CLH Report

Proposal for Harmonised Classification and Labelling

**Based on Regulation (EC) No 1272/2008 (CLP Regulation),
Annex VI, Part 2**

International Chemical Identification:

Propyl [3-(dimethylamino)propyl]carbamate monohydrochloride; propamocarb hydrochloride

EC Number: **247-125-9**

CAS Number: **25606-41-1**

Index Number:

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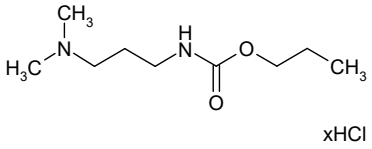
CONTENTS

1 IDENTITY OF THE SUBSTANCE

1.1 Name and other identifiers of the substance

Table 1: Substance identity and information related to molecular and structural formula of the substance

Name(s) in the IUPAC nomenclature or other international chemical name(s)	propyl [3- (dimethylamino) propyl] carbamate monohydrochloride) *
Other names (usual name, trade name, abbreviation)	Not applicable
ISO common name (if available and appropriate)	propamocarb hydrochloride
EC number (if available and appropriate)	247-125-9
EC name (if available and appropriate)	propyl [3-(dimethylamino) propyl] carbamate monohydrochloride
CAS number (if available)	25606-41-1
Other identity code (if available) = CIPAC No.:	399.601
Molecular formula	$C_9 H_{21} Cl N_2 O_2$
Structural formula	 xHCl
SMILES notation (if available)	Cl.CCCOC(=O)NCCCN(C)C
Molecular weight or molecular weight range	224.7 g/mol
Information on optical activity and typical ratio of (stereo) isomers (if applicable and appropriate)	Not applicable
Description of the manufacturing process and identity of the source (for UVCB substances only)	Not applicable
Degree of purity (%) (if relevant for the entry in Annex VI)	TK* – 690 g/kg to 740 g/kg TC – theoretical water-free material 920 g/kg

* propamocarb hydrochloride is the chemical substance manufactured and used in the formulated products. It is a very hygroscopic and highly water-soluble substance. Chemically it is possible to generate a material that is higher in purity than *e.g.* 96 % w/w, however such a material will most readily absorb moisture from the surrounding atmosphere resulting in a fast and significant decrease of the initial assay to a content readily below *e.g.* 90 % w/w.

Thus, the technical grade active substance propamocarb hydrochloride manufactured is a technical concentrate (TK) in water.

The "Food and Agriculture Organization of the United Nations" (FAO Specification propamocarb, May 2013) has set the minimum assay in the aqueous TK to 690 g/kg (corresponding to a theoretical water-free

material, which does not exist as an isolated one, with a purity of 920 g/kg) and the maximum content in the TK to 740 g/kg. Therefore, the content of propamocarb hydrochloride has to be expressed as technical concentrate grade (TK).

1.2 Composition of the substance

Table 2: Constituents (non-confidential information)

Constituent (Name and numerical identifier)	Concentration range (% w/w minimum and maximum in multi-constituent substances)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)
propamocarb hydrochloride	69.0 – 74,0 %	-	Skin Sens. 1 H317
Water	Ca. 31.0%	-	-.

Table 3: Impurities (non-confidential information) if relevant for the classification of the substance

Impurity (Name and numerical identifier)	Concentration range (% w/w minimum and maximum)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)	The impurity contributes to the classification and labelling
Dichloromethane	0.5 g/kg	Carc. 2 … H351		No (only relevant if concentration ≥ 1%)

Table 4: Additives (non-confidential information) if relevant for the classification of the substance

Additive (Name and numerical identifier)	Function	Concentration range (% w/w minimum and maximum)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)	The additive contributes to the classification and labelling
No additive added					

Table 5: Test substances (non-confidential information) (this table is optional)

Identification of test substance	Purity	Impurities and additives (identity, %, classification if available)	Other information	The study(ies) in which the test substance is used
05370 31491	Proplant®: propamocarb hydrochloride, liquid Code 5370: 70.63% Code 31491: 75.05%	no data		M-310427-01-1

Identification of test substance	Purity	Impurities and additives (identity, %, classification if available)	Other information	The study(ies) in which the test substance is used
31491	Proplant®: propamocarb hydrochloride 722 g/l, eq. to 691 g/kg propamocarb hydrochloride	no data		M-310751-01-1 M-310748-01-1 M-310551-01-1 M-310453-01-1 M-310449-01-1 M-310445-01-1 M-310442-01-1 M-310439-01-1 M-310432-01-1 M-310256-01-1
A490464	propamocarb hydrochloride technical concentrate: 70.7% w/w purity	no data		M-414757-01-1
AABA00921	PREVICUR N: 66.1% w/w	confidential		M-252483-01-1
AE B066752 00 1B97 0001	propamocarb hydrochloride: 97.2 % w/w	no data		M-203110-01-1 M-203108-01-1 M-181858-01-1

Identification of test substance	Purity	Impurities and additives (identity, %, classification if available)	Other information	The study(ies) in which the test substance is used
AE B066752 00 1E72 0001	[^{14}C]-propamocarb hydrochloride: Radioactive purity: 95.46% Non-radioactive purity: 780 g/L eq. 71.2% (w/w)	confidential		M-156084-03-1
AE B066752 00 SL67 A201	Previcur N: Content of propamocarb hydrochloride: 67.38 % w/w	no data		M-157339-02-1 M-157337-01-1 M-157246-01-1
AE B066752 00 TK72 A101	propamocarb hydrochloride, liquid. Concentrate 780 g/1. The test article was 71.1% pure.	no data		M-197256-01-1 M-183560-02-1 M-183340-01-1 M-182006-01-1
AE B066752 00 TK72 A112	propamocarb hydrochloride, technical concentrate, 780 g/l, eq. to 72.5 %-w/w propamocarb hydrochloride	no data		M-186226-01-1
EK1C00064 8	propamocarb hydrochloride, technical concentrate, 70.1 % w/w	no data		M-494160-01-1
OP2	Proplant®: (propamocarb hydrochloride 722 g/1 SL): Propyl 3- (dimethyl amino) propylcarbamate hydrochloride = 715 g/litre of formulation	no data		M-310337-01-1

2 PROPOSED HARMONISED CLASSIFICATION AND LABELLING

2.1 Proposed harmonised classification and labelling according to the CLP criteria

Table 6: Proposed harmonised classification and labelling according to the CLP criteria

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	No current Annex VI entry										
Dossier submitters proposal		propyl [3-(dimethylamino)propyl]carbamate monohydrochloride; propamocarb hydrochloride	247-125-9	25606-41-1	Skin sensitisation: Category 1B H317	H317	GHS07 Wng	H317			
Resulting Annex VI entry if agreed by RAC and COM		propyl [3-(dimethylamino)propyl]carbamate monohydrochloride; propamocarb hydrochloride	247-125-9	25606-41-1	Skin sensitisation: Category 1B H317	H317	GHS07 Wng	H317			

Table 7: Reason for not proposing harmonised classification and status under public consultation

Hazard class	Reason for no classification	Within the scope of consultation
Explosives	Conclusive but not sufficient for classification	Yes
Flammable gases (including chemically unstable gases)	Hazard class not applicable	No
Oxidising gases	Hazard class not applicable	No
Gases under pressure	Hazard class not applicable	No
Flammable liquids	Conclusive but not sufficient for classification	Yes
Flammable solids	Hazard class not applicable	No
Self-reactive substances	Conclusive but not sufficient for classification.	Yes
Pyrophoric liquids	Conclusive but not sufficient for classification	Yes
Pyrophoric solids	Hazard class not applicable	No
Self-heating substances	Conclusive but not sufficient for classification	Yes
Substances which in contact with water emit flammable gases	Hazard class not applicable	No
Oxidising liquids	Conclusive but not sufficient for classification	Yes
Oxidising solids	Hazard class not applicable	No
Organic peroxides	Hazard class not applicable	No
Corrosive to metals	Conclusive but not sufficient for classification	Yes
Acute toxicity via oral route	Conclusive but not sufficient for classification	Yes
Acute toxicity via dermal route	Conclusive but not sufficient for classification	Yes
Acute toxicity via inhalation route	Conclusive but not sufficient for classification	Yes
Skin corrosion/irritation	Conclusive but not sufficient for classification	Yes
Serious eye damage/eye irritation	Conclusive but not sufficient for classification	Yes
Respiratory sensitisation	Conclusive but not sufficient for classification	Yes
Skin sensitisation	harmonised classification proposed	Yes
Germ cell mutagenicity	Conclusive but not sufficient for classification	Yes
Carcinogenicity	Conclusive but not sufficient for classification	Yes
Reproductive toxicity	Conclusive but not sufficient for classification	Yes

Hazard class	Reason for no classification	Within the scope of consultation
Specific target organ toxicity-single exposure	Conclusive but not sufficient for classification	Yes
Specific target organ toxicity-repeated exposure	Conclusive but not sufficient for classification	Yes
Aspiration hazard	Hazard class not applicable	No
Hazardous to the aquatic environment	Conclusive but not sufficient for classification	Yes
Hazardous to the ozone layer	Hazard class not applicable	No

3 HISTORY OF THE PREVIOUS CLASSIFICATION AND LABELLING

Pesticide view:

Bayer and its Regulatory Task Force partner Arysta LifeScience Benelux sprl. (formerly Agriphar S.A.) performed self-classification for propamocarb based on study packages mainly conducted with the salt propamocarb hydrochloride. In the past such data package was submitted for Annex I inclusion of the fungicide propamocarb (base compound) and evaluated on EU level under Council Directive 91/414/EEC by the Rapporteur Member State (RMS) Ireland. Entry into force was effective from October 1st, 2007.

Currently the evaluation process for the renewal of the approval of propamocarb in Europe (AIR) is ongoing under Regulation (EC) No. 1107/2009. The official submission date of the AIR-dossier to the RMS Portugal was on 31 January 2016.

Chemical view:

Ireland, the previous RMS submitted a CLH Dossier for propamocarb as active ingredient in plant protection products to ECHA on 30 September 2011 (Submission Number: CR006298-29). On January 10, 2012, ECHA completed the "Accordance Check Report" and provided to the RMS Ireland proposals for revision of the CLH Dossier on January 25, 2012. However, since a revised version was not submitted to ECHA afterwards, Portugal as the new RMS was requested by the Commission to submit a CLH Report to ECHA at the same time as the draft RAR to EFSA for the renewal of approval of propamocarb as chemical active substance.

The C&L inventory shows the following self classifications:

Classification		Labelling			Specific Concentration limits, M-Factors	Notes	Classification affected by Impurities / Additives	Additional Notified Information	Number of Notifiers	Joint Entries
Hazard Class and Category Code(s)	Hazard Statement Code(s)	Hazard Statement Code(s)	Supplementary Hazard Statement Code(s)	Pictograms, Signal Word Code(s)						
Skin Sens. 1	H317	H317		GHS07 Wng				State/Form	34	
Not Classified									3	
Skin Irrit. 2	H315	H315	EUH401	GHS07 Wng				State/Form	2	
Aquatic Chronic 4	H413	H413								
Skin Sens. 1	H317	H317	EUH401	GHS07 Wng					1	

4 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

A substance that is a chemical active substance in the meaning of Regulation (EC) No. 1107/2009 or Regulation (EU) No. 528/2012 (biocidal products) shall normally be subject to harmonised classification and labelling, and justification is not required (Article 36 CLP Regulation).

5 IDENTIFIED USES

Propamocarb hydrochloride, belongs to the group of fungicidal carbamates and had been discovered by Schering AG Berlin, Germany, and developed during the seventies with first registrations in 1978. Propamocarb hydrochloride containing products are used worldwide in agriculture/horticulture via drench application on young plants in nursery, via drip application or foliar sprays in vegetable crops (including potatoes, tomatoes and cabbages), and ornamentals, particularly targeting *Oomycete* diseases, such as *Pythium spp., Peronospora spp., Pseudoperonospora spp., Phytophthora infestans* and *Bremia spp.*

6 DATA SOURCES

Reference is made to Point 14 (Reference list) at the end of this document.

7 PHYSICOCHEMICAL PROPERTIES

Table 8: Summary of physicochemical properties

Property	Value	Reference	Comment (e.g. measured or estimated)
Physical state at 20°C and 101,3 kPa	AE B066752 00 TK72 A110 780 g/L (TK): Clear colourless liquid AE B066752 00 1B97 0001 97.2% w/w (pure): Sticky crystals cream coloured OP2 99.1% (pure): Opaque, crystalline soft solid	Sixl, F.; Rexer, K.; 1998; M-183222-01-1 (C001717) **BCS** (KCA* 2.3/01), Sixl, F.; Rexer, K.; 1998; M-183218-01-1 (C001715) **BCS** (KCA 2.3/02) Weilbaecher, R.; 1998; M-181858-01-1 (C001142) **BCS** (KCA 2.3/03) Walker, A. J.; Mulle, D. M.; Barlett, A. J.; 1995; M-309665-01-1 (722/013) **AGR** (KCA 2.3/04)	Measured according to Directive 94/37/EEC, AII, Section 1, Point 2.4.1
Melting/freezing point	Melting point 64.2 °C (100.3% w/w pure)	Lehne, V.; 1990; M-164549-01-1 (A89312) **BCS** (KCA 2.1/01)	Measured with capillary method, CIPAC MT 2
Boiling point	-	-	Not applicable, as the pure substance is a solid
Relative density	AE B066752 00 TK72 A112 72.5% w/w 1.0851 g/cm3 at 20°C OP2 99.1% w/w(pure) 1.1478 at 20.5 ± 0.5°C	Bittner, P.; Rexer, K.; 1999; M-186226-01-1 (C003480) **BCS** (KCA 2.14/01) Walker, A. J.; Mulle, D. M.; Barlett, A. J.; 1995; M-309665-01-1 (722/013) **AGR** (KCA 2.14/02)	Measured according to EEC Directive 92/69 A.5; OECD 109- oscillating densitometer Determination was carried out using an air comparison pycnometer
Vapour pressure	AE B066752 00 107/90 97.7% w/w propamocarb hydrochloride: 20°C: 3.8 x 10-5 Pa 25°C: 8.1 x 10-5 Pa 30°C: 1.6 x 10-4 Pa	Miklautz, H.; 1990; M-157253-01-1 (A85057) **BCS** (KCA 2.2/01)	Measured according to OECD 104 – vapour pressure balance

Property	Value	Reference	Comment (e.g. measured or estimated)
Surface tension	AE B066752 00 TK72 A112 72.5% w/w 40.90 mN/m at 40°C (undiluted) 934578 74.4% w/w 62.92 mN/m at 20°C (1% sol.; TK) WB 071 97.2% w/w 71.98 mN/m at 20°C (1% sol.; pure substance) OP2 99.1 % (pure) 72.5 mN/m at 19.0 ± 0.5 °C (1.03 g/L solution)	Bittner, P.; Rexer, K.; 1999; M-186230-01-1 (C003482) **BCS** (KCA 2.12/01) Muehlberger, B.; Lemke, G.; 2004; M-235782-01-1 (C044112) **BCS** (KCA 2.12/02) Muehlberger, B.; Lemke, G.; 2004; M-235780-01-1 (C044111) **BCS** (KCA 2.12/03) Walker, A. J.; Mulle, D. M.; Barlett, A. J.; 1995; M-309665-01-1 (722/013) **AGR** (KCA 2.12/04)	Measured according to EEC Directive 92/69 A.5; OECD 115 – ring method Measured with surface tensiometer based on ISO 304 (ring method)
Water solubility	AE B066752 00 1B970001 97.2% w/w (pure): 1005 g/L at 20°C OP2 99.1% (pure) at 20°C pH 4: 89.2 – 93.5% w/w pH 7: 89.1 – 93.8% w/w pH 10: 89.6 – 94.6%w/w AE B066752 00 1B970001 97.2% w/w (pure): > 500 g/L in the pH range 1.6 – 9.6 Statements: Applying the 5 fold amount of the test item in accordance with the flask method guidance is not possible due to the high viscosity of the mixture. Due to the chemical properties of the PCH solution, it seems not relevant to compare the water solubility of this substance under alkaline and acid conditions.	Mueller, T.; 1988; M-157201-01-1 (A85005) **BCS** (KCA 2.5/01) Walker, A. J.; Mulle, D. M.; Barlett, A. J.; 1995; M-309665-01-1 (722/013) **AGR** (KCA 2.5/02) Muehlberger, B.; 2001; M-203108-01-1 (PA01/009) **BCS** (KCA 2.5/03) Statements: Muehlberger, B.; 2004; M-232456-01-1 (AF04/027) **BCS** (KCA 2.5/04) Renaud, D.; 2004; M-236979-01-1 (C045318) **BCS** (KCA 2.5/05)	Measured according to EEC Directive 92/69 A.6; Measured according to OECD 105 flask method This position paper makes reference to Muehlberger, (Muehlberger, B.; 2001; M-203108-01-1) propamocarb hydrochloride has an extremely high solubility in water with no pH dependence

Property	Value	Reference	Comment (e.g. measured or estimated)
Partition coefficient n-octanol/water	WB 071 97.2% w/w (pure): Determination at 22 °C: **pH** / **Log Pow** 2 / -2.87 7 / -1.27 9 / 0.67 OP2 99.1% (pure): Determination at 21-22°C: **pH** / **Log Pow** 4 / -0.98 7 / -1.36 9 / 0.32	Muehlberger, B.; 2001; M-203110-01-1 (C012642) **BCS** (KCA 2.7/01) Walker, A. J.; Mulle, D. M.; Barlett, A. J.; 1995; M-309665-01-1 (722/013) **AGR** (KCA 2.7/02)	Measured according to EEC Directive 92/69 A.8; OECD 107 The results indicate that propamocarb hydrochloride is not fat soluble.
Flash point	Formulation 722 g/L**: No flash point below its boiling temperature	Francois, J. M.; 2001; M-202029-01-1 (C016246) **BCS** (KCA 2.11/02)	propamocarb hydrochloride (TK) is an aqueous solution
Flammability	not applicable		Not required as the melting point of pure Propamocarb hydrochloride is 64.2°C and thus above the trigger of 40°C.
Explosive properties	propamocarb: In the temperature range between 25 and 400°C no endothermic or exothermic peak could be detected Formulation 722 g/L: No danger of explosion OP2 99.1% (pure): propamocarb hydro-chloride is non-explosive	Rehme, G.; 1985; M-157175-01-1 (A84979) **BCS** (KCA 2.11/01) Francois, J. M.; 2001; M-202029-01-1 (C016246) **BCS** (KCA 2.11/02) Poerschke, R.; 2001; M-206828-01-1 (C014554) **BCS** (KCA 2.11/03 Tremain, S. P.; Bartlett, A. J.; 1995; M-310252-01-1 (722/016) **AGR** (KCA 2.11/04)	Measured DTA according OECD Testing of chemicals; propamocarb hydrochloride does not contain structural features associated with hazardous physico-chemical properties (see document M-202029-01-1 under KCA 2.9/01 and 2.11/02). Thus additionally, a test with the formulation Previcur N was conducted and commented in a Statement (see document M-206828-01-1 under KCA 2.9/02 and 2.11/03) Measured according to EEC Directive 92/69 A.14

Property	Value	Reference	Comment (e.g. measured or estimated)
Self-ignition temperature	EXP10382A: Autoflammable with a self ignition temperature of 400 °C	Francois, J. M.; 2001; M-202029-01-1 (C016246) **BCS** (KCA 2.9/01)	Measured Test was conducted with the formulation Previcur N (see Statement Poerschke, R.; 2001; M-206828-01-1) according to EEC Directive 92/69, Part A.15
	Test was conducted with the formulation Previcur N (722 g/L)	Poerschke, R.; 2001; M-206828-01-1 (C014554) **BCS** (KCA 2.9/02)	Statement
	OP2 99.1% (pure): Auto-ignition temperature: 312 ± 5 °C	Tremain, S. P.; Bartlett, A. J.; 1995; M-310252-01-1 (722/016) **AGR** (KCA 2.9/03)	Measured according to EEC Directive 92/69, Part A.15
Oxidising properties	No hazardous physico-chemical properties; propamocarb hydrochloride is non-oxidising. Structural formula established beyond doubt incapability of exothermic reaction	Baker, G.; 1998; M-180285-01-1 (C000128) **BCS** (KCA 2.13/01) Krips, H. J.; 2000; M-310256-01-1 (308611) **AGR** (KCA 2.13/02)	Theoretical assessment In agreement with EEC Directive 92/69 Part A.17: Statement Statement
Granulometry	-	-	Not applicable, propamocarb hydrochloride is manufactured as technical concentrate in solution.
Stability in organic solvents and identity of relevant degradation products	270901 B00000 100.3% w/w **Solubility g/L at 20°C** Hexane < 0.01 Toluene 0.14 Methanol > 656.0 Dichloromethane >626.0 Ethylacetate 4.34 Acetone 560.3	Mueller, T.; 1990; M-157242-01-1 (A85046) **BCS** (KCA 2.6/01)	Measured according to CIPAC MT 157
	OP2 99.1%w/w Heptane $<1 \times 10^{-4}$ Xylene 1.06×10^{-2} Ethylacetate 4.8	Walker, A. J.; Mulle, D. M.; Barlett, A. J.; 1995; M-309665-01-1 (722/013) **AGR** (KCA 2.6/02)	Measured according to EEC Directive 92/69 A.6

Property	Value	Reference	Comment (e.g. measured or estimated)
Dissociation constant	24/90 97.7% (pure): pKa = 9.3 ± 0.03 at 20°C	Miklautz, H.; 1991; M-157256-01-1 (A85060) **BCS** (KCA 2.8/01)	Measured according to OECD 112 potentiometric titration method
	Statement: Due to the chemical structure the tertiary amine N atom (see N+) will become protonated. Thus, the dissociated species are the propamocarb ammonium cation on one hand and the chloride anion on the other.	Poerschke, R.; 2001; M-205699-01-1 (C014007) **BCS** (KCA 2.8/02)	
	OP2 99.1% (pure): pKa = 9.63 (± 0.03) at 20°C; only one pair of species (Cl-/R-CH3-H3O+); only one dissociation constant.	Walker, A. J.; Mulle, D. M.; Barlett, A. J.; 1995; M-309665-01-1 (722/013) **AGR** (KCA 2.8/03)	Measured according to potentiometric titration method
Viscosity	propamocarb hydro-chloride 722 g/L; Batch OP 2)**: In the range of 83.8 to 287 s^{-1} the test item shows Newtonian flow behaviour. 48 mPa×s at 20°C 21 mPa×s at 40°C	Lecocq, V.; 2010; M-541525-01-1 Study: 22312) **AGR** (KCP* 2.5/01)	Measured according to CIPAC MT 192 (rotational viscometer)

KCA*/KCP*: indicates the position of the reference in the dossier for renewal of the approval of propamocarb submitted to RMS Portugal in January 2016

** The test conducted with the formulation covers also the active substance being an aqueous solution with min. 690 g/kg and max. 740 g/kg propamocarb hydrochloride TK.

8 EVALUATION OF PHYSICAL HAZARDS

8.1 Explosives

Table 9: Summary table of studies on explosive properties

Method	Results	Remarks	Reference
DTA according OECD testing of chemicals	In the temperature range between 25 and 400°C no endothermic or exothermic peak could be detected.	-	Rehme, G.; 1985; M-157175-01-1
EEC Directive 92/69, Part A.14	Test with the formulation Previcur N and comment in a statement: No danger of explosion	-	Francois, J. M.; 2001; M-202029-01-1, Poerschke, R.; 2001; M-206828-01-1
EEC Directive 92/69, Part A.14	propamocarb hydrochloride is non-explosive.	-	Tremain, S. P.; Bartlett, A. J.; 1995; M-310252-01-1

8.1.1 Short summary and overall relevance of the information provided on explosive properties

Propamocarb hydrochloride is non-explosive.

Propamocarb hydrochloride does not contain structural features associated with hazardous physico-chemical properties (Francois, J. M.; 2001; M-202029-01-1).

8.1.2 Comparison with the CLP criteria

Explosive properties are associated with the presence of certain chemical groups in a molecule which can react to produce very rapid increases in temperature or pressure. The screening procedure is aimed at identifying the presence of such reactive groups and the potencial for rapid energy release.

Through the first step of the test methods described in Part I of the UN RTDG, Manual of tests and criteria (test series 1) it was demonstrated that propamocarb hydrochloride has no explosive effects.

8.1.3 Conclusion on classification and labelling for explosive properties

Propamocarb hydrochloride is not considered to be explosive. Therefore, no classification or labelling as explosive is indicated/required.

8.2 Flammable gases (including chemically unstable gases)

Table 10: Summary table of studies on flammable gases (including chemically unstable gases)

Method	Results	Remarks	Reference
Not applicable.			

8.2.1 Short summary and overall relevance of the provided information on flammable gases (including chemically unstable gases)

Not applicable.

8.2.2 Comparison with the CLP criteria

Not applicable.

8.2.3 Conclusion on classification and labelling for flammable gases

Not applicable, since propamocarb hydrochloride aqueous concentrate is a liquid.

8.3 Oxidising gases

Table 11: Summary table of studies on oxidising gases

Method	Results	Remarks	Reference
Not applicable.			

8.3.1 Short summary and overall relevance of the provided information on oxidising gases

Not applicable.

8.3.2 Comparison with the CLP criteria

Not applicable.

8.3.3 Conclusion on classification and labelling for oxidising gases

Not applicable, since propamocarb hydrochloride aqueous concentrate is a liquid..

8.4 Gases under pressure

Table 12: Summary table of studies on gases under pressure

Method	Results	Remarks	Reference
Not applicable			

8.4.1 Short summary and overall relevance of the provided information on gases under pressure

Not applicable.

8.4.2 Comparison with the CLP criteria

Not applicable.

8.4.3 Conclusion on classification and labelling for gases under pressure

Not applicable, since propamocarb hydrochloride aqueous concentrate is a liquid.

8.5 Flammable liquids

Table 13: Summary table of studies on flammable liquids

Method	Results	Remarks	Reference
In compliance with EEC Directive 92/69, Part A.9 – Pensky-Martens	No flash point below its boiling point	Test was conducted with the formulation Previcur N (water diluted) containing 722 g/l propamocarb hydrochloride	Francois, J. M.; 2001; M-202029-01-1,

8.5.1 Short summary and overall relevance of the provided information on flammable liquids

The reference dealing with flammability of the propamocarb hydrochloride dilution as present in Previcur N (722 g/l active ingredient) M-202029-01-1 conclude no flammability properties for the tested material and for propamocarb hydrochloride (803 g/l active ingredient). Propamocarb hydrochloride 722 g/l showed not to be flammable under the conditions of the test

8.5.2 Comparison with the CLP criteria

Classification criteria

Category	Criteria
1	Flash point < 23ºC and initial boiling point ≤ 35 ºC
2	Flash point < 23ºC and initial boiling point > 35 ºC
3	Flash point < 23ºC and ≤ 60 ºC

Comparing the results no flash point below its boiling point no classification of flammability is indicated.

8.5.3 Conclusion on classification and labelling for flammable liquids

Not flammable.

8.6 Flammable solids

Table 14: Summary table of studies on flammable solids

Method	Results	Remarks	Reference
Not applicable			

8.6.1 Short summary and overall relevance of the provided information on flammable solids

Not applicable.

8.6.2 Comparison with the CLP criteria

Not applicable.

8.6.3 Conclusion on classification and labelling for flammable solids

Not applicable, since propamocarb hydrochloride aqueous concentrate is a liquid.

8.7 Self-reactive substances

Table 15: Summary table of studies on self-reactivity

Method	Results	Remarks	Reference
Not applicable			

8.7.1 Short summary and overall relevance of the provided information on self-reactive substances

Propamocarb hydrochloride showed to be thermally stable when tested for flammability or explosiveness, see points 8.1 and 8.5. No pyrophoric or exothermic reaction was observed when exposed to room temperatures of up to 400°C. Further, the molecule does not have a peroxide function nor is it classified as oxidising.

Propamocarb hydrochloride is prepared as aqueous solution, which excludes water-reactivity.

There is no indication of structural features associated with properties such as self-decomposition or self-reactivity in propamocarb hydrochloride.

8.7.2 Comparison with the CLP criteria

The classification procedures for self-reactive substances need not to be applied if:

(a) There are no chemical groups present in the molecule associated with explosive or self-reactive properties; examples of such groups are given in Tables A6.1 and A6.3; or

Table A6.3: Examples of chemical groups indicating self-reactive properties in organic materials

Structural feature	Examples
Mutually reactive groups	Aminonitriles, haloanilines, organic salts of oxidizing acids
S=O	Sulphonyl halides, sulphonyl cyanides, sulphonyl hydrazides
P-O	Phosphites
Strained rings	Epoxides, aziridines
Unsaturation	Olefins, cyanates

Propamocarb does not have chemical groups associated with explosive or self-reactive properties.

8.7.3 Conclusion on classification and labelling for self-reactive substances

No classification or labelling as self-reactive is indicated/required.

8.8 Pyrophoric liquids

Table 16: Summary table of studies on pyrophoric liquids

Method	Results	Remarks	Reference
	No data submitted		

8.8.1 Short summary and overall relevance of the provided information on pyrophoric liquids

There is no indication of structural features associate with pyrophoric properties in propamocarb hydrochloride.

8.8.2 Comparison with the CLP criteria

A liquid may be classified as pyrophoric after self-ignition within five minutes exposure to air. Propamocarb hydrochloride does not have pyrophoric properties.

The classification procedure for pyrophoric liquids need not be applied when experience in manufacture or handling shows that the substance or mixture does not ignite spontaneously on coming into contact with air at normal temperatures (i.e. the substance is known to be stable at room temperature for prolonged periods of time (days)).

According to experience in manufacture or handling of propamocarb, there is no ignition spontaneously on coming into contact with air at normal temperatures.

8.8.3 Conclusion on classification and labelling for pyrophoric liquids

No classification or labelling as pyrophoric is required.

8.9 Pyrophoric solids

Table 17: Summary table of studies on pyrophoric solids

Method	Results	Remarks	Reference
Not applicable			

8.9.1 Short summary and overall relevance of the provided information on pyrophoric solids

Not applicable.

8.9.2 Comparison with the CLP criteria

Not applicable.

8.9.3 Conclusion on classification and labelling for pyrophoric solids

Not applicable, since propamocarb hydrochloride aqueous concentrate is a liquid.

8.10 Self-heating substances

Table 18: Summary table of studies on self-heating substances

Method	Results	Remarks	Reference
EU Directive 92/69, Part A.15	EXP10382A: Autoflammable with a self ignition temperature of 400 °C	Test was conducted with the formulation Previcur N (722 g/L	Francois, J. M.; 2001; M-202029-01-1
Statement			Poerschke, R.; 2001; M-206828-01-1

8.10.1 Short summary and overall relevance of the provided information on self-heating substances

Propamocarb hydrochloride showed to be thermally stable when tested for flammability or explosiveness, see points 8.1 and 8.5. No pyrophoric or exothermic reaction was observed when exposed

to room temperatures of up to 400°C. Further, the molecule does not have a peroxide function nor is it classified as oxidising.

There is no indication of structural features associate with self-heating properties in propamocarb hydrochloride.

8.10.2 Comparison with the CLP criteria

A liquid may be classified as self-heating when self-heating can be observed in the presence of air without energy supply. Such material ignites only at bigger amounts and after a long period of time (hours or days).

Propamocarb hydrochloride aqueous concentrate is a liquid with a self ignition temperature of 400 °C, no classification of self-heating is indicated.

8.10.3 Conclusion on classification and labelling for self-heating substances

Not a self-heating substance.

8.11 Substances which in contact with water emit flammable gases

Table 19: Summary table of studies on substances which in contact with water emit flammable gases

Method	Results	Remarks	Reference
Not applicable			

8.11.1 Short summary and overall relevance of the provided information on substances which in contact with water emit flammable gases

Based on information provided above: not applicable.

8.11.2 Comparison with the CLP criteria

Not applicable.

8.11.3 Conclusion on classification and labelling for substances which in contact with water emit flammable gases

Not applicable.

8.12 Oxidising liquids

Table 20: Summary table of studies on oxidising liquids

Method	Results	Remarks	Reference
EEC Directive 92/69 Part A.17	No hazardous physico-chemical properties. propamocarb hydrochloride is non-oxidising.	Statement	Baker, G.; 1998; M-180285-01-1
EEC Directive 92/69 Part A.17	Structural formula established beyond doubt incapability of exothermic reaction.	-	Krips, H. J.; 2000; M-310256-01-1

8.12.1 Short summary and overall relevance of the provided information on oxidising liquids

Propamocarb hydrochloride does not contain structural features associated with hazardous physico-chemical properties. Hazardous physico-chemical properties can therefore be discounted. Therefore, testing to measure such properties is not necessary.

8.12.2 Comparison with the CLP criteria

A substance is considered to be an oxidising substance when the burning rate of a mixture of the test substance and cellulose is higher or equal to the maximum burning rate of a reference mixture of cellulose and barium nitrate.

For organic substances or mixtures the classification procedure for this hazard class need not to be applied if:

a. the substance or mixture does not contain oxygen, fluorine or chlorine; or

b. the substance or mixture contains oxygen, fluorine or chlorine and these elements are chemically bonded only to carbon or hydrogen.

Propamocarb does not have chemical groups associated with oxidising properties.

Examination of the structural formula of the active ingredient propamocarb hydrochloride (722 g/l) establishes beyond reasonable doubt that the test substance is incapable of burning, when mixed with cellulose, at a higher or equal rate compared with the maximum burning rate of a reference mixture of cellulose and barium nitrate.

None of categories 1-3 for oxidising liquids apply.

8.12.3 Conclusion on classification and labelling for oxidising liquids

Not-oxidising.

8.13 Oxidising solids

Table 21: Summary table of studies on oxidising solids

Method	Results	Remarks	Reference
Not applicable			

8.13.1 Short summary and overall relevance of the provided information on oxidising solids

Not applicable.

8.13.2 Comparison with the CLP criteria

Not applicable.

8.13.3 Conclusion on classification and labelling for oxidising solids

Not applicable, since propamocarb hydrochloride aqueous concentrate is a liquid.

8.14 Organic peroxides

Table 22: Summary table of studies on organic peroxides

Method	Results	Remarks	Reference
Not applicable			

8.14.1 Short summary and overall relevance of the provided information on organic peroxides

Not applicable.

8.14.2 Comparison with the CLP criteria

Not applicable.

8.14.3 Conclusion on classification and labelling for organic peroxides

Not applicable, no organic peroxides contained.

8.15 Corrosive to metals

Table 23: Summary table of studies on the hazard class corrosive to metals

Method	Results	Remarks	Reference
Direct contact method and visual inspection of effects at 25°C (77°F) and 46.1°C (115°F)	Not corrosive to metals		Lambert, M.; 1979; M-157163-01-1, Mueller, T.; 1990; M-157255-01-1

8.15.1 Short summary and overall relevance of the provided information on the hazard class corrosive to metals

Corrosivity to metals and other materials was studied following two experimental procedures with Previcur N (ca. 67% propamocarb; M-157255-01-1 and M-157163-01-1). Propamocarb hydrochloride shows some changes or/and corrosive effects on different tested metallic metals. Propamocarb hydrochloride did not affect polyethylene, latex, rubber and teflon.

8.15.2 Comparison with the CLP criteria

The corrosion rate can be measured according to the test method of Part III sub-section 37.4 of the ►M4 UN RTDG ◄, Manual of Tests and Criteria (UN Test C.1).

The studies at hand do not reproduce the required method to decide on classification for corrosive to metals. Notable differences between the standard procedure and the procedure applied in the study M-157163-01-1 are the exposure time and temperature of the metal specimens to the test item.

However, the corrosion observed in study M-157163-01-1 shows that an increase of temperature of ca. 20°C produces between no increase of corrosion (compare aluminium corrosion at 25°C and at 46.1°C after one month) and ca. four times increase of corrosion (compare steel at 25°C and 46.1°C after 1 month). Additionally, all weight losses found in this study lie between one and two orders of magnitude less than the trigger values to classify for corrosivity to metals.

Weight loss due to corrosion after 1, 3 and 12 months:

	Temperature	1 month	3 month	12 month
Plain steel	25°C	0.2 %	0.47 %	1.26 %
Plain steel	46.1°C	0.76 %	1.52 %	3.20 %
Aluminium	25°C	0.06 %	0.17 %	0.40 %
Aluminium	46.1°C	0.06 %	0.25 %	0.92 %

The CLP criteria requires corrosion being studied at 55°C and these requirements consider a test item as corrosive to metals if for any specimen the mass loss on the metal specimen is more than the amount stated in the relevant test method.

Minimum mass loss of specimens after different exposure times:

Exposure time	Mass loss
7 days	13.5 %
14 days	26.5 %
21 days	39.2 %
28 days	51.5 %

Thus, extrapolating, it is considered safe to assume that running test C.1 would produce mass losses below the trigger value for classification.

8.15.3 Conclusion on classification and labelling for corrosive to metals

Not corrosive to metals.

9 TOXICOKINETICS (ABSORPTION, METABOLISM, DISTRIBUTION AND ELIMINATION)

Preface

The majority of the toxicological studies had been conducted with the straight formulations Previcur N (BCS) and Proplant (AGR), containing 722 g/L Propamocarb hydrochloride, rather than with the Technical active ingredient Propamocarb due to its high hygroscopicity. As such Propamocarb was tested as Propamocarb hydrochloride. Since after resorption of Propamocarb hydrochloride the molecule is ionized, there is systemic exposure to the base form Propamocarb.

Table 24: Summary table of toxicokinetic studies

Method	Results	Remarks	Reference
ADME: Absorption, distribution, elimination studies in the rat following single and repeated oral dosing and single intravenous dosing Group 1: single oral dose of 10 mg/kg (1 mL/200 g bw), by gavage. Group 2: single oral dose of 1000 mg/kg (1 mL/200 g bw), by gavage. Group 3: repeated oral dose of 10 mg/kg (1 mL/200 g bw), by gavage, for 14 days of nonradiolabelled propamocarb HCl, followed by a single radiolabelled dose at the same level. Group 4: single i.v. dose of 10 mg/kg (0.2 mL/200 g	Absorption was rapid and extensive (78 - 96% < 72 h). No evidence of retention of the substance in tissues, however residues were considerably higher in the animals in the single high dose group than in in the low dose group. Readily excreted by the rat, with the urinary route as the major route of elimination.	Key study of the ADME studies, experimental results. Reliable without restriction	Anonymous; 1994; M-157337-01-1
ADME: Absorption, distribution, metabolism and excretion following oral administration to the rat. Groups A/B: single oral dose of 100 mg/kg to 2 rats/sex, by gavage (Pilot study). Groups C/D: single oral dose of 1 and 100mg/kg to 4 rats/sex, by gavage (PK studies). Groups E/F: single oral dose of 1 and 100mg/kg to 4 rats/sex by gavage (Ex. Bal studies). Groups G/H: single oral dose of 1 and 100mg/kg to 3 rats/sex by gavage (TD studies). Group I: repeated daily oral dose (by gavage) of 1 mg/kg of non-radiolabelled propamocarb HCl to 12 rats/sex for 14 days, followed by a single radiolabelled dose of 1 mg/kg propamocarb hydrochloride on day 15.	Upon oral administration, the active substance is rapidly absorbed and extensively metabolised before excretion. Maximum radioactivity in all tissues at 0.75 hours post-dosing, independent of the dose level. No accumulation of active substance and/or its metabolites in any tissue even upon administering a high dose or upon repeated dosing. The highest level in liver and kidneys between 0.75 and 3 hours post-dosing. Excretion extensive with a relatively high clearance. Dose level or gender of the rats did not influence the excretion characteristics. From 92 to 97% of the radioactivity administered was recovered in the balance, and more than 80% were detected in the urine. Proposed metabolic pathway: oxidation of the propyl chain followed by N-oxidation and N-demethylation of the N-methyl groups. The major metabolites in urine were carbonyl propamocarb (met II) and hydroxy propamocarb (met VI).	Key study of the ADME studies, experimental results. Reliable without restriction	Anonymous.; 2000; M-310331-01-1

Method	Results	Remarks	Reference
Clearance from tissues: Propamocarb HCl: Clearance of a single oral dose from rat tissues. Group 1: single oral dose of 10 mg/kg (1 mL200 g bw), by gavage. Group 2: single oral dose of 1000 mg/kg (1 mL/200 g bw), by gavage.	Rapid clearance. After 48 or 72 hours, tissue residue levels generally at or below the limit of quantification. Highest residue levels in the liver, kidney, carcass and gastro-intestinal tract, additionally in the high dose group, the lungs and thyroid also contained high residues.	Key study of the metabolism studies, experimental results. Reliable without restriction	Anonymous; 1997; M-157339-02-1
Metabolite identification: Identification of selected metabolites in the rat. Groups E/F: single oral dose of 1 and 100 mg/kg to 4 rats/sex by gavage (Ex. Bal studies). Group I: repeated daily oral dose (by gavage) of 1 mg/kg of non-radiolabelled propamocarb HCl to 12 rats/sex for 14 days, followed by a single radiolabelled dose of 1 mg/kg bw propamocarb hydrochloride on day 15.	Metabolites 3-(dimethyl-amino)propylamine (Met X) and its N-oxide (Met XI) confirmed as the major components in the polar region of radioactivity. Met X was formed by the cleavage of the amide bond of propamocarb. Met XI was either formed by the cleavage of the amide bond of propamocarb N-oxide or by the N-oxidation of Met X. Both metabolites are products formed by the cleavage of the amide bond in propamocarb. Terminal half-life similar for all tissues analysed (11-26 h)	Key study of the metabolism studies, experimental results. Reliable without restriction	Anonymous.; 2000; M-310335-01-1
Metabolism: Metabolism in the Rat. Group 1: Single oral dose of 14C-propamocarb HCl at 10 mg/kg bw. Group 2: Single oral dose of 14C-propamocarb HCl at 1000 mg/kg bw. Group 3: Single oral dose of 14C-propamocarb HCl preceded by 14 consecutive daily oral doses of unlabelled propamocarb HCl at 10 mg/kg bw. Group 4: Single i.v. dose of 14C-propamocarb HCl at 10 mg/kg bw (TOX 91137).	Urine as major route of elimination (77 and 96% of the dose excreted). Faecal excretion accounted for only 1.2 – 4.6% of the dose. Propamocarb was extensively metabolised in the rat, by aliphatic oxidation of the propyl chain, N-oxidation of the tertiary amine and N-dealkylation yielding with 4 major metabolites, I, IV, VI and mono-N-desmethylpropamocarb. Unchanged propamocarb was only a minor metabolite at the low dose (3 – 11%), but at the higher dose, it increased to a mean of 20% of the dose. No evidence of conjugation with glucuronic or sulfuric acid.	Key study of the metabolism studies, experimental results. Reliable without restriction	Anonymous; 1994; M-157337-01-1

Method	Results	Remarks	Reference
Toxicokinetics: Toxicokinetic studies in the rat. Group 1: Single oral dose of 14C-propamocarb HCl at 10 mg/kg bw. Animals used for elimination/tissue residue studies. Group 2: Single oral dose of 14C-propamocarb HCl at 1000 mg/kg bw. Animals used for metabolite identification studies.	Propamocarb hydrochloride was rapidly excreted in the urine (88 – 92% in 72 h). Faecal excretion only accounted for 1.5 and 2.8%, respectively. The concentration of tissue residues was greatest in the liver in the low dose group and in the carcass and the liver in the high dose group. The compound was extensively metabolised with the metabolic profile being qualitatively similar at both dose levels. Overall, 87.68% of the low dose and 93.44% of the high dose was identified as Hoe 155306/ AE B155306, Hoe 132679/AE B132 679, Hoe 132674/AE B132674 and Hoe 132677/AE B132677. Unchanged propamocarb was a minor metabolite (1.1%) at the low dose but accounted for 20.35% of the metabolites at the high dose.	Key study of the metabolism studies, experimental results. Reliable without restriction	.Anonymous; 1998; M-156084-03-1

9.1 Short summary and overall relevance of the provided toxicokinetic information on the proposed classification(s)

In the rat, propamocarb hydrochloride was extensively and rapidly absorbed (78 – 96% within 72 h), with maximum tissue concentrations achieved within 0.75 h when dosed orally at levels of either 1 or 100 mg/kg bw.

Tissue retention was highest in organs associated with excretion i.e. liver, kidney, and in one study, the lungs. At all dose levels, residues were low and were rapidly cleared, and therefore there is no evidence of accumulation of the active substance or its metabolites. Residue levels were generally an order of magnitude greater in the high-dosed rats compared with the low dosed animals.

Propamocarb hydrochloride was rapidly excreted by the rat, primarily via the urinary route (>77 – 96% within 72 h). This was independent of dose or gender. Only a small amount was accounted for in the faeces (1.2 – 4.6%).

Metabolism was extensive, with only 1.1 – 11% of the low doses (single oral, single i.v., or repeat oral) being excreted as unchanged parent material (PM) in the urine. In the high dose animals, the amount of PM excreted in the urine increased to a mean of 20% of the dose.

The proposed metabolism of propamocarb hydrochloride involved aliphatic oxidation of the propyl chain, N-oxidation of the tertiary amine and N-dealkyation yielding the following compounds:
a) 2-hydroxypropyl 3-(dimethylamino) propylcarbamate
b) propyl [3-(methylamino) propyl] carbamate
c) propyl-3-(dimethylamino) propylcarbamate-N-oxide
d) 3-(3-dimethylaminopropyl) -4-hydroxy-4-methyloxazolidin-2-one

10 EVALUATION OF HEALTH HAZARDS

Acute toxicity

10.1 Acute toxicity - oral route

Table 25: Summary table of animal studies on acute oral toxicity

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance	Dose levels, duration of exposure	Value LD_{50}	Reference
Acute oral LD_{50} USEPA (=EPA) proposed guide-lines (1978) Reliability 1 (Klimisch score) GLP: Yes	Rat, Wistar	Propamocarb hydrochloride (66.5%)	Males (mg/kg bw): 2000, 2300, 2645, 3042, 3498, 4023 Females (mg/kg bw): 1512, 1739, 2000, 2300, 2645, 3042, 3498 14-day post exposure observation period	LD_{50}: 2900 mg/kg bw (m) LD_{50}: 2000 mg/kg bw (f)	Anonymous; 1982; M-157621-01-1
Acute oral LD_{50} OECD # 420; Method B1 of Directive 92/69/EEC Reliability 1 (Klimisch score) GLP: Yes	Rat, Sprague-Dawley	Propamocarb HCl 722 g/L SL	Limit dose of 2000 mg/kg bw 14-day post exposure observation period	LD_{50}: > 2000 mg/kg bw (m, f)	A Anonymous; 1995; M-310337-01-1
Acute oral toxicity study in mice USEPA (=EPA) proposed guidelines (1978) Reliability 1 (Klimisch score) GLP: Yes	Mouse, ICR	Propamocarb-hydrochloride (66.5%)	1300, 1690, 2197, 2856, 3713, 4826 mg/kg bw 14-day post exposure observation period	LD_{50} = 2650 mg/ kg bw (m) LD_{50} = 2800 mg/ kg bw (f)	. Anonymous; 1982; M-157621-01-1

M = males, f = females

Table 26: Summary table of human data on acute oral toxicity

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data available				

Table 27: Summary table of other studies relevant for acute oral toxicity

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data available				

10.1.1 Short summary and overall relevance of the provided information on acute oral toxicity

In an acute oral toxicity study in rats, mortality was seen at dose levels of 2300 mg/kg bw and above in males and at 1739 mg/kg bw and above in females. All mortalities occurred on day 1, the day of dosing.

Clinical signs: hypokinesia, clonic convulsion, nasal hemorrhage, mouth hemorrhage, bleeding eyelid, piloerection, sleek disappearing hair and staggering gait. Body weights of surviving animals were generally unaffected at 1 and 2 weeks after dosing. At necropsy, hyperemia of lungs and hemorrhage in small intestine of the dead animals, but no abnormalities were observed in any organs from surviving animals in all treated groups. The LD_{50} was 2900 mg/kg bw in males and 2000 mg/kg bw in females.

In another study, no mortalities or clinical signs were recorded after dosing at 2000 mg/kg bw. All animals had a normal body weight gain over the 14-day observation period. No abnormalities were detected at necropsy. The acute oral LD_{50} of Proplant (propamocarb hydrochloride 722 g/l SL) in male and female Sprague-Dawley rats in this study was greater than 2000 mg/kg bw.

In an acute oral toxicity study in mice, clinical signs of toxicity included hypokinesia, clonic convulsion, staggering gait, hearing loss and prone position. Body weights of surviving animals were generally unaffected at 1 and 2 weeks post-dosing. No abnormalities were observed in any organs from surviving animals at any dose level. Hyperemia of the lungs in the animals which died was observed. The acute oral LD_{50} of Previcur N (66.5%propamocarb hydrochloride) in ICR mice was 2650 mg/kg bw (male) and 2800 mg/kg bw (female).

10.1.2 Comparison with the CLP criteria

A compound has to be classified if the oral LD_{50} is below 2000 mg/kg bw. The acute oral LD_{50} values were as follows:

Oral LD_{50} values:
Rat: >2000 mg/kg bw
Rat: 2900 mg/kg bw (males), 2000 (females) mg/kg bw
Mouse: 2650 mg/kg bw (males), 2800 mg/kg bw (females)

In all acute toxicity studies propamocarb hydrochloride had an LD_{50} of higher than 2000 mg/kg bw. The studies were reliable.

10.1.3 Conclusion on classification and labelling for acute oral toxicity

In all acute toxicity studies Propamocarb hydrochloride had an oral LD_{50} of higher than 2000 mg/kg bw, so that a classification is not warranted.

10.2 Acute toxicity - dermal route

Table 28: Summary table of animal studies on acute dermal toxicity

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance	Dose levels duration of exposure	Value LD_{50}	Reference
Acute dermal LD_{50} OECD # 402; Method B3 of Directive 92/69/EEC Reliability 1 (Klimisch score) GLP: Yes	Rat, Sprague-Dawley	Propamocarb hydrochloride (722 g/L SL)	2000 mg/kg bw 14-day post exposure observation period	LD_{50} : > 2000 mg/kg bw (m, f)	. Anonymous; 1995; M-310341-01-1
Acute dermal LD50 Directive 92/69/EEC Part B.3, 31st July 1992, OECD Guideline No. 402,24th February 1987, USA/EPA/OPPTS 870.1200 Guideline, August 1998. Reliability 1 (Klimisch score) GLP: Yes	Rat, Wistar ICO: WI (IOPS AF/Han)	PREVICUR-N (AE B06675200 SL67 A2 - EXP 10382 A 68.0 % w/w	5000 mg/kg bw 14-day observation period	LD_{50} : > 5000 mg/kg bw (m, f)	Anonymous; 2001; M-205222-01-1

Table 29: Summary table of human data on acute dermal toxicity

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data				

Table 30: Summary table of other studies relevant for acute dermal toxicity

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data				

10.2.1 Short summary and overall relevance of the provided information on acute dermal toxicity

In one study in rats, no mortalities occurred in either sex at 2000 mg/kg bw during the course of the study. No overt signs of toxicity and no skin irritating effects were observed except erythema on the skin of 1 male and 2 female rats in one of the studies but all treated skin sites had returned to normal within 2 to 7 days after application. No abnormalities were recorded at necropsy.

In another study with dermal administration of 5000 mg/kg bw no clinical signs and no deaths were observed during the study. The overall body weight gain of the animals was not affected by treatment with the test substance. No cutaneous reactions were observed. Also macroscopic examination did not reveal apparent abnormalities in all the animals. The dermal LD_{50} was > 5000 mg/kg bw.

10.2.2 Comparison with the CLP criteria

A compound has to be classified if the dermal LD50 is below 2000 mg/kg bw. The acute dermal LD_{50} values were as follows:

Dermal LD_{50} values:

Rat > 2000 mg/kg bw

Rat > 5000 mg/kg bw

In the acute dermal toxicity studies propamocarb hydrochloride had a dermal LD_{50} of higher than 2000 and 5000 mg/kg bw.

10.2.3 Conclusion on classification and labelling for acute dermal toxicity

In all acute toxicity studies, propamocarb hydrochloride had a dermal LD_{50} of higher than 2000 mg/kg bw so that a classification is not warranted.

10.3 Acute toxicity - inhalation route

Table 31: Summary table of animal studies on acute inhalation toxicity

Method, guideline, deviations if any	**Species, strain, sex, no/group**	**Test substance, form and particle size (MMAD)**	**Dose levels, duration of exposure**	**Value** LC_{50}	**Reference**
Acute inhalation LC_{50} OECD # 403; Method B2 of Directive 92/69/EEC Reliability 1 (Klimisch score) GLP: Yes	Rat, Sprague-Dawley	Propamocarb hydrochloride 722 g/L SL MMAD: 1.8 µm.	Mean achieved atmospheric concentration: 5.01 mg/L Animals were observed for signs of overt toxicity for 14 days.	LC_{50}: > 5.01 mg/ L (m, f)	. Anonymous; 1995; M-310999-01-1
Acute inhalation LC_{50} EEC 92/69/EEC, B2 (1992) OECD 403 (1981) USEPA (=EPA) 81-3 (1984) JMAFF Nohsan No.: 4200 (1985) Reliability 1 (Klimisch score) GLP: Yes	Rat, Sprague-Dawley	Propamocarb HCl 71.2% w/v liquid concentrate	5.54 mg/L	LC_{50}: > 5.54 mg/ L (m, f)	. Anonymous; 1998; M-167986-01-1

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance, form and particle size (MMAD)	Dose levels, duration of exposure	Value LC_{50}	Reference
Acute inhalation toxicity (nose-only) study in the rat. OECD (1981) No. 403 "Acute Inhalation Toxicity" referenced as Method B2 in Comm. Directive 92/69/EEC Acute Toxicity – Inhalation Reliability 1 (Klimisch score) GLP: Yes	Rat, Sprague-Dawley Crl:CD® (SD) IGS BR	Previcur N (AE B06675200 SL67 A2–EXP 10382A 68.0 % w/w (propamocarb hydrochloride; water-soluble concentrate; 722 g/L)	4.95 mg/L	LC_{50}: > 4.95 mg/ L (m, f)	. Anonymous; 2001; M-206501-01-1

Table 32: Summary table of human data on acute inhalation toxicity

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No human data				

Table 33: Summary table of other studies relevant for acute inhalation toxicity

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No other data available				

10.3.1 Short summary and overall relevance of the provided information on acute inhalation toxicity

The acute inhalation LC_{50} of propamocarb hydrochloride liquid concentrate was rather low in rat inhalation studies with LC_{50} of > 4.95, > 5.01 and of > 5.54 mg/L (both sexes).

Animals were observed for signs of overt toxicity for 14 days. In the studies no mortalities occurred in either sex during the course of the study. The principal clinical signs seen in the studies were wet fur, hunched posture and piloerection, but all animals were normal two to four days post-exposure. Body weight gain was unaffected apart from two females in one of the studies that lost body weight during either week 1 or week 2. In one study, no findings were noted at necropsy, whereas in the other one female showed a raised reddened area on the lungs and pale kidneys. Another female had dark foci on the lungs. No other macroscopic abnormalities were seen.

10.3.2 Comparison with the CLP criteria

The criterion for classification is an inhalative LC_{50} of less than 5 mg/L (dust/mist). In all acute inhalation toxicity studies propamocarb hydrochloride had an inhalative LC_{50} of higher than 5 mg/L. Also the LC_{50} of > 4.95 mg/L is regarded as higher than 5 mg/L.

10.3.3 Conclusion on classification and labelling for acute inhalation toxicity

In all acute inhalation toxicity studies propamocarb hydrochloride had an inhalative LC_{50} of higher than 5 mg/L bw. Therefore, the data are conclusive and support that a classification is not warranted.

10.4 Skin corrosion/irritation

Table 34: Summary table of animal studies on skin corrosion/irritation

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance	Dose levels duration of exposure	Results -Observations and time point of onset -Mean scores/animal -Reversibility	Reference
Acute dermal irritation test in the rabbit OECD # 404; Method B4 of Directive 92/69/EEC; EPA-FIFRA 81-5; TSCA, E, 798.4470 Reliability 1 (Klimisch score) GLP: Yes	Rabbit, NZW 6 females	715 g/l (aqueous formulation)	0.5 mL of undiluted compound under a 2.5 cm x 2.5 cm gauze patch on the shorn skin 4-hour exposure	Very slight erythema was seen at 3 treated sites 1 hour after patch removal. All reactions had resolved by 24 hours and appeared normal.	Anonymous; 1995; M-310346-01-1
PREVICUR-N (AE B06675200 SL67 A2 - EXP10382 A). Acute dermal irritation in rabbits OECD guideline No. 404,17th July 1992, EC Directive No. 92/ 69/EEC, B.4,31st July 1992, USA/ EPA/OPPTS 870.2500 Guideline, August 1998 Reliability 1 (Klimisch score) GLP: Yes	Male New Zealand White rabbits 3 males	PREVICUR-N (AE B06675200 SL67 A2 - EXP10382 A 68.0 % w/w	0.5 mL of the test substance were placed on a dry gauze pad, which was then applied to the right flank 4-hour exposure	No erythema and no oedema was observed.	Anonymous; 2001; M-205222-01-1

Table 35: Summary table of human data on skin corrosion/irritation

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No human data available				

Table 36: Summary table of other studies relevant for skin corrosion/irritation

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No other data available				

In a primary dermal irritation study, each of 6 young adult NZW rabbits (3/sex) were exposed via the dermal route to 0.5 mL Previcur N (68.7% propamocarb hydrochloride). The test material was applied for 4 hours, under an occlusive dressing. The animals were then observed for 3 days. Irritation was scored using the Draize scheme. Very slight erythema was seen in all animals 1 hour after removal of the dressing.

However, all reactions had resolved by 24 hours apart from one animal in which the skin was normal by 48 hours. No other effects were seen.

In another primary dermal irritation study, each of 6 young adult NZW rabbits were exposed via the dermal route to 0.5 mL Proplant (propamocarb hydrochloride722 g/L SL). The test material was applied for 4 hours, under a gauze patch. The animals were then observed for 3 days. Irritation was scored using the Draize scheme. No erythema and no oedema was observed. Thus under the experimental conditions, the test substance PREVICUR-N (AE B06675200 SL67 A2 - EXP 10382 A) was a non-irritant when applied topically to rabbits.

10.4.1 Comparison with the CLP criteria

According to the criteria of the CLP (Regulation 1272/2008/EC), a substance is classified as irritating to skin if the mean score for erythema or edema over 24, 48, and 72 h is ≥ 2.3 - ≤ 4.0 in 2 out of 3 tested animals after removal of the patch or if reactions are delayed, from grades on 3 consecutive days after the onset of skin reactions. Furthermore a substance is considered irritating, if an inflammation persists to the end of the observation period in at least 2 of the animals, taking into account alopecia, hyperkeratosis, hyperplasia, and scaling. In addition, in some cases where there is pronounced variability of response among animals, with very definite positive effects related to chemical exposure in a single animal but less than the criteria above, a substance may also be classified as irritant to the skin.

Propamocarb hydrochloride was tested in 2 skin irritation studies in which none of the criteria was reached or exceeded.

10.4.2 Conclusion on classification and labelling for skin corrosion/irritation

The available data on skin irritation of propamocarb hydrochloride do not meet the criteria for classification according to Regulation (EC) 1272/2008.

10.5 Serious eye damage/eye irritation

Table 37: Summary table of animal studies on serious eye damage/eye irritation

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance	Dose levels duration of exposure	Results - Observations and time point of onset - Mean scores/animal - Reversibility	Reference
Acute eye irritation test in the rabbit. OECD # 405; Method B5 of Directive 92/69/EEC; EPA-FIFRA 81-4; TSCA, E, 798.4500 Reliability 1 (Klimisch score) GLP: Yes	Rabbit, NZW 6 females	Propamocarb hydrochloride 722 g/l SL	0.1 mL of un-diluted test substance (Proplant® in the right eye, left as control	A single instillation of the test material to the non-irrigated eye of six rabbits produced iridial inflammation and/or minimal to moderate conjunctival irritation. Treated eyes appeared normal 24 to 48-hours after treatment. The test material produced a maximum group mean score of 6.5 and was classified as a minimal irritant (Class 3 on a 1 to 8 scale) to the rabbit eye according to the modified Kay and Calandra/ Draize classification system.	Anonymous; 1995; M-310352-01-1
Acute eye irritation in rabbits OECD guideline No. 405,24th February 1987, EC Directive No. 92/69/EEC, B.5,31st July 1992, USA/EPA/OPPTS 870.2400 Guideline, August 1998 Reliability 1 (Klimisch score) GLP: Yes	New Zealand White rabbits 3 males	PREVICUR-N (AE B06675200 SL67 A2 - EXP 10382 A	0.1 mL of the test substance was instilled into the conjunctival sac of the left eye	The mean scores calculated for each animal over 24, 48 and 72 hours were 0.0, 0.0 and 0.0 for chemosis, 0.0, 0.0 and 0.3 for redness of the conjunctiva, 0.0, 0.0 and 0.0 for iris lesions and 0.0, 0.0 and 0.0 for corneal opacity. Thus, no eye irritating potential in this test.	Anonymous; 2001; M-205226-01-1

Table 38: Summary table of human data on serious eye damage/eye irritation

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No human data available				

Table 39: Summary table of other studies relevant for serious eye damage/eye irritation

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No other data available				

10.5.1 Short summary and overall relevance of the provided information on serious eye damage/eye irritation

In one study, a single instillation of the test material to the non-irrigated eye of six rabbits produced iridial inflammation and/or minimal to moderate conjunctival irritation. Treated eyes appeared normal 24 to 48 hours after treatment. The test material was classified as a minimal irritant (Class 3 on a 1 to 8 scale) to the rabbit eye according to the modified Kay and Calandra/Draize classification system.

In the other test, the mean scores calculated for each animal over 24, 48 and 72 hours were 0.0, 0.0 and 0.0 for chemosis, 0.0, 0.0 and 0.3 for redness of the conjunctiva, 0.0, 0.0 and 0.0 for iris lesions and 0.0, 0.0 and 0.0 for corneal opacity. Under the experimental conditions, the test substance PREVICUR-N (AE B06675200 SL67 A2 - EXP 10382 A) is a non-irritant when administered by ocular route to rabbits.

10.5.2 Comparison with the CLP criteria

According to the criteria of the CLP Regulation a substance is classified as irritating to the eye, when applied to the eye of the animal, if it causes significant ocular lesions which occur within 72 hours after exposure and which persist for at least 24 hours. Ocular lesions are significant and lead to category 1 classification if the mean value of the corneal opacity is ≥ 3, the iris lesion is ≥ 1.5, and to category 2 classification if corneal opacity is ≥ 1.0, irits ≥ 1, conjunctival redness ≥ 2.0, and/or chemosis ≥ 2, calculated as the mean scores following grading at 24, 48 and 72 hours after instillation and which fully reverses within 21 days. If three animals were used in the test, the scores have to occur in at least 2 animals.

In one study with propamocarb hydrochloride in rabbits, slight eye irritating effects were seen, but the scores did not reach the classification criteria. In the 2nd study with propamocarb in rabbits, no evidence of an eye irritating effect was seen.

10.5.3 Conclusion on classification and labelling for serious eye damage/eye irritation

Since in 2 studies with propamocarb hydrochloride in rabbits, no eye irritating effects beyond the classification criteria were seen, the data were conclusive, but a classification is not warranted.

10.6 Respiratory sensitisation

Table 40: Summary table of animal studies on respiratory sensitisation

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance	Dose levels, duration of exposure	Results	Reference
28-day immuno-toxicity study in the female Sprague-Dawley rat by dietary administrat-ion U.S.E.P.A., OPPTS Series 870, Health Effects Testing Guidelines, No 870.7800 (August 1998) Reliability 1 (Klimisch score) GLP: Yes	Rats, Crl:CD (SD) 10 females/ dose	Propamo-carb hydro-chloride	0, 1400, 4500, 15000 ppm 28 days	In this study the potential immunotoxic properties of Propamocarb hydrochloride technical concentrate were tested in female Sprague-Dawley rats (SD) following continuous dietary administration for at least 28 days at concentrations of 0, 1400, 4500 and 15000 ppm (equivalent to doses of 92.4, 290.8 and 1142.5 mg/kg bw/day). In conclusion, up to the highest dose tested of 15000 ppm, no relevant change was noted in anti-SRBC IgM concentrations compared to controls, so that there was no evidence of an immunotoxic potential of Propamocarb hydrochloride technical concentrate. The NOEL for immunotoxic potential iexpressed as propamocarb hydrochloride is 1065 ppm corresponding to 807.7 mg/kg bw/day.	Anonymous; 2011; M-414757-01-1

Table 41: Summary table of human data on respiratory sensitisation

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No human data available				

Table 42: Summary table of other studies relevant for respiratory sensitisation

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No other data available				

10.6.1 Short summary and overall relevance of the provided information on respiratory sensitisation

No relevant human data are available. No formally recognised and validated animal tests currently exist for respiratory sensitisation. However data from some animal studies may be indicative of the potential of a substance to cause respiratory sensitisation in humans and may provide supportive evidence in case human evidence is available. This information may also be combined with information on structural alerts for respiratory sensitisation and information on the skin sensitising properties of a substance and should be used in a weight of evidence assessment.

In the animal studies with propamocarb hydrochloride under sections 10.1 to 10.5 and 10.7, no evidence of respiratory tract irritation (local cytotoxic effects) was obvious, also the acute rat inhalation data do not provide evidence for functional impairment of the respiratory system.. The skin and eye irritation studies in rabbits, and the rat acute and repeated dose dermal toxicity studies did not indicate an irritating potential on skin and mucous membranes, so that a respiratory irritation potential is not likely. Also a study on the immunotoxic potential of propamocarb hydrochloride was negative.

10.6.2 Comparison with the CLP criteria

According to the CLP criteria for respiratory sensitisation, evidence that a substance can lead to specific hypersensitivity will normally be based on human experience. In this context, hypersensitivity is normally seen as asthma, but other hypersensitivity reactions such as rhinitis/conjunctivitis and alveolitis are also considered. The condition will have the clinical character of an allergic reaction.

In the animal studies with propamocarb hydrochloride, no evidence of respiratory tract irritation (local cytotoxic effects) was obvious, also the acute rat inhalation data do not provide evidence for functional impairment of the respiratory system. Also a study on the immunotoxic potential of propamocarb was negative. The skin and eye irritation studies in rabbits, and the rat acute and repeated dose dermal toxicity studies did not indicate a severe irritating or corrosive potential on skin and mucous membranes, so that a respiratory irritation potential is not likely.

10.6.3 Conclusion on classification and labelling for respiratory sensitisation

Since in the animal studies with propamocarb hydrochloride, no evidence of respiratory tract irritation was obvious, the data are conclusive but not sufficient to warrant a respiratory sensitisation classification.

10.7 Skin sensitisation

Table 43: Summary table of animal studies on skin sensitisation

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance	Dose levels duration of exposure	Results	Reference
Guinea-pig skin sensitisation study (Magnusson & Kligman method) EU (=EEC) 92/69/EEC, B.6 (1992), OECD 406 (1992), USEPA (=EPA) 870.2600	Guinea pig, Dunkin/Hartley 20 test, 10 control animals	Propamocarb hydrochloride liquid con-centrate 71.2% w/w.	Induction intradermal injection of 7.5 % v/v in sterile water (48 h) Induction topical application of 10 % v/v in distilled water (48 h) Topical	After the challenge, slight persistent dermal responses were recorded in 9 out of 20 test animals (45%), compared with none in controls. Slight non-persistent reactions were seen in 2 other test animals and therefore these were considered to be inconclusive. The remaining 9 animals gave negative responses.	. Anonymous; 1999; M-184379-01-1

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance	Dose levels duration of exposure	Results	Reference
(1998), JMAFF NohSan no. 4200 (1985) Reliability 1 (Klimisch score) GLP: Yes			challenge of 5 and 2.5 % v/v in distilled water (24 h)	Conclusion: Propamocarb hydrochloride liquid concentrate was a weak skin sensitiser in the Magnusson and Kligman test.	
Modified Nine-Induction Buehler Delayed Contact Hypersensitivity Study in the Guinea Pig OECD Guidelines for Testing of Chemicals (1981) No. 406 "Skin Sensitisation", Buehler Test and Method B6 in Commission Directive 84/449/EEC Reliability 1 (Klimisch score) GLP: Yes	Guinea pig, Dunkin/Hartley 20 test, 10 control animals	PROPLANT (Propamocarb hydrochloride 722 g/L SL)	A topical application (0.5 mL) of the undiluted test material was applied on absorbent lint Induction was performed on days 0, 2, 4, 7, 9, 11, 14, 16 and 18 A quantity of 0.5 mL of the undiluted test material was applied to the shorn right flank of each animal on absorbent lint as challenge, concentration of 75% v/v in distilled water was similarly applied to a separate skin site on the right shorn flank.	The test material, PROPLANT (Propamocarb hydrochloride 722 g/L SL), produced a 0% (0/20) sensitisation rate and was classified as a non-sensitizer to guinea pig skin.	Anonymous; 1995; M-310356-01-1
Evaluation of potential dermal sensitisation in the Local Lymph Node Assay (LLNA) in the mouse. OECD guideline 429 (2002)	Mice, CBA/J	Propamocarb hydrochloride (66.1 %)	Concentrations (%): 0, 10, 25, 50, 100 3 days	Previcur N was found to be a sensitizing formulation in the Local Lymph Node Assay at a concentration of 100 % as it exceeded the SI of 3 at a concentration which was not demonstrated irritating in a preliminary test.	Anonymous; 2005; M-252483-01-1

Table 44: Summary table of human data on skin sensitisation

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No human data				

Table 45: Summary table of other studies relevant for skin sensitisation

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No other data				

10.7.1 Short summary and overall relevance of the provided information on skin sensitisation

In a Guinea-pig skin sensitisation study (Magnusson & Kligman method) slight persistent dermal responses were recorded in 9 out of 20 test animals (45%) compared with none in controls after the challenge phase. Slight non-persistent reactions were seen in 2 other test animals and therefore these were considered to be inconclusive. The remaining 9 animals gave negative responses. Therefore, Propamocarb hydrochloride liquid concentrate was a weak skin sensitiser in this Magnusson and Kligman test.

In a Buehler test, the test material, propamocarb hydrochloride 722 g/1 SL, L produced a 0% (0/20) sensitisation rate and was thus not a sensitizer to guinea pig skin.

In a Local Lymph Node Assay (LLNA) in the mouse for evaluation of potential dermal sensitisation positive lymphoproliferative responses (SI > 3) were at a concentration of 100%, negative lymphoproliferative response (SK3) were noted for at concentrations of 10, 25 and 50%. In the positive control group given p-Benzoquinone, a SI value of 3 was noted which demonstrated the validity of this assay using the specific test formulation, with a positive response to treatment with p-Benzoquinone.

Therefore, propamocarb hydrochloride was found to be a sensitizing formulation in the Local Lymph Node Assay at a concentration of 100%.

10.7.2 Comparison with the CLP criteria

Effects seen in either humans or animals will normally justify classification in a weight of evidence approach for skin sensitisers. According to CLP there are three standard animal test methods used to evaluate skin sensitisation for substances: the mouse local lymph node assay (LLNA), the guinea pig maximisation test (GPMT) and the Buehler assay. Substances may be allocated to one of the two sub-categories 1A or 1B using a weight of evidence approach in accordance with the criteria as follows. Substances shall be classified as skin sensitisers (Category 1) where data are not sufficient for sub-categorisation in accordance with the following criteria: (a) if there is evidence in humans that the substance can lead to sensitisation by skin contact in a substantial number of persons; or (b) if there are positive results from an appropriate animal test. Sub-category 1A: Substances showing a high frequency of occurrence in humans and/or a high potency in animals can be presumed to have the potential to produce significant sensitisation in humans. Severity of reaction may also be considered. Sub-category 1B: Substances showing a low to moderate frequency of occurrence in humans and/or a low to moderate potency in animals can be presumed to have the potential to produce sensitisation in humans. Severity of reaction may also be considered and on the basis of reliable and good quality evidence from human cases or epidemiological studies and/or observations from appropriate studies in experimental animals according to the guidance values for sub-category 1A and for sub-category 1B. For propamocarb no

evidence of a sensitizing potential in humans exists, whereas the animal studies indicate a weak potential.

10.7.3 Conclusion on classification and labelling for skin sensitisation

Propamocarb hydrochloride liquid concentrate was a weak skin sensitiser in a Magnusson and Kligman test, but not in a Buehler test with topical application. In a Local Lymph Node Assay (LLNA) in the mouse for evaluation of potential dermal sensitisation positive lymphoproliferative responses (SI > 3) were seen at a concentration of 100 %, so that Previcur N was found to be a sensitizing formulation in the Local Lymph Node Assay at a concentration of 100 %. Thus, the studies were conclusive and warrant a classification as skin sensitizer H317 (May cause an allergic skin reaction).

Since in the LLNA study, the EC3 value was above 2% and the response in the guinea pig maximization test was ≥ 30% at > 1 % intradermal induction, it is classified as Category 1B.

10.8 Germ cell mutagenicity

Table 46: Summary table of mutagenicity/genotoxicity tests in vitro

Method, guideline, deviations if any	Test substance	Relevant information about the study including rationale for dose selection (as applicable)	Observations	Reference
Bacterial mutation (Ames Test) *Salmonella typhimurium* strains TA 1535, Ta 1537, TA 1538, TA 98 and TA 100 *Escherichia coli* strain WP2 uvrA Guideline: Not stated but substantially compliant with OECD 471 and 472 (1983). GLP: No Reliability: 2 (Klimisch score)	Previcur N 66.5% propamocarb hydrochloride (SN 66752)	Previcur N was not toxic and did not increase the numbers of revertant colonies in any of the bacterial strains in either the presence or absence of metabolic activation. The positive control compounds produced the expected increases in the numbers of revertant colonies in the presence of metabolic activation thereby demonstrating the efficacy of the S9 mix and the sensitivity of the bacterial strains. Previcur N (containing propamocarb hydrochloride as active substance) was not mutagenic in bacteria in either the presence or absence of metabolic activation. 5 – 5000 µg/plate (with and without S-9 mix)	Not mutagenic in bacteria in either the presence or absence of metabolic activation	Anonymous; 1981; M-157610-01-1

Method, guideline, deviations if any	**Test substance**	**Relevant information about the study including rationale for dose selection (as applicable)**	**Observations**	**Reference**
Bacterial mutation (Ames Test) *Salmonella typhimurium* strains TA 1535, Ta 1537, TA 1538, TA 98 and TA 100 *Escherichia coli* strain WP2 uvrA Guidelines: OECD 471 and 472 (1983) GLP: Yes (OECD, 1982; USFDA, 1978; USEPA, 1983; JMAFF, 1984; JMHW, 1982) Reliability: 1 (Klimisch score)	Propamocarb Hydrochloride (Nominal 70%)	Technical propamocarb hydrochloride was not toxic to any bacterial strain and did not induce any significant increases the number of revertant colonies in any strain in either the presence or absence of metabolic activation. The concurrent positive control compounds produced expected increases in the number of revertant colonies thereby demonstrating the sensitivity of the assay and the efficacy of the S9 mix. 15 – 5000 µg/plate (with and without S-9 mix)	Negative	Anonymous; 1987; M-157642-01-1

Method, guideline, deviations if any	Test substance	Relevant information about the study including rationale for dose selection (as applicable)	Observations	Reference
Bacterial mutation (Ames Test) *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537 and TA 1538 Guidelines: OECD # 471; Method B14 of Directive 92/69/EEC; US-EPA, section 84-2. GLP: Yes Reliability: 1 (Klimisch score)	Propamocarb HCl 722 g/L SL in aqueous solution	Compared to the number of spontaneous mutations obtained in the negative controls, there was no significant increase in the number of revertants for any of the five strains of Salmonella used at any of the five test concentrations with or without metabolic activation. All the positive controls induced marked increases in the frequency of revertant colonies and the activity of the S9 fraction was found to be satisfactory. 5 – 5000 µg/plate (with and without S-9 mix)	Propamocarb hydrochloride is considered non-mutagenic under the conditions of the Ames test with Salmonella typhimurium strains TA1535, TA1537, TA1538, TA98 and TA100. Negative	Anonymous; 1997; M-310446-01-1
Bacterial mutation (Ames Test) *Escherichia coli* strain WP2 uvrA Guidelines: OECD # 471; Method B13/14 of Dir. 92/69/EEC; US-EPA-OPPTS 870.5100. GLP: Yes Reliability: 1 (Klimisch score)	Propamocarb HCl 750.5g/L aqueous solution	Compared to the number of spontaneous mutations obtained in the negative controls, there was no significant number of revertants in any of experiments at any of the test concentrations, with or without metabolic activation. 69 – 5000 µg/plate (with and without S-9 mix)	Propamocarb hydrochloride is considered non-mutagenic under the conditions of the Ames test with Escherichia coli strain WP2uvrA	Anonymous; 2001; M-310449-01-1

Method, guideline, deviations if any	Test substance	Relevant information about the study including rationale for dose selection (as applicable)	Observations	Reference
Chromosome aberrations Human lymphocytes Guidelines: OECD 473 (1983) GLP: Yes (OECD, 1982; USEPA, 1983; JMAFF, 1984) Reliability: 1 (Klimisch score)	70% solution of tech. propamocarb in 1N HCl	Technical propamocarb hydrochloride did not significantly increase the incidence of chromosomal aber-rations, positive control compounds, ethylmethane sulphonate and cyclophosphamide confirmed the sensitivity of this test system. 110-1100 µg/mL (without S-9 mix); 470-4700 µg/mL (with S-9 mix)	Negative	Anonymous; 1987; M-157641-01-1
Chromosome aberrations Human lymphocytes Guidelines: OECD guideline # 473 (1997); US-OPPTS 870.5375 (EPA, 1998); Dir. 67/548/EEC, Annex V, B.10 (2000) GLP: Yes Reliability: 1 (Klimisch score)	750.5 g/L Propamocarb HCl aqueous solution	Propamocarb hydrochloride shows no clastogenic potential under the conditions of this in vitro test. There was no recorded increase in the numbers of chromosome aberrations in cultured human lymphocytes, either in the presence or the absence of metabolic activation (S9), up to a concentration of 5000 µg a.s./mL culture. 518-4000 µg/mL (without S-9 mix) 691-5000 µg/mL (with S-9 mix)	No clastogenic potential under the conditions of this in vitro test	Anonymous; 2001; M-310453-01-1

Method, guideline, deviations if any	Test substance	Relevant information about the study including rationale for dose selection (as applicable)	Observations	Reference
Mammalian cell gene mutation Mouse lymphoma L5178Y (TK+/-) cells Guidelines: OECD 476 (1997); EU (=EEC) 88/302/EEC (1988); USEPA (=EPA) OPPTS 870.5300 (1998) GLP: Yes (UK, 1999) Reliability: 1 (Klimisch score)	Propamocarb Hydrochloride Liquid Concentrate, 71% w/w	The concentrations were based on the results of a preliminary toxicity test. 100-2500 µg/mL (without S-9 mix) 125-4000 µg/mL (with S-9 mix)	Propamocarb hydrochloride liquid concentrate was not mutagenic in mouse lymphoma L5178Y cells in either the absence or presence of metabolic activation.	Anonymous; 2001; M-197256-01-1
Mammalian cell gene mutation Mouse lymphoma L5178Y (TK+/-) cells Guidelines: OECD # 476 (1997); US-OPPTS 870.5300 (EPA, 1998); Dir. 67/548/EEC, Annex V, B.17 (2000). GLP: Yes Reliability: 1 (Klimisch score)	Propamocarb HCl 750.5g/L aqueous solution	The dose range finding demonstrated that the test item was soluble in the exposure medium up to the recommended high dose of 5000 µg a.s./ml. Propamocarb hydrochloride is con-sidered non-mutagenic in the TK-locus mutation test system under the conditions of this study 3-5000 µg/ml (±S-9 mix and 3h treatment); 3-2000 µg/ml (-S9 and 24h treatment)	Negative	Anonymous; 2001; M-310551-01-1

Table 47: Summary table of mutagenicity/genotoxicity tests in mammalian somatic or germ cells in vivo

Method, guideline, deviations if any	Test substance	Relevant information about the study (as applicable)	Observations	Reference
Micronucleus test in CD-1 mouse (bone marrow erythrocytes) Guidelines: Not stated but substantially compliant with OECD 474 (1983). Samples taken GLP: No Reliability: 2 (Klimisch score)	Previcur N 70.2%	From the results of the preliminary toxicity test, a top dosage of 5000 mg/kg bw was chosen for the micronucleus test. Administration of CP 604 had no effect on the incidences of micronucleated polychromatic and normochromatic erythrocytes. All group mean values were comparable with the concurrent control. However, the positive control, Mitomycin C, produced the expected statistically significant increases in these cells.1250, 2500 and 5000 mg/bw body weight (as two equal doses of separated by 24 hours). The test compound containing 70.2% of propamocarb hydrochloride, did not induce micronuclei at total dose levels up to 5000 mg/kg. In SHG 182/79183 (Sampling took place 6 hours following the last dose), administration of total doses of 2500 and 5000 mg/kg of test compound caused statistically significant differences in the ratio of normochromatic to polychromatic erythrocytes indicating bone marrow toxicity. In SHG/191/79737 (Sampling took place 12, 24, 36, and 48 hours following the last dose), a dose of 2500 mg/kg produced evidence of bone marrow toxicity at the 12-hour sampling time. The test compound therefore failed to show any evidence of mutagenic potential when administered orally, in this test procedure. However, evidence of bone marrow depression was observed.	Negative	Anonymous; 1980; M-157582-01-1

Method, guideline, deviations if any	Test substance	Relevant information about the study (as applicable)	Observations	Reference
Micronucleus NMRI BR mouse (bone marrow erythrocytes) Guidelines: OECD # 474 (1997); US-OPPTS 870.5395 (EPA, 1998); Dir. 67/548/EEC, Annex V, B.12 (2000). GLP: Yes Reliability: 1 (Klimisch score)	Propamocarb HCl 722g/L	Based on the results of the dose range finding study, dose levels of 69, 138 and 276 mg/kg body weight were selected as appropriate doses for the main test. Clinical signs related to the treatment were only seen in the high dose group (276 mg a.i./kg), and these had completely receded within 20 hours of dosing. No increase in the frequency of micronucleated polychromatic erythrocytes was observed in the polychromatic erythrocytes of the bone marrow of Proplant treated animals compared to the vehicle treated animals. 0, 69, 138, 276 mg/kg body weight (as single intraperitoneal injection) Neither the Propamocarb HCl 722g/L treated nor the negative control animals showed any decrease in the ratio of polychromatic to normochromatic erythrocytes, reflecting a lack of toxicity of this compound on erythropoiesis. The positive control groups showed a decrease in the ratio.	Negative	Anonymous; 2001; M-310555-01-1
Dominant lethal mutation ICR/SIM mouse (spermatogenic cells) Guidelines: Not stated but substantially compliant with OECD 478 (1984). GLP: Yes Reliability: 2 (Klimisch score)	Previcur N 69.2 %	Test compound was administered to adult male mice for 8 consecutive weeks in their drinking water, treatment of mice for 8 weeks with up to 8000 ppm of Previcur N did not induce dominant lethal mutations. The no observable adverse effect level (NOAEL) was 8000 ppm, equivalent to an overall mean achieved intake of 1237 mg/kg bw/day. In terms of active substance, 8000 ppm corresponded to 5536 ppm of propamocarb hydrochloride and to an overall mean intake of 856 mg/kg/day. 2000 - 8000 ppm in drinking water	Negative	Anonymous; 1979; M-157583-01-1

Table 48: Summary table of human data relevant for germ cell mutagenicity

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No human data				

10.8.1 Short summary and overall relevance of the provided information on germ cell mutagenicity

The results of the conducted guideline genotoxicity studies, i.e. many Ames tests, chromosome aberration tests, mammalian gene mutation tests in vitro and two micronucleus and a dominant lethal test *in vivo* did not reveal a genotoxic potential of propamocarb.

10.8.2 Comparison with the CLP criteria

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Epidemiological studies have been to date unable to provide evidence to classify a substance as a Category 1A mutagen. Hereditary diseases in humans for the most part have an unknown origin and show a varying distribution in different populations. Due to the random distribution of mutations in the genome it is not expected that one particular substance would induce one specific genetic disorder. Therefore, it is unlikely that such evidence may be obtained by epidemiological studies to enable you to classify a substance in Category 1B may be based on positive results of at least one valid in vivo mammalian germ cell mutagenicity test. In case there are also negative or equivocal data, a weight of evidence approach using expert judgement has to be applied.

If there are only positive results of at least one valid in vivo mammalian somatic mutagenicity test but no respective data on mammalian germ cells are available, additional evidence is required to be able to classify as mutagen in Category 1B. Such additional data must prove that the substance or its metabolite(s) interacts in vivo with the genetic material of germ cells. It is also possible to obtain supporting evidence in an in vivo genotoxicity test with mammalian germ cells. In addition, genetic damage to germ cells in exposed humans proven to be caused by substance exposure may offer respective information. In case of other supporting evidence or where there are also negative or equivocal data, a weight of evidence approach using expert judgement has to be applied.

Classification in Category 2 may be based on positive results of a least one in vivo valid mammalian somatic cell mutagenicity test, indicating mutagenic effects in somatic cells. A Category 2 mutagen classification may also be based on positive results of a least one in vivo valid mammalian somatic cell genotoxicity test, supported by positive in vitro mutagenicity results. Genetic damage to somatic cells in exposed humans shown to be caused by substance exposure supported by positive in vitro mutagenicity results may also offer respective information warranting classification as a Category 2 mutagen. In vitro results can only lead to a Category 2 mutagen classification in a case where there is support by chemical structure activity relationship to known germ cell mutagens. In the case where there are also negative or equivocal data, a weight of evidence approach using expert judgement has to be applied.

In general, mutations can be differentiated into gene mutations (e.g. point or frame shift mutation), chromosome mutations (structural chromosome changes) and genome mutations (loss or gain of whole chromosomes). Different mutagenicity tests may detect different types of mutations and genotoxic effects which have to be taken into account in the weight of evidence determination.

If there are positive results in at least one valid in vivo mutagenicity test using intraperitoneal application, or from at least one valid in vivo genotoxicity test using intraperitoneal application plus supportive in vitro data, classification is warranted. In cases where there are additional data from further in vivo tests with oral, dermal or inhalative substance application, a weight of evidence approach using expert judgement has to be applied in order to come to a decision.

In summary, classification as a Category 2 mutagen would generally apply if only intraperitoneal in vivo tests show mutagenicity/genotoxicity and the negative test results from the in vivo tests using other routes of application are plausible. Factors influencing plausibility are e.g. the doses tested and putative kinetic data on the test substance. However, on a case-by-case analysis using a weight of evidence approach and expert judgement, non-classification may also result.

Since the results of the conducted guideline genotoxicity studies in vitro and in vivo did not reveal a genotoxic potential of propamocarb, none of the aforementioned criteria for any category are fulfilled.

10.8.3 Conclusion on classification and labelling for germ cell mutagenicity

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According to the CLP Guidance a classification for germ cell mutagenicity category 2 is based on positive somatic cell mutagenicity tests in vivo, in mammals, or other positive in vivo somatic cell genotoxicity tests which are supported by positive results from in vitro mutagenicity assays, or positive in vitro mammalian mutagenicity assays for substances which also show chemical structure activity relationship to known germ cell mutagens.

Based on the genotoxicity results with propamocarb hydrochloride, the aforementioned classification criteria are not met. Classification criterion for substances which show chemical structure activity relationship to known germ cell mutagens is also not met since propamocarb hydrochloride does not show a chemical structure activity relationship to known germ cell mutagens. Since the results of the conducted guideline genotoxicity studies with propamocarb hydrochloride, i.e. many Ames tests, chromosome aberration tests, mammalian gene mutation tests in vitro and two micronucleus and a dominant lethal test in vivo did not reveal a genotoxic potential of propamocarb the criteria for genotoxicity classification are not met. Thus, the data for propamocarb are conclusive, but they do not warrant genotoxicity classification.

10.9 Carcinogenicity

Table 49: Summary table of animal studies on carcinogenicity

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results	Reference
Toxicity and potential tumourigenicity in dietary administration to rats for 104 weeks Rat, Sprague-Dawley 50 male and 50 female rats per sex/dose (main groups). Study was not conducted to any currently-recognised guideline. Deviations from currently accepted guidelines: Based on OECD Guideline 453 "Combined chronic toxicity / carcinogenicity studies", the following deviations were identified:- The recommended number of animals in the high-dose satellite group is 20 / sex as opposed to 10 / sex in this study. The survival rate after 104 weeks of treatment, taking the main and satellite groups together, was greater than 50% in high-dose	Previcur N (SN 66 752) 0, 28, 140, 702 ppm	No treatment-related effects on body weight or body weight gain, food consumption or food conversion and water intake. No treatment-related ocular effects and no obvious treatment-related effects on haematological, clinical biochemistry or urinalysis measurements. Organ weights were unaffected by treatment. Non-neoplastic histopathological findings were unremarkable. The NOAEL was 1000 ppm test material (equivalent to 36.5 mg/kg bw/day in males and 45.4 mg/kg bw/day in females). This corresponds to 702 ppm active ingredient (equivalent to 25.6 mg/kg bw/day in males and 31.9 mg/kg bw/day in females). The incidence of mammary gland fibro-adenoma in terminal sacrifice females was increased	Anonymous; 1983; M-157599-01-1

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results	Reference
males only (57%) and varied from 30 – 48% in the other groups. A haematological examination is recommended on samples from 20 rats/sex from all groups. In this study, samples were taken from 10 rats/sex from all groups. However, the haematological parameters tested were as recommended in the guideline. Tissue samples from the thymus, rectum, peripheral nerve and femur were not preserved for histopathology. GLP: No. Although the in-life phase of the study commenced prior to the issuing of GLP regulations, such regulations as set forth in Title 21 of the US Code of Federal Regulations, Part 58 were implemented during the study. Overall the study was conducted according to the principles of GLP with a signed statement to this effect. Reliability: 4 (Klimisch score)		at the mid and high doses compared to controls. The frequencies were within the normal range for Charles River Sprague-Dawley female rats. However, no normative data was supplied for this laboratory covering the time period inclusive of this study. This is a pre-guideline study and consequently a number of significant deviations from current guidelines were identified. Most notably, the mortality rate exceeded 50% by 24-months ranging from 43 – 70% (mean 58%) which invalidates the conclusions drawn in the study with respect to the negative toxicological effects of the test material. In addition, the incidence of viral sialodacryo-adenitis was very high, especially in males with two distinct outbreaks during the course of the study. Therefore, this study is considered to be supplemental.	

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results	Reference
Rat combined chronic toxicity and oncogenicity (dietary) study. Rat, CRL:CD (SD)BR 70/sex/dose Guidelines: EEC Directive 88/302/EEC (1988); OECD Guideline for testing of chemicals, Section 4, Health effects, No. 453, Combined Chronic Toxicity / Carcinogenicity Studies (1981); US EPA Pesticide Assessment Guideline 83-5, Combined Chronic Toxicity / Oncogenicity Studies (1984); Japan MAFF SACI Combined Chronic Toxicity / Oncogenicity Study (1985) Deviations from currently accepted guidelines: Based on OECD Guideline 453 "Combined chronic toxicity / carcinogenicity studies", the following deviations were identified: The guidelines recommended the lowest dose be no lower than 10% of the high dose. In this instance, the low dose is 350 ppm which is approximately 1.6% the high dose of 22400 ppm. A haematological examination is recommended on samples from 20 rats/sex from all groups. In this study, samples were taken from 10 rats/sex from all groups. However, the haematological parameters tested were as recommended in the guideline. GLP. Yes Reliability: 2 (Klimisch score)	Propamocarb hydrochloride liquid concentrate 71.2% w/w 0, 350, 2800, 22400 ppm, (equivalent to mean a.i. intakes of 0, 249, 1994, 15949 ppm)	No treatment-related effect on mortality, male and female body weight, body weight gain and food and water consumption were significantly reduced at the high dose throughout the treatment period. No treatment-related ocular effects were recorded. Significant increases in urine volume in high-dose females were noted in months 3-18 coinciding with decreased specific gravity that may have been treatment-related. Changes in absolute and relative organ weights were not corroborated by gross pathological or histopathological findings. Gross pathology findings were unremarkable. Vacuolation of the ependymal cells of the choroid plexus of the brain in essentially all high-dose animals at both sacrifice times. NOAEL: 1994 ppm active ingredient (equivalent to 84 mg/kg bw/day in males and 112 mg/kg bw/day in females). There was no evidence of a treatment-related carcinogenic effect. The NOEL for carcinogenicity is 15949 ppm active ingredient (equivalent to 682 mg/kg bw/day in males and 871 mg/kg bw/day in females).	Anonymous; 1998; M-183340-01-1

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results	Reference
		The mortality rate at the terminal sacrifice exceeded 50% in males in the low dose group (65%) and in females in the low-dose, mid-dose and control groups (67 – 71%). The validity of the negative toxicological findings in these groups is therefore questionable. However, in control and high-dose males, where acceptable survival rates were achieved by week 104, there was no obvious increase in the incidence of neoplasia. Similarly, this was not observed between control and high-dose females; even though the survival rate among high-dose females was effectively double that of control females. On this basis, the negative oncogenicity findings of this study are considered acceptable Addendum by Jackson, C.M. and Millar, P.M., 1999, on vacuolation of choroid plexus ependymal cells in rats from a chronic toxicity and oncogenicity study. It was concluded that the observed vacuolation was likely the result of a species-specific localised effect on fluid homeostasis, i.e. accumulation of excess intracellular fluid. The authors conclude that the observed vacuolation of the choroid plexus ependymal cells is insignificant in terms of human health hazard because (a) it was recorded at very high doses in rats during chronic exposures, (b) it was not recorded in the mouse or dog or 90-day studies in rats, (c) it was not associated with other histopathological findings in the brain or perturbations in behaviour and (d) it is highly unlikely that human exposure will occur at such high and prolonged levels. However, in a 2-year oral rat study (Blair, 2001), the incidence of vacuolation of the choroid plexus at the low doses of 150 mg/kg bw/day (males) and 155 mg/kg	

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results	Reference
		bw/day (females) was 90% and 82%, respectively. This finding was also made in 28-day gavage and 28-day dietary studies in rats (both 1997), a 90-day dietary study in rats (2001) and a 28-day dermal study in rats (2002). While an association with treatment could not be established, nonetheless vacuolation of the choroid plexus was recorded in mice in 2 control females and 3 high-dose males. While such vacuolation was not recorded in dogs, the claim of species-specificity has not been substantiated by investigations in other species such as non-human primates. Therefore, vacuolation of the choroid plexus is considered significant for human health risk assessment purposes.	
Two year oral (dietary) com-bined chronic toxicity and oncogenicity study in rats with Proplant®. Guideline: US EPA OPPTS Guideline 870.4300 Deviations from currently accepted guidelines: Based on OECD Guideline 453 "Combined chronic toxicity / carcinogenicity studies", the following deviations were identified:- • A haematological evaluation was conducted, as per Guideline OPPTS 870.4300 recommendations, on blood sampled during weeks 27, 52, 78 and 104 (sampling at 13 weeks is dependent on the outcome of subchronic studies). However, OECD guideline 453 also recommends sampