Irritation

Annex Point IIA VI.6.1.4 6.1.4 Acute dermal irritation

5.3	**Conclusion**	**According to the criteria of Directive 2001/59/EC, fenoxycarb is non-irritating to skin and a classification for this endpoint is not required**
5.3.1	Reliability	1
5.3.2	Deficiencies	No

Section A6.1.4 Acute Dermal Irritation

Annex Point IIA VI.6.1.4 6.1.4 Acute dermal irritation

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2006/08/03
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A6.1.4 Acute Dermal Irritation

Annex Point IIA VI.6.1.4 6.1.4 Acute dermal irritation

Table A6_1-4S-1. Table for skin irritation study

Time	Erythema						Oedema					
Animal number #	**M80**	**M81**	**M82**	**F83**	**F84**	**F85**	**M80**	**M81**	**M82**	**F83**	**F84**	**F85**
after 30 minutes	0	0	0	0	0	0	0	0	0	0	0	0
after 24 hours	0	0	0	0	0	0	0	0	0	0	0	0
after 48 hours	0	0	0	0	0	0	0	0	0	0	0	0
after 72 hours	0	0	0	0	0	0	0	0	0	0	0	0
mean score 24-72 h	0,0						0.0					

all with the prescript of F426 or M426 for male and females, respectively
M – male F – female
Additional criteria specified in Directive 2001/59/EC Point 3.2.6.1 fulfilled: No

Section A6.1.4 Acute Eye Irritation

Annex Point IIA VI.6.1.4 6.1.4 Acute eye irritation

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		1 REFERENCE
1.1	**Reference**	[redacted] (1992b), Primary Eye Irritation Study of Fenoxycarb Technical in Rabbits. [redacted] Report No. [redacted] 20800882, 11 November 1992 (unpublished).
1.2	**Data protection**	Yes
1.2.1	Data owner	Syngenta
1.2.2	Company with letter of access	[redacted]
1.2.3	Criteria for data protection	[redacted]
		2 GUIDELINES AND QUALITY ASSURANCE
2.1	**Guideline study**	Yes 92/69/EEC B.5 (1992) ≅ OECD 405 (1987) ≅ FIFRA § 81-4
2.2	**GLP**	Yes
2.3	**Deviations**	None
		3 MATERIALS AND METHODS
3.1	**Test material**	Fenoxycarb (CGA 114597) technical
3.1.1	Lot/Batch number	[redacted]
3.1.2	Specification	As given in Section 2 of dossier.
3.1.2.1	Description	No data
3.1.2.2	Purity	[redacted]
3.1.2.3	Stability	No data
3.2	**Test Animals**	
3.2.1	Species	Rabbit
3.2.2	Strain	Hra:(NZW)SPF
3.2.3	Sex	♂ + ♀
3.2.4	Age/weight at study initiation	Age: adult
3.2.5	Number of animals per group	3 ♂ (30 s exposure); 3 ♂/ 3 ♀ (24 h exposure)
3.2.6	Control animals	No; the untreated eye served as control.
3.3	**Administration/ Exposure**	Ocular instillation
3.3.1	Preparation of test substance	Test substance was used as delivered.
3.3.2	Amount of active substance instilled	0.1 mL (0.04 g)
3.3.3	Exposure period	30 s, 24 h
3.3.4	Postexposure period	72 h

Section A6.1.4 Acute Eye Irritation

Annex Point IIA VI.6.1.4 6.1.4 Acute eye irritation

3.4	**Examinations**	
3.4.1	Ophthalmoscopic examination	Yes
3.4.1.1	Scoring system	Grades of ocular lesions: Cornea 0 – 4 (0 = no finding, 1 = slight, disperse, diffuse opacity, 2 = extensive, diffuse opacity, iris blurred, 3 = mother-of-pearl-like opacity, iris and pupil hardly recognisable, 4 = complete opacity, ulceration) Iris 0 – 2 (0 = no finding, 1 = swelling, reddening, positive light reaction, 2 = severe reddening and swelling, no light reaction) Conjunctivae Redness 0 – 3 (0 = blood vessels normal, 1 = vessels abnormally filled, 2 = diffuse reddening, 3 = diffuse deep reddening) Swelling 0 – 4 (0 = no swelling, 1 = slight swelling, 2 =severe swelling, lids everted, 3 = lids cover one half of eye, 4 = lids cover more than half eye, necroses and ulcers on the conjunctivas)
3.4.1.2	Examination time points	1 h, 24 h, 48 h, 72 h
3.4.2	Other examinations	None
3.5	**Further remarks**	None

4 RESULTS AND DISCUSSION

4.1	**Average score**	see Table A6_1-4E-1
4.1.1	Cornea	0.0
4.1.2	Iris	0.0
4.1.3	Conjunctiva	
4.1.3.1	Redness	0.4
4.1.3.2	Chemosis	0.0
4.2	**Reversibility**	Yes, within 72 h
4.3	**Other**	None
4.4	**Overall result**	Not irritating

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	One group of three (male) and one group of six (three male and three female) adult albino rabbits of the Hra:(NZW)SPF strain were used in this study. 0.1 mL (0.04 g) of fenoxycarb was instilled into one eye of each rabbit and the lids held gently closed for 1 second. After 30 seconds the eyes of the group of 3 rabbits were irrigated for 1 minute with lukewarm tap water. The eyes of the group of 6 rabbits were irrigated after 24 hours. The treated eyes were examined to assess the grade of ocular reaction at 1, 24, 48 and 72 hours after instillation. A sodium fluorescein examination was used at 72 hours to aid detection of possible corneal damage. Irritation was graded and scored according to the Draize scale.

Section A6.1.4 Acute Eye Irritation

Annex Point IIA VI.6.1.4 6.1.4 Acute eye irritation

5.2	**Results and discussion**	There was no corneal or iridial involvement in any of the animals from either group. In the group irrigated after 30 seconds, slight conjunctival irritation, including slight redness, slight chemosis and slight discharge was present in all three rabbits one hour after instillation. No chemosis or discharge persisted at the 24 hour reading and all animals had fully recovered after 72 hours. In the group irrigated after 24 hours, slight to moderate conjunctival irritation, including slight to moderate redness, slight chemosis and slight discharge, was present in all animals after 1 hour. No chemosis or discharge persisted at the 24 hour reading and at 48 hours slight redness was seen in one rabbit only and all rabbits were normal at the 72 hour reading.
5.3	**Conclusion**	**According to the criteria of Directive 2001/59/EC fenoxycarb is non-irritating to eyes and a classification for this endpoint is not required.**
5.3.1	Reliability	1
5.3.2	Deficiencies	–

Section A6.1.4 Acute Eye Irritation

Annex Point IIA VI.6.1.4 6.1.4 Acute eye irritation

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2006/08/03
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A6.1.4 Acute Eye Irritation

Annex Point IIA VI.6.1.4 6.1.4 Acute eye irritation

Table A6_1-4E-1. Eye irritation scores according to the Draize scheme (Irrigated after 24 hours)

Time	Cornea						Iris						Conjunctiva											
													Redness						Chemosis					
Animal number	**8**	**9**	**0**	**1**	**2**	**3**	**8**	**9**	**0**	**1**	**2**	**3**	**8**	**9**	**0**	**1**	**2**	**3**	**8**	**9**	**0**	**1**	**2**	**3**
after 1 hour	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	2	2	1	1	1	0	1	1	1
after 24 hours	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	1	1	1	0	0	0	0	0	0
after 48 hours	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
after 72 hours	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
mean scores 24-72h	0						0						0.4						0					

Additional criteria specified in Directive 2001/59/EC Point 3.2.6.2 fulfilled: No

Section A6.1.5 Skin sensitisation

Annex Point IIA VI.6.1.5 6.1.5 Skin sensitisation test in guinea pigs (Maximisation Test)

			Official use only
		1 REFERENCE	
1.1	**Reference**	[redacted] (1998), Skin Sensitization in the Guinea Pig (Maximization Test). CGA 114597 tech. [redacted], Report No. 972170, 22 April 1998 (unpublished)	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Syngenta	
1.2.2	Companies with letter of access	[redacted]	
1.2.3	Criteria for data protection	[redacted]	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Yes 96/54/EC B.6 (1996) ≅ OECD 406 (1992) ≅ FIFRA § 81-6	
2.2	**GLP**	Yes	
2.3	**Deviations**	None	
		3 MATERIALS AND METHODS	
3.1	**Test material**	Fenoxycarb technical (CGA 114597)	
3.1.1	Lot/Batch number	[redacted]	
3.1.2	Specification	As given in Section 2	
3.1.2.1	Description		
3.1.2.2	Purity	[redacted]	
3.1.2.3	Stability	Not reported	
3.1.2.4	Preparation of test substance for application	Dissolved in peanut oil (intradermal) or vaseline (topical induction + challenge)	
3.1.2.5	Pretest performed on irritant effects	Yes	
3.2	**Test Animals**		
3.2.1	Species	Guinea pigs	
3.2.2	Strain	Himalayan Spotted (GOHI)	
3.2.3	Sex	♀	X
3.2.4	Age/weight at study initiation	Young adult	X
3.2.5	Number of animals per group	20 (test substance group) 10 (controls)	X
3.2.6	Control animals	Yes	
3.3	**Administration/ Exposure**	Maximisation Test	
3.3.1	Induction schedule	Day 0: intradermal induction Day 7: topical idunction	

Section A6.1.5 Skin sensitisation

Annex Point IIA VI.6.1.5 6.1.5 Skin sensitisation test in guinea pigs (Maximisation Test)

3.3.2	Duration of induction exposures	48 h
3.3.3	Way of induction	Intradermal induction followed by topical induction
3.3.4	Concentrations used for induction	a) Intradermal induction: fenoxycarb in peanut oil or fenoxycarb in 1:1 adjuvant/physiological saline mixture b) Topical induction: fenoxycarb/vaseline 50:50
3.3.5	Challenge schedule	Day 21
3.3.6	Duration of challenge exposure	24 h
3.3.7	Concentrations used for challenge	10% fenoxycarb in vaseline
3.3.8	Rechallenge	No
3.3.9	Scoring schedule	24 h and 48 after removal of dressings
3.3.10	Removal of the test substance	Yes
3.3.11	Positive control substance	Yes Mercaptobenzothiazole (1% intradermal, 50% topical, 30% challenge)
3.4	**Examinations**	Skin sites were examined approximately 1 and 2 days after removal of the dressings.
3.4.1	Pilot study	Skin irritation
3.5	**Further remarks**	–

4 RESULTS AND DISCUSSION

4.1	**Results of pilot studies**	A preparation of 10% fenoxycarb in vaseline was the highest non-irritant concentration.
4.2	**Results of test**	see Table A6_1_5-1
4.2.1	24 h after challenge	Test compound group: 4/20; negative control*: 0/10 (Number of animals with signs of allergic reactions/number of animals)
4.2.2	48 h after challenge	Test compound group: 3/20; negative control*: 0/10 (Number of animals with signs of allergic reactions/number of animals)
4.2.3	Other findings	None of the animals died and there was no evidence of toxicity.
4.3	**Overall result**	A positive response was seen in 20% of the test animals. For an adjuvant test, a positive response in 30% of the animals would justify classification as a skin sensitizer. The test result is thus negative.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	The sensitisation potential of fenoxycarb technical was assessed using a method based on the maximisation test of Magnusson and Kligman (1969). Groups of 20 test and 10 control young adult female Himalayan Spotted (GOHI) guinea pigs were used for the main study. Two main procedures were involved; (a) the induction of an immune response; (b) a challenge of that response. In test animals, the induction phase involved 3 intradermal injections of adjuvant/physiological saline mixture, 1:1 v/v; fenoxycarb in peanut oil; and fenoxycarb in 1:1 adjuvant/physiological saline mixture to a shorn area of the scapular region. This was followed 1

Section A6.1.5 Skin sensitisation

Annex Point IIA VI.6.1.5 6.1.5 Skin sensitisation test in guinea pigs (Maximisation Test)

week later by a topical induction using a fenoxycarb/vaseline 50:50 mixture under an occlusive dressing for 48 hours. For control animals the intradermal injections were adjuvant/physiological saline, 1:1 v/v; peanut oil; and peanut oil, 50% w/v with 1:1 adjuvant/physiological saline mixture, and the topical applications were as for the test animals except that vaseline only was applied. Application sites were checked 1 day after removal of the dressings.

In the challenge phase, study day 21, the flanks of all animals were shaved immediately prior to treatment. The animals of both groups had one self-adhesive dosing chamber, which was loaded with a 10% (the highest non-irritant dose) fenoxycarb/vaseline mixture (approximately 0.35 mL), placed on the test flank. A chamber loaded with vehicle only was placed on the other flank. The chambers were held in place with an occlusive dressing for 24 hours.

Skin sites were examined approximately 1 and 2 days after removal of the dressings.

A positive control study was conducted using essentially the same methodology and using mercaptobenzothiazole as the test substance. The method used an intradermal induction of a 1% preparation in peanut oil and 50% preparations in vaseline for the topical induction and 30% in vaseline in the challenge phase.

5.2 Results and discussion

Positive reactions were observed in 3 males and 1 female of the test group animals on the test flanks at the 24 hour examination, and in 3 males at the 48 hour examination; the sensitisation rate for fenoxycarb was therefore 20%. There were no positive skin responses on the vehicle flanks or in the vehicle control group.

5.3 Conclusion

Following challenge with a 10% preparation of fenoxycarb in vaseline, four animals (20%) showed an erythematous response.

According to the criteria of Directive 2001/59/EC, fenoxycarb is considered not to be a skin sensitizer in the guinea pig maximisation test and a classification for this endpoint is not required.

5.3.1 Reliability 1

5.3.2 Deficiencies –

Evaluation by Competent Authorities

Use separate "evaluation boxes" to provide transparency as to the comments and views submitted

EVALUATION BY RAPPORTEUR MEMBER STATE

Date 2006/08/03

Materials and Methods [redacted]

Results and discussion [redacted]

Conclusion [redacted]

Reliability [redacted]

Acceptability [redacted]

Remarks

Section A6.1.5 Skin sensitisation

Annex Point IIA VI.6.1.5 6.1.5 Skin sensitisation test in guinea pigs (Maximisation Test)

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A6_1_5-1. Maximisation test: Number of animals with positive skin reactions after challenge application

	Vehicle flank		Test flank	
Scored after:	**24 hours**	**48 hours**	**24 hours**	**48 hours**
Negative/vehicle control group	0/10	0/10	0/10	0/10
Test item group	0/20	0/20	4/20	3/20

Section A6.2 Percutaneous absorption (in vitro test)

Annex Point IIA VI.6.2 6.2 In vitro dermal absorption study with rat and human skin

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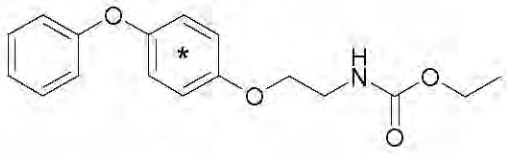
1 REFERENCE

1.1	**Reference**	[redacted] (2003a), The Percutaneous Penetration of [Hydroquinone-U-^{14}C] CGA 114597 Formulated as INSEGAR® 25 WG (A-8995 B) Through Rat and Human Split-Thickness Skin Membranes (in vitro). [redacted], Report No. 029AM02, 27 August 2003 (unpublished)
1.2	**Data protection**	Yes
1.2.1	Data owner	Syngenta
1.2.2	Companies with letter of access	[redacted]
1.2.3	Criteria for data protection	[redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes OECD Guideline for Testing of Chemicals, Skin Absorption: in vitro Method, Draft new guideline 428, December 2000
2.2	**GLP**	Yes
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Test material**	CGA 114597 (fenoxycarb)
3.1.1	Non-labelled compound	CGA 114597 (fenoxycarb)
3.1.2	Lot/Batch number	[redacted]
3.1.3	Specification	As given in section 2 of dossier.
3.1.3.1	Purity	[redacted]
3.1.3.2	Stability	–
3.1.4	Labelled compound	[Hydroquinone-U-^{14}C]- fenoxycarb
3.1.4.1	Lot/Batch number	ILA-92.1
3.1.4.2	Purity	98.6% radiochemical purity
3.1.4.3	Radiolabelling	 (* Position of [^{14}C]-label)
3.1.5	Formulation	
3.1.5.1	Description	WG formulation
3.1.5.2	Active ingredient concentration	0.05, 0.75, and 50 g/L fenoxycarb
3.2	**Test System**	
3.2.1	Species	**Human**
3.2.2	Source	Abdominal cadaver skin from Caucasian donors was stored at ca. -18°C

Section A6.2		**Percutaneous absorption (in vitro test)**	
Annex Point IIA VI.6.2		6.2 In vitro dermal absorption study with rat and human skin	
		until preparation of the skin membranes.	
3.2.3	Species	**Rat**	
3.2.4	Source	Skin from male rats (strain: HanBrl: WIST (SPF)), approximately 8-9 weeks old, was used for the preparation of the skin membranes. Upon receipt the state of health was checked in all animals. The rats were sacrificed by an overdose of carbon dioxide gas and the fur on the dorsal site was clipped and the full thickness skin excised. The skin was wrapped in aluminium foil and stored at ca. -18°C.	
3.3	**Administration/ Exposure**		
3.3.1	Concentration of test substance	0.05, 0.75, and 50 mg/mL fenoxycarb ≅ 0.0005, 0.0070, and 0.469 mg/cm²	X
3.3.2	Specific activity of test substance	2050 kBq/mg (55 µCi/mg)	
3.3.3	Volume applied	6 µL	
3.3.4	Size of test site	0.64 cm²	
3.3.5	Exposure period	24 hours	
3.3.6	Sampling time	0 - 6 hours: 1 h intervals 6 - 24 hours: 2 h intervals	
3.3.7	Samples	Receptor fluid, cell wash, skin rinses, skin membranes.	
		4 RESULTS AND DISCUSSION	
4.1	**Recovery of labelled compound**	The total recovery of radioactivity ranged between 97.4% and 125.8% (see Table A6_2-1).	
4.2	**Percutaneous absorption**	**after 24 h** / **Rat** / **Human** 0.05 mg/mL: 66.3% 41.6% 0.75 mg/mL: 55.2% 7.7% 50 mg/mL: 1.2% 0.4% see Table A6_2-2 and Table A6_2-3	X
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	*Test Material:* The test material was incorporated into a blank WG formulation concentrate representative of formulation A-8995 B, which contains a nominal 250 g fenoxycarb/L. The prepared formulation concentrate was diluted in water to give a nominal concentration of 50 g fenoxycarb/L (Dose Level A3). Two further aqueous dilutions of the formulation concentrate (1:331 w/v and 1:5128 w/v), nominally containing a 0.75 g fenoxycarb/L (Dose Level A2) and 0.05 g fenoxycarb/L (Dose Level A1), were also prepared. *Preparation of Split-Thickness Skin Membranes:* The skin samples were removed from the freezer and allowed to thaw at room temperature. The subcutaneous fat was carefully removed from the full thickness skin and pieces of about 4 x 5 cm^2 were stretched evenly over a cork block, with stratum corneum uppermost. Skin sections of about 200 µm thickness were cut from the top using an electric dermatome. The skin sections were cut in pieces (ca. 1.8 x 1.8 cm²) and mounted in the diffusion cells. *Diffusion Cell Apparatus:* An automated flow-through cell system was used. Flow-through diffusion cells were placed in an aluminium manifold connected to a water bath to maintain the temperature of the	X

Section A6.2	Percutaneous absorption (in vitro test)	
Annex Point IIA VI.6.2	6.2 In vitro dermal absorption study with rat and human skin	
	skin membranes at 31±1°C. Each diffusion cell consisted of a donor and receptor chamber separated by the skin membrane. The area of skin membrane exposed to the donor chamber was 0.64 cm^2. The receptor chambers were connected to a multi-channel peristaltic pump and the pump speed was adjusted to about 3 mL/h. At recorded time intervals, the effluent from each cell was collected directly into vials on a fraction collector. *Treatment:* The receptor fluid was ethanol/water (1:1 v/v). A 6 µL aliquot of the application solution/emulsion was applied to the surface of the skin membranes. The donor chamber was left open (non-occluded conditions). Twenty four hours after application, the skin membrane surface was rinsed with ethanol (10 mL) and the radioactivity in the skin rinse was determined by LSC. The skin membrane was removed from the in-line cells and dissolved in tissue solubilizer prior to LSC. The cells were finally washed with ethanol and the radioactivity in the cell wash determined by LSC.	
5.2 Results and discussion	After application of CGA 114597 at the low (A1) and middle (A2) dose levels, 66% and 55% of the applied dose penetrated through the rat skin membrane within 24 hours. At the high dose level (A3) the portion penetrating through the skin membrane accounted only for 1.2% of the dose. The total amounts which penetrated the skin within this period were 0.30 µg/cm^2 at the low dose level, 3.3 µg/cm^2 at the middle dose level, and 6.3 µg/cm^2 at the high dose level. The flux, under steady state conditions, was 0.025 µg/cm^2/h at the low dose level, 0.189 µg/cm^2/h at the middle dose level and 0.593 µg/cm^2/h at the high dose level. Within 24 hours, 42% of the low dose (A1), 8% of the middle dose (A2), and 0.4% of the high dose (A3) penetrated through the human skin membrane, corresponding to a penetration of 0.19 µg/cm^2, 0.46 µg/cm^2, and 2.11 µg/cm^2. The calculated flux, under steady state conditions (0-4 h after application), was 0.029 µg/cm^2/h, 0.102 µg/cm^2/h, and 0.191 µg/cm^2/h at the low, middle, and high dose level, respectively. In contrast to the rat skin membranes, human skin membranes showed a biphasic pattern with high penetration rates for the first few hours only (0-4 hours after start of exposure), followed by a second phase with significantly decreased penetration rates for most of the cells Aliquots of skin rinse were pooled according to species and dose level and the pools analysed by TLC. For the low dose level (A1) the TLC analysis revealed a fraction of impurity accounting for 28.8% of rat skin rinse pool and 5.8% of the human skin rinse pool. It was assumed that this impurity was the result of the contamination of the samples, as discussed above. For the middle and high dose level, CGA 114597 amounted to more than 98% of the radioactivity present in the skin rinses. Hence, it was concluded that the test substance remained unchanged during the 24 hours of exposure on the skin membrane.	X
5.3 Conclusion		
5.3.1 Reliability	1	X
5.3.2 Deficiencies	None	

Section A6.2 Percutaneous absorption (in vitro test)

Annex Point IIA VI.6.2 6.2 In vitro dermal absorption study with rat and human skin

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2006/08/04
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A6_2-1: Recovery of radioactivity

Recovery [% of Dose]						
Test System	**Rat Skin Membrane**			**Human Skin Membrane**		
Dose Level	**A1**	**A2***	**A3**	**A1**	**A2**	**A3**
Applied Dose [µg/cm²]	**0.5**	**6**	**522**	**0.5**	**6**	**522**
Perfusates						
0-24 h	66.31	55.19	1.20	41.58	7.73	0.40
Remaining Dose						
Cell wash	6.74	1.62	1.38	5.08	1.00	0.20
Skin Rinse	44.78	35.27	93.52	60.76	97.12	99.45
Skin Membrane	7.97	6.15	1.28	4.78	2.81	0.13
Subtotal	59.48	43.04	96.18	70.61	100.93	99.79
Recovery	125.80	97.91	97.39	112.19	108.65	100.19

* Two cells showing an extremely low penetration rate were excluded from mean calculation. In addition a contamination of the skin rinse vessel of another cell led to a value of 183% of dose, which was also excluded from mean calculation.

Table A6_2-2: CGA 114597 Absorption through Rat Skin

Test System	**Rat Skin Membrane**					
Dose Level	**A1**		**A2***		**A3**	
Applied Dose [µg/cm²]	**0.5**		**6**		**522**	
Applied Volume [µL]	**6**		**6**		**6**	
Application Area [cm²]	**0.64**		**0.64**		**0.64**	
Concentration [mg/cm³]	**0.05**		**0.6**		**55.7**	
Penetration within	**% of dose**	**µg/cm²**	**% of dose**	**µg/cm²**	**% of dose**	**µg/cm²**
6 h	25.04	0.11	14.65	0.88	0.42	2.21
12 h	46.77	0.21	32.19	1.93	0.62	3.26
24 h	66.31	0.30	55.19	3.30	1.20	6.29
Flux [µg/cm²/h]	0.025		0.189		0.593	

* Two cells showing an extremely low penetration were excluded from mean calculation

Table A6_2-3: CGA 114597 Absorption through Human Skin

Test System	Human Skin Membrane					
Dose Level	**A1**		**A2**		**A3**	
Applied Dose [µg/cm²]	**0.5**		**6**		**522**	
Applied Volume [µL]	**6**		**6**		**6**	
Application Area [cm²]	**0.64**		**0.64**		**0.64**	
Concentration [mg/cm³]	**0.05**		**0.6**		**55.7**	
Penetration within	**% of dose**	**µg/cm²**	**% of dose**	**µg/cm²**	**% of dose**	**µg/cm²**
6 h	20.52	0.09	4.63	0.28	0.11	0.57
12 h	28.80	0.13	5.64	0.34	0.17	0.90
24 h	41.58	0.19	7.73	0.46	0.40	2.11
Flux [µg/cm²/h]	0.029		0.102		0.191	

CA-Table A6_2-1.1: Revised figures for dermal absorption rates and calculation of rat-to-human interconversion factors

Dose Level	A1		A2		A3	
Applied Dose [µg/cm²]	**0.5**		**6**		**522**	
Applied Volume [µL]	**6**		**6**		**6**	
Application Area [cm²]	**0.64**		**0.64**		**0.64**	
Concentration [mg/cm³]	**0.05**		**0.6**		**55.7**	
Penetration [% of dose] within 24 h	**Rat**	**Human**	**Rat**	**Human**	**Rat**	**Human**
As % nominally applied dose	74.28	46.36	61.34	10.54	2.48	0.93
As % total recovery[§]	59.05	41.32	62.65	9.70	2.54	0.93
Rat-to-human interconversion factor[&]	1.43		6.46		2.73	

[§] obtained by dividing the absolute percentage of absorbed radioactivity (perfusates + skin membrane) by the overall recovery.

[&] obtained by dividing the percentage of radioactivity absorbed through rat skin by that absorbed through human skin (both percentages as % total recovery)

Section A6.2 Percutaneous absorption (*in-vivo* test)

Annex Point IIA VI.6.2 6.2 Dermal Absorption and Excretion in rats

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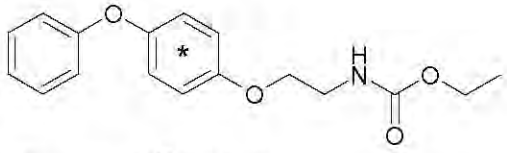
1 REFERENCE

1.1	**Reference**	[redacted] (2003b). Dermal Absorption of [hydroquinone-U-^{14}C] CGA 114597 formulated as INSEGAR® 25 WG (A-8995 B) in the rat (*in vivo*). [redacted]; Report 029AM03, 27 August 2003 (unpublished)
1.2	**Data protection**	Yes
1.2.1	Data owner	Syngenta
1.2.2	Company with letter of access	[redacted]
1.2.3	Criteria for data protection	[redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes OECD (2000). Test Guideline 427: Skin Absorption: *in vivo* Method (OECD 2003, in press)
2.2	**GLP**	Yes
2.3	**Deviations**	None

3 MATERIALS AND METHODS

3.1	**Test material**	
3.1.1	**Non-labelled parent compound**	CGA 114597 (common name: fenoxycarb)
3.1.2	Lot/Batch number	[redacted]
3.1.3	Specification	As given in Section 2 of dossier.
3.1.3.1	Description	No data
3.1.3.2	Purity	[redacted]
3.1.3.3	Stability	Not reported
3.1.4	**Labelled parent compound**	[Hydroquinone-U-^{14}C]- fenoxycarb
3.1.5	Lot/Batch number	[redacted]
3.1.6	Specification	
3.1.6.1	Purity	[redacted]
3.1.6.2	Stability	Stable throughout the study.
3.1.6.3	Radiolabelling	 (* Position of [^{14}C]-label)
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain	HanBrl: WIST (SPF)

Section A6.2 Percutaneous absorption (*in-vivo* test)

Annex Point IIA VI.6.2 6.2 Dermal Absorption and Excretion in rats

3.2.3	Sex	Males	
3.2.4	Age/weight at study initiation	Body weights: 189-256 g	
3.2.5	Number of animals per group	4 per dose and time point	
3.2.6	Control animals	No	
3.3	**Administration/ Exposure**	**Dermal**	
3.3.1	Preparation of test site	An O-ring was attached to the clipped skin (~10 cm^2). The O-ring was covered with non-occlusive tape.	
3.3.2	Concentration of test substance	0.05, 0.75 and 61.2 mg/mL ≅ 0.0005, 0.0075, and 0.612 mg/cm^2 (subgroups P1, P2, and P3, respectively)	
3.3.3	Specific activity of test substance	2050 kBq/mg (55 µCi/mg)	
3.3.4	Volume applied	100 µL	
3.3.5	Size of test site	10 cm^2	
3.3.6	Exposure period	6 hours	
3.3.7	Sampling time	Subgroups of four rats from each dose level were terminated at 6, 24, 72 and 120 hours after dosing (subgroups T1, T2, T3 and T4, respectively). Blood was collected by tail vein bleeding from each animal of the T4 subgroup at intervals of 0.5, 1, 2, 4, 6, 8, 24 and 48 hours after dosing.	
3.3.8	Samples	O-rings, covers, 6-h skin wash, application site, untreated skin, tape strippings (*stratum corneum*), carcasses, whole blood, gastrointestinal tract, cage wash, urine, faeces.	
		4 RESULTS AND DISCUSSION	
4.1	**Toxic effects, clinical signs**	At all dose levels, some animals showed slight stress symptoms (chromodacryorrhoea and diarrhoea) during the first few hours after dosing, and the observed weight loss is attributed to the stress and discomfort of the experiment. One animal from subgroup P1T3 showed reduced food intake and corresponding reduction in faecal excretion between 24 and 48 hours after dosing, and the O-ring had fallen off one animal from subgroup P1T3 between 24 and 48 hours after dosing, and therefore oral ingestion of radioactivity from the O-ring cannot be excluded for this animal.	
4.2	**Dermal irritation**	None.	
4.3	**Recovery of labelled compound**	The total recovery of radioactivity ranged between 90.1% and 96.0%.	
4.4	**Percutaneous absorption**	0.05 mg/mL: 35.7% 0.75 mg/mL: 34.6% 61.2 mg/mL: 0.54% see Table A6_2.1	X
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	The objective of this study was to investigate the dermal penetration of radioactivity following the application, to rat skin, of 1:5000, 1:333 and 1:4 (w/v) dilutions of [^{14}C]-CGA 114597 formulated as INSEGAR® 25	

Section A6.2 Percutaneous absorption (*in-vivo* test)

Annex Point IIA VI.6.2 6.2 Dermal Absorption and Excretion in rats

		WG (A-8995 B), corresponding to a nominal low dose level of 0.0005 mg/cm^2 (group P1), an intermediate dose level of 0.0075 mg/cm^2 (group P2) and a high dose level of 0.5 mg/cm^2 (group P3). The low and intermediate dose levels were selected to represent typical in-use dilutions. The high dose level represented an exaggerated concentration of INSEGAR® 25 WG suitable for dermal application. During the acclimatisation period, rats were group housed for at least 4 days and then housed individually in metabolism cages for 1 day. A measured amount of each [^{14}C]-formulated dose (100 µL) was applied to 10 cm^2 of clipped skin per rat, corresponding to mean achieved doses of CGA 114597 of 0.005 mg, 0.075 mg and 6.12 mg per rat, respectively. Each [^{14}C]-dose was applied to the skin of 16 rats with application sites protected, but not occluded, using O-rings covered with permeable tape. A collar was placed around the neck of each rat to prevent ingestion of the test substance. Rats were housed singly in metabolism cages for the regular collection of urine and faeces. Blood was collected by tail vein bleeding from each animal of subgroup T4 at intervals of 0.5, 1, 2, 4, 6, 8, 24 and 48 hours after doing. After a 6 hour exposure interval, the application sites of all rats were washed with a mild soap solution to remove the unabsorbed dose. After the washing procedure, a new cover tape was applied to each O-ring. For the animals in subgroups P1T4, P2T4 and P3T4, a bandage was wrapped around each rat to secure and protect the O-rings for the remainder of the experimental period of 3 days. Subgroups of four rats from each dose level were terminated at 6, 24, 72 and 120 hours after dosing (subgroups T1, T2, T3 and T4, respectively). The O-rings and covers were removed and the application site skin was tape-stripped to remove the *stratum corneum*. All samples, including carcasses, were analysed for radioactivity, either directly or after tissue solubilisation or sample combustion. Aliquots of the skin wash extracts were pooled by dose level and analysed by TLC to determine the purity of the test substance after exposure.	
5.2	**Results and discussion**	Analyses confirmed that the [^{14}C]-dose preparations simulated 1:4, 1:333 and 1:5000 dilutions of the commercial WG formulation concentrate and that the formulated active ingredient was stable for longer than its period of use during this study. The radioactivity recovered from the application site skin wash and O-rings and covers was considered to be unabsorbed. Radioactivity present in the skin beneath each application site was also considered as unabsorbed, although it is recognised that some of this material may be absorbed beyond the duration of exposure investigated. The absorbed dose included the radioactivity in urine, faeces, cage wash, gastrointestinal tract, untreated skin, blood and residual carcass. Dermal absorption of [^{14}C]-CGA 114597 from aqueous dilutions of INSEGAR® 25 WG (A-8995 B) was moderate at the low and intermediate dose levels, and very low at the high dose level. After a six hour dermal exposure, the majority of the radioactivity was removed by a mild aqueous wash, accounting for 49-54% of the low dose, 51-59% of the intermediate dose and 92-94% of the high dose. After the washing procedure, 22% of the low dose, 12% of the intermediate dose and 0.32% of the high dose remained associated with	X

Section A6.2	Percutaneous absorption (*in-vivo* test)	
Annex Point IIA VI.6.2	6.2 Dermal Absorption and Excretion in rats	

the application site, some of which was available for subsequent absorption. Tape stripping demonstrated that the majority of the radioactivity remaining on the application site after skin washing was associated with the *stratum corneum*, accounting for 20%, 10% and 0.29% of the dose at the low, intermediate and high dose levels, respectively. Radioactive residues remaining in the *stratum corneum* continued to be absorbed into the epidermis and finally into systemic circulation.

The amount of dose absorbed increased from 21% after 6 hours to 36% after 72 hours at the low dose level, from 21% after 24 hours to 35% after 72 hours at the intermediate dose level, and from 0.22% after 24 hours to 0.54% after 72 hours at the high dose level.

Penetration rates were calculated based on the amount of radioactivity entering systemic circulation within the 6 hour exposure interval, and assumed that the rate of penetration was constant during this time. The mean penetration rate was calculated to be 0.018 µg/cm^2/h at the low dose level, 0.259 µg/cm^2/h at the intermediate dose level and 0.227 µg/cm^2/h at the high dose level. The penetration rate increased proportionately from the low to the intermediate dose levels, whereas the penetration rate at the high dose level was similar to the intermediate dose level. This is attributed to the limited solubility of the CGA 114597 in the application vehicle.

The absorbed dose was rapidly excreted in approximately equal proportions in urine and faeces. 72 hours after dosing, only 0.5%, 0.5% and 0.02% of the dose remained in the gastrointestinal tract and carcass at the low, intermediate and high dose levels, respectively.

The concentration of radioactive residues in blood during and after dermal exposure was very low at all dose levels. The blood residues were all below the limit of determination for the low and high dose levels. At the intermediate dose level, the maximum concentration of radioactive residues in blood (0.0172 µg/g) was reached at the end of the 6 hour exposure period (see Figure A6_2.1). After skin washing, the concentration in blood decreased rapidly, reaching the limit of determination within 24 hours.

5.3	**Conclusion**	**Following a 6 hour exposure interval and recovery for up to 3 days, the in vivo dermal absorption of [^{14}C]-CGA 114597 from 1:5000 and 1:333 spray strength dilutions of INSEGAR® 25 WG (A-8995 B) was moderate. The extent of absorption for the 1:5000 dilution (low dose level) and 1:333 dilution (intermediate dose level) was 21% and 21% at the end of the 6 hour exposure period, increasing to 36% and 35%, respectively after 3 days. Absorption from a 1:4 dilution (high dose level) was very low, accounting for only 0.2% after 6 hours and 0.5% after 3 days.**	X
5.3.1	Reliability	1	
5.3.2	Deficiencies	None	

Section A6.2 Percutaneous absorption (*in-vivo* test)

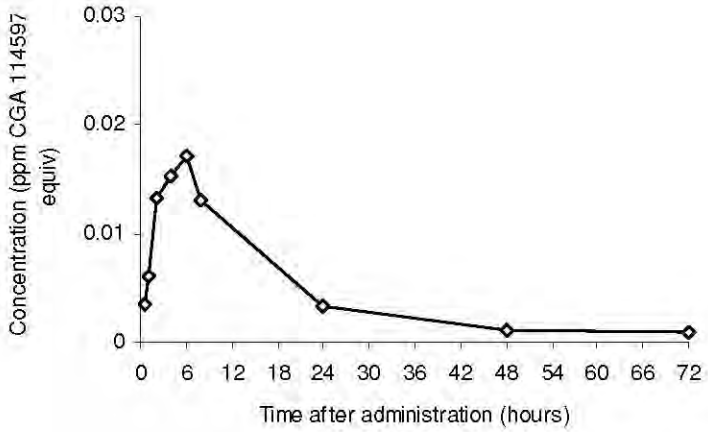
Annex Point IIA VI.6.2 6.2 Dermal Absorption and Excretion in rats

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2006/08/04
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A6_2.1: Percentage distribution of radioactivity following the application of aqueous dilutions of [^{14}C]-fenoxycarb to rat skin

Dose level (Group)	Mean percentage recoveries of applied dose											
	Low dose level 0.0005 mg/cm^2 (P1)				Intermediate dose level 0.0075 mg/cm^2 (P2)				High dose level 0.612 mg/cm^2 (P3)			
Termination time	**6 h**	**24 h**	**48 h**	**72 h**	**6 h**	**24 h**	**48 h**	**72 h**	**6 h**	**24 h**	**48 h**	**72 h**
6 hour skin wash	51.02	54.42	54.46	49.13	59.44	50.67	56.48	53.87	94.01	92.50	92.06	92.45
O-rings & covers	0.56	1.72	4.12	0.72	1.87	0.51	1.37	0.74	1.41	0.42	0.10	2.61
Dislodged dose	**51.59**	**56.14**	**58.59**	**49.85**	**61.31**	**51.18**	**57.85**	**54.61**	**95.42**	**92.92**	**92.16**	**95.05**
Stratum corneum	20.00	10.11	8.76	7.79	10.15	7.42	5.09	3.47	0.29	0.19	0.10	0.16
Application site skin	1.81	0.17	0.09	0.04	1.59	0.17	0.08	0.49	0.03	<0.01	<0.01	<0.01
Application site	**21.81**	**10.28**	**8.85**	**7.83**	**11.74**	**7.59**	**5.17**	**3.96**	**0.32**	**0.19**	**0.11**	**0.16**
Urine	2.41	10.35	11.06	12.08	1.58	9.35	9.54	13.79	0.03	0.17	0.15	0.26
Faeces	0.12	12.95	12.98	22.54	0.02	18.49	15.17	19.84	<0.01	0.14	0.18	0.24
Cage wash	0.20	0.60	0.74	0.49	0.23	0.70	0.40	0.38	<0.01	0.01	0.01	0.01
Untreated skin	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Gastrointestinal tract	11.99	5.20	3.26	0.53	12.10	5.12	1.23	0.31	0.12	0.08	0.02	0.02
Whole blood	0.15	<0.01	<0.01	<0.01	0.14	0.03	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Carcass	6.48	<0.01	<0.01	<0.01	6.61	1.77	0.69	0.22	0.06	<0.01	<0.01	<0.01
Absorbed dose	**21.34**	**29.09**	**28.05**	**35.65**	**20.69**	**35.47**	**27.04**	**34.55**	**0.22**	**0.40**	**0.37**	**0.54**
Total recovered	**94.74**	**95.51**	**95.49**	**93.33**	**93.75**	**94.24**	**90.05**	**93.12**	**95.96**	**93.52**	**92.63**	**95.75**

Figure A6_2.1: Blood kinetics following the application of a 1:333 aqueous dilution of INSEGAR® 25 WG (A-8995 B) at the intermediate dose level of 0.0075 mg [14C]-CGA 114597/cm2 skin



Section A6.2 Absorption, distribution, and excretion

Annex Point IIA VI.6.2 6.2 Absorption, distribution, and excretion of [^{14}C]-Fenoxycarb in rats

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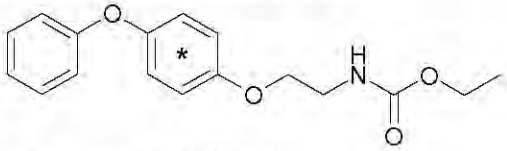
1 REFERENCE

1.1	**Reference**	[redacted] (1993). Metabolism of ^{14}C-Fenoxycarb in rats (preliminary and definitive phases). [redacted]; Report No. [redacted] 6117-209, 04 August 1993 (unpublished)
1.2	**Data protection**	Yes
1.2.1	Data owner	Syngenta
1.2.2	Companies with letter of access	[redacted]
1.2.3	Criteria for data protection	[redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes 87/302/EEC B.36. ≅ 94/79/EC (1994) ≅ OECD 417 (1984) ≅ EPA 85-1 (1984) ≅ Japanese MAFF (1985)
2.2	**GLP**	Yes
2.3	**Deviations**	None

3 MATERIALS AND METHODS

3.1	**Test material**	Fenoxycarb
3.2	**Non-labelled parent compound**	Fenoxycarb
3.2.1	Lot/Batch number	[redacted]
3.2.2	Specification	
3.2.2.1	Purity	[redacted]
3.2.2.2	Stability	Not reported
3.2.3	**Labelled parent compound**	
3.2.4	Lot/Batch number	[redacted]
3.2.5	Specification	
3.2.5.1	Purity	Radiochemical purity: [redacted] Chemical purity: [redacted]
3.2.5.2	Stability	The purity and verification of stability of the test substance in the dose solutions was determined by HPLC.
3.2.5.3	Radiolabelling	 *(* Position of [^{14}C]-label)*
3.3	**Test animals**	
3.3.1	Species	*Rattus norvegicus*
3.3.2	Strain	HSD:Sprague Dawley SD

Section A6.2 Absorption, distribution, and excretion

Annex Point IIA VI.6.2 6.2 Absorption, distribution, and excretion of [^{14}C]-Fenoxycarb in rats

3.3.3	Sex	♂ + ♀	
3.3.4	Age/weight at study initiation	Body weights: 182-236 g (males), 164-221 g (females).	
3.3.5	Number of animals	see Table A6_2-1	
3.3.6	Control animals	Yes	
3.4	**Administration/ Exposure**	Oral gavage or intravenous injection	
3.4.1	Application	**Intravenous**	
3.4.1.1	Type	Single bolus injection	
3.4.1.2	Post-exposure period	7 days	
3.4.1.3	Specific activity of test substance	GAN-XXV-93: 37 kBq/mg (1 µCi/mg) GAN-XXV-74: 1203 kBq/mg (32.5 µCi/mg)	X
3.4.1.4	Vehicle	Polyethylene glycol 200 (PEG 200)	
3.4.1.5	Volume applied	Approx 0.5 mL	
3.4.2	Application	**Oral**	
3.4.2.1	Type	Gavage	
3.4.2.2	Post-exposure period	7 days	
3.4.3	Specific activity of test substance	GAN-XXV-93: 37 kBq/mg (1 µCi/mg) GAN-XXV-74: 1203 kBq/mg (32.5 µCi/mg)	
3.4.3.1	Vehicle	Polyethylene glycol 200 (PEG 200)	
3.4.3.2	Volume applied	Approx 1 mL	
3.5	**Examinations**		
3.5.1	Biokinetic parameters	Absorption, distribution, excretion	
3.5.2	Samples	Urine, faeces, expired air (preliminary test only), blood, skin, bone (femur), brain, fat (from reproductive area), ovaries, testes, heart, kidneys, liver, lungs, muscle (thigh), spleen, uterus and residual carcass Cage washes and wipes were collected for each animal at the end of the collection period..	
3.5.3	Sampling time (0 h = start of application)	Excreta: 0-6 h; 6-12 h; 12-24 h; 24-48 h ;48-72 h; 72-96 h; 96-120 h; 120-144 h; 144-168 h Tissues: 7 days	
		4 RESULTS AND DISCUSSION	
4.1	**Toxic effects, clinical signs**	All animals in group A (single intravenous dose) appeared to have red urine immediately after dosing. All animals in groups A and E appeared languid after dosing, and returned to normal after approximately 15 minutes. One animal from group A fell to its right side, returned to its upright position (dyspnoea and languid) and appeared normal approximately 45 minutes later. One animal from group A died immediately after dosing and was replaced. The death was not attributed to the test material.	

Section A6.2 Absorption, distribution, and excretion

Annex Point IIA VI.6.2		6.2 Absorption, distribution, and excretion of [^{14}C]-Fenoxycarb in rats	
4.2	**Recovery of labelled compound**	91.3% (i.v. low dose) – 105.4% (oral low dose, preconditioned)	
4.3	**Absorption**	The percentage absorption figures for groups B and C (oral low dose groups) were calculated by dividing the total recovery in urine, tissues and carcass with the corresponding values from group A (intravenous low dose group). The percentage absorption figure was 100% for animals dosed intravenously in group A. Data from the high dose group (group D) was not compared with the low dose groups due to the greater proportion of radioactivity eliminated in urine at the high dose level. Absorption from the gastrointestinal tract into the systemic circulation was similar for males and females within each dose group, however absorption was greater for the animals that received multiple oral doses (98.6% in males and 97.7% in females) compared with the animals that received a single oral dose (77.0% in males and 66.7% in females). See Table A6_2-3.	
4.4	**Excretion**	In the preliminary groups (group P-H), following administration of a single oral dose of [^{14}C]-fenoxycarb at a high dose level of 300 mg/kg, the majority of the radioactivity was excreted in faeces (55.8% in males and 57.9% in females) and urine (37.8% in males and 38.7% in females), with less than 0.3% of the dose retained in the carcass (see Table A6_2-3). Negligible amounts of radioactivity were recovered in the expired air (CO_2 and volatiles) and therefore expired air was not collected for groups A to H. Following oral or intravenous administration of [^{14}C]-fenoxycarb at both high (300 mg/kg) and low (1 mg/kg) dose levels, elimination was moderately rapid with the majority of the radioactivity excreted within 48 hours after dosing. Faecal excretion was the primary route of elimination in all groups for both male and female rats, with biliary excretion being an important route of elimination following intravenous dosing (group A). A mean of 74.7% (males) and 75.5% (females) of the dose was excreted in faeces by the low dose groups and 59.6% (males) and 56.4% (females) was excreted in faeces by the high dose group. A smaller amount of radioactivity was excreted in urine, accounting for a mean of 19.5% (males) and 21.3% (females) for the low dose groups and 36.0% (males) and 35.9% (females) in the high dose group. No apparent sex difference in the route or rate of elimination was observed within dose groups, however it was noted that less radioactivity was excreted in faeces for animals that received a high dose compared with those that received a low dose.	X
4.5	**Distribution**	7 days after administration of a single oral or intravenous [^{14}C]-fenoxycarb dose of 1 mg/kg, 0.02-0.03% of the dose remained in tissues and up to 0.33% and 0.67% in the carcass of male and female rats, respectively. Following administration of a single oral dose at the high dose level of 300 mg/kg, residues in the tissues accounted for 0.01-0.02% of the dose and carcass accounted for 0.17% and 0.29% of the dose in male and female rats, respectively. For the low dose groups (groups A, B and C), the highest tissue residue concentrations were found in the liver (♂: 0.004 ppm, ♀: 0.006 ppm), fat (♂: 0.003 ppm, ♀: 0.002 ppm) and kidneys (♂: 0.001 ppm, ♀: not detectable), with all other tissues residue concentrations being not detectable or <0.001 ppm. Radioactive residues in blood cells and	

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plasma were not detectable 7 days after dosing.

For the high dose group (group D), residues were correspondingly higher with the highest tissue residue concentrations again found in the liver (♂: 0.683 ppm, ♀: 1.14 ppm), fat (♂: 1.62 ppm, ♀: 1.795 ppm), ovaries (♀: 0.675 ppm) and kidneys (♂: 0.335 ppm, ♀: 0.282 ppm). Radioactive residues in blood cells and plasma accounted for 0.023 ppm and 0.093 ppm (males and females) and 0.079 ppm and 0.066 ppm (males and females), respectively.

See Table A6_2-4.

4.6 Metabolism

Metabolites were identified in a follow-up study ([redacted], 1995) that is summarised in a separate document.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

Animals were acclimatised for at least 7 days prior to dosing and were housed individually in stainless steel metabolism cages during that time. Unlabelled or [^{14}C]-labelled fenoxycarb was dissolved in polyethylene glycol 200 (PEG 200) for dosing at 1 mg/kg bw or 300 mg/kg bw. Individual dose levels are tabulated below. Approximately 0.5 mL of the dose solution was administered intravenously or approximately 1.0 mL was administered by oral gavage to male and female rats. Control animals (1 male and 1 female rat per group) were dosed with PEG 200 without the test material.

The absorption, distribution and elimination of radioactivity was investigated in rats administered fenoxycarb by oral or intravenous administration as listed below.

Rats in the preliminary group (group P-H) were housed in glass metabolism cages to enable the collection of urine, faeces and expired CO_2 and volatile compounds at intervals over 7 days after dosing. Animals were sacrificed 7 days after dosing and the carcass retained for radioactivity analysis.

Rats in groups A to H were housed in metabolism cages and urine and faeces collected separately at intervals over 7 days after dosing. Cage washes and wipes were collected for each animal at the end of the collection period. At the end of the collection period (7 days), the animals were killed and the following tissues taken for radioactivity analysis; bone (femur), brain, fat (from reproductive area), ovaries, testes, heart, kidneys, liver, lungs, muscle (thigh), spleen, uterus and residual carcass. Blood was collected by cardiac puncture into heparinised tubes and centrifuged to separate the blood cells and plasma.

All samples were counted for radioactivity by liquid scintillation counting (LSC), either directly or following sample oxidation. Urine, cage wash, plasma and fat samples were analysed directly by LSC. Cage wipes and dose wipes were extracted with ethanol and the extracts analysed directly by LSC. Aliquots of the CO_2 trapping solutions were mixed with methanol prior to direct analysis by LSC. Charcoal samples from the volatile traps and all other tissues were analysed by sample oxidation. No radioactivity was found in tissues from control animals and these samples were used for validation of the radioanalysis procedures.

5.2 Results and discussion

No marked sex difference was apparent in the absorption, tissue distribution or excretion of fenoxycarb following administration of single oral or intravenous doses or multiple oral doses at the low dose

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		level of 1 mg/kg, or following a single oral dose at the high dose level of 300 mg/kg. Fenoxycarb was extensively absorbed from the gastrointestinal tract into the general circulation. The degree of absorption was greater following multiple oral doses, with 98.6% (males) and 97.7% (females) of the dose being absorbed compared with 77.0% (males) and 66.7% (females) being absorbed following a single oral dose. The majority of the administered radioactivity was excreted in faeces, accounting for a mean of approximately 75% of the dose at the low dose level and approximately 58% at the high dose level. Biliary excretion was an important route of elimination following intravenous dosing. A smaller amount of the administered radioactivity was excreted in urine, accounting for approximately 20% of the dose at the low dose level and approximately 36% at the high dose level. Negligible amounts of radioactivity were recovered in expired air (CO_2 and volatiles). At the low dose level, mean tissues residue concentrations were all at or below 0.001 ppm, with the exception of liver (0.004 ppm in males, 0.006 ppm in females) and fat (0.003 ppm in males, 0.002 ppm in females). At the high dose level, residues were correspondingly higher with the highest tissue residue concentrations again found in the liver (0.683 ppm in males, 1.14 ppm in females) and fat (1.62 ppm in males, 1.795 ppm in females).	
5.3	**Conclusion**		X
5.3.1	Reliability	1	
5.3.2	Deficiencies	None	

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	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2006/07/25
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

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Table A6_2-1 Toxicokinetic studies in the rat - experimental scheme

Group	Number and sex	Route and dose level of [^{14}C]-fenoxycarb	Sample collection times
P-H	2♂, 2♀	Single oral dose at high dose level of 300 mg/kg	Urine and faeces: 0-12 and 12-24 hours and then daily up to 7 days. Expired air: 0-12 and 12-24 hours and then daily up to 7 days.
A	5♂, 5♀	Single intravenous dose at low dose level of 1.0 mg/kg	Urine and faeces: 0-6, 6-12 and 12-24 hours and then daily up to 7 days. Tissues: Collected 7 days after dosing.
B	5♂, 5♀	Single oral dose at low dose level of 1.0 mg/kg	
C	5♂, 5♀	14 daily non-radiolabelled oral doses followed by a single radiolabelled oral dose at low dose level of 1.0 mg/kg	
D	5♂, 5♀	Single oral dose at high dose level of 300 mg/kg	
E	1♂, 1♀	Control single intravenous dose (for low dose level)	Urine, faeces, blood and tissues collected at selected time intervals.
F	1♂, 1♀	Control single oral dose (for low dose level)	
G	1♂, 1♀	Control 15 consecutive daily oral doses (for low dose level)	
H	1♂, 1♀	Control single oral dose (for high dose level)	

Table A6_2-2 Excretion of fenoxycarb following administration of a single oral [^{14}C]-fenoxycarb dose of 300 mg/kg to rats (Results are expressed as percentages of administered radioactivity)

		Group P-H (preliminary oral high dose)	
Sex		**Male**	**Female**
Dose level (mg/kg)		**281**	**280**
Urine	0-168 h	37.80	38.71
Faeces	0-168 h	55.76	57.89
Expired CO_2	0-168 h	nd	nd
Volatiles	0-168 h	nd	nd
Cage wash and wipe	168 h	0.75	0.53
Total Excretion		**94.31**	**97.13**
Carcass		0.19	0.25
Total Recovery		**94.48**	**97.02**

nd = not detectable

Table A6_2-3 Excretion of fenoxycarb following administration of a single oral dose of 1 or 300 mg [^{14}C]-fenoxycarb/kg to rats

(Results are expressed as percentages of administered radioactivity)

		Group A (i.v. low dose)		Group B (oral low dose)		Group C (oral low dose, preconditioned)		Group D (oral high dose)	
Sex		**Male**	**Female**	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**
Dose level (mg/kg)		**0.929**	**0.943**	**0.998**	**1.00**	**0.899**	**0.919**	**289**	**292**
Urine	0-6 h	5.20	6.46	4.11	5.47	5.37	8.19	2.38	4.06
	6-12 h	4.17	5.01	3.30	3.35	5.61	5.21	3.72	3.50
	12-24 h	6.57	6.40	5.26	3.84	6.26	5.01	7.73	4.78
	24-48 h	3.61	4.29	2.81	2.80	2.90	3.02	19.74	20.19
	48-72 h	1.05	1.47	0.50	0.63	0.58	0.65	1.54	2.26
	72-96 h	0.23	0.63	0.14	0.20	0.15	0.27	0.45	0.50
	96-120 h	0.10	0.24	0.08	0.11	0.07	0.15	0.18	0.34
	120-144 h	0.06	0.10	0.06	0.07	0.06	0.09	0.12	0.14
	144-168 h	0.04	0.07	0.03	0.05	0.04	0.07	0.11	0.14
	Subtotal	*21.03*	*24.67*	*16.29*	*16.52*	*21.04*	*22.67*	*35.97*	*35.91*
Faeces	0-6 h	0.01	0.28	ns	<0.01	ns	<0.01	ns	0.01
	6-12 h	1.10	1.55	9.27	22.40	14.04	23.00	3.68	4.96
	12-24 h	38.69	29.83	40.96	37.69	46.97	38.09	13.35	10.30
	24-48 h	25.57	28.51	19.67	14.62	16.71	16.38	32.74	27.26
	48-72 h	3.71	6.50	2.90	2.47	2.70	2.37	8.76	11.86
	72-96 h	0.71	1.46	0.40	0.36	0.34	0.39	0.83	1.47
	96-120 h	0.16	0.34	0.12	0.10	0.10	0.09	0.14	0.34
	120-144 h	0.05	0.07	0.03	0.02	0.02	0.05	0.05	0.09
	144-168 h	<0.01	0.05	nd	<0.01	nd	<0.01	0.02	0.05
	Subtotal	*70.00*	*68.59*	*73.35*	*77.66*	*80.88*	*80.38*	*59.58*	*56.36*
Cage wash and wipe	168 h	0.25	0.47	0.27	0.46	0.32	2.30	0.55	0.89
Total Excretion		**91.28**	**93.73**	**89.91**	**94.64**	**102.24**	**105.35**	**96.10**	**93.16**
Tissues		0.02	0.02	0.03	0.03	0.03	0.03	0.01	0.02
Carcass		0.33	0.67	0.02	0.15	nd	0.17	0.17	0.29
Total Recovery		**91.63**	**94.41**	**89.95**	**94.82**	**102.27**	**105.54**	**96.25**	**93.47**
Calculated % absorption		100	100	77.0	66.7	98.6	97.7	-	-

ns = no sample
nd = not detectable

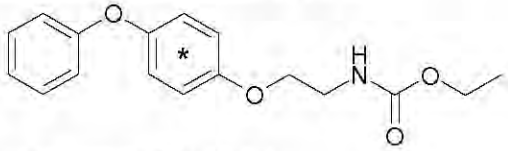
Table A6_2-4 Tissue residues of radioactivity 7 days after administration of a single oral [^{14}C]-fenoxycarb dose of 1 or 300 mg/kg to rats
(Results are expressed as µg equivalents fenoxycarb/g)

Group	Group A (IV low dose)		Group B (oral low dose)		Group C (oral low dose preconditioned)		Group D (oral high dose)	
Sex	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**
Dose level (mg/kg)	**0.929**	**0.943**	**0.998**	**1.00**	**0.899**	**0.919**	**289**	**292**
Plasma	nd	nd	nd	nd	nd	nd	0.079	0.066
Blood cells	nd	nd	nd	nd	nd	nd	0.023	0.093
Bone (femur)	nd	nd	nd	nd	nd	nd	0.103	0.205
Brain	nd	nd	nd	nd	nd	nd	nd	nd
Fat (reproductive)	0.003	0.002	0.002	0.002	0.001	0.002	1.62	1.795
Heart	nd	nd	nd	nd	nd	nd	0.011	0.015
Kidneys	<0.001	nd	<0.001	nd	0.001	nd	0.335	0.282
Liver	0.003	0.005	0.004	0.006	0.004	0.006	0.683	1.14
Lungs	nd	nd	nd	nd	nd	nd	0.083	0.121
Muscle (thigh)	nd	nd	nd	nd	<0.001	nd	0.068	0.066
Ovaries	na	nd	na	nd	na	nd	na	0.675
Spleen	nd	nd	nd	nd	nd	nd	0.023	0.031
Testes	nd	na	nd	na	nd	na	nd	na
Uterus	na	nd	na	nd	na	nd	na	0.102

nd = not detected
na = not applicable

Section A6.2 Metabolism

Annex Point IIA VI.6.2 6.2 Metabolism [^{14}C]-Fenoxycarb in rats

			Official use only
		1 REFERENCE	
1.1	**Reference**	[redacted] (1995). Characterisation and identification of metabolites in rats administered phenyl-^{14}C-(B)-Fenoxycarb. [redacted]; Unpublished Report No. ABR-94068, 12 October 1995 (unpublished)	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Syngenta	
1.2.2	Companies with letter of access	[redacted]	
1.2.3	Criteria for data protection	[redacted]	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Yes 87/302/EEC B.36 ≅ 94/79/EC (1994) ≅ OECD 417 (1984) ≅ EPA 85-1 (1984) ≅ Japanese MAFF (1985)	
2.2	**GLP**	Yes	
2.3	**Deviations**	None	
		3 MATERIALS AND METHODS	
3.1	**Test material**	Fenoxycarb	
3.2	**Non-labelled parent compound**	Fenoxycarb	
3.2.1	Lot/Batch number	[redacted]	
3.2.2	Specification		
3.2.2.1	Purity	[redacted]	
3.2.2.2	Stability	Not reported	
3.2.3	**Labelled parent compound**		
3.2.3.1	Lot/Batch number	[redacted]	
3.2.3.2	Specification		
3.2.3.3	Purity	Radiochemical purity: [redacted] Chemical purity: [redacted]	
3.2.3.4	Stability	The purity and verification of stability of the test substance in the dose solutions was determined by HPLC.	
3.2.3.5	Radiolabelling	 *(* Position of [^{14}C]-label)*	X
3.3	**Test animals**		
3.3.1	Species	*Rattus norvegicus*	
3.3.2	Strain	HSD:Sprague Dawley SD	

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3.3.3	Sex	♂ + ♀	
3.3.4	Age/weight at study initiation	Body weights: 182-236 g (males), 164-221 g (females).	
3.3.5	Number of animals	see Table A6_2-1	
3.3.6	Control animals	Yes	
3.4	**Administration/ Exposure**	Oral gavage or intravenous injection	
3.4.1	Application	**Intravenous**	
3.4.1.1	Type	Single bolus injection	
3.4.1.2	Post-exposure period	7 days	
3.4.1.3	Specific activity of test substance	GAN-XXV-93: 37 kBq/mg (1 µCi/mg) GAN-XXV-74: 1203 kBq/mg (32.5 µCi/mg)	X
3.4.1.4	Vehicle	Polyethylene glycol 200 (PEG 200)	
3.4.1.5	Volume applied	Approx 0.5 mL	
3.4.2	Application	**Oral**	
3.4.2.1	Type	Gavage	
3.4.2.2	Post-exposure period	7 days	
3.4.3	Specific activity of test substance	GAN-XXV-93: 37 kBq/mg (1 µCi/mg) GAN-XXV-74: 1203 kBq/mg (32.5 µCi/mg)	
3.4.3.1	Vehicle	Polyethylene glycol 200 (PEG 200)	
3.4.3.2	Volume applied	Approx 1 mL	
3.5	**Examinations**		
3.5.1	Parameters	Metabolism	
3.5.2	Samples	see Table A6_2-2	
3.5.3	Sampling time (0 h = start of application)	see Table A6_2-1 and Table A6_2-2	

4 RESULTS AND DISCUSSION

4.1 Metabolism

Nine metabolites of fenoxycarb were isolated and characterised (see Table A6_2-3).

In summary, [^{14}C]-fenoxycarb was extensively metabolised following oral or intravenous dosing at both the high and low dose levels, with little unchanged fenoxycarb eliminated in urine and only small amounts in faeces. The biotransformation products were qualitatively similar in male and female rats for all dose levels and routes of administration. [^{14}C]-fenoxycarb was rapidly converted to a series of metabolites that were excreted in urine and faeces in both free and conjugated forms. The metabolites CGA 294850, CGA 294851 and F-8 (U-10b) were formed by sequential oxidation of fenoxycarb.

Urinary metabolites (see Table A6_2-4): Little inter-rat variability was seen in the urinary profiles, however a significant quantitative sex difference was observed. The major urinary metabolites identified were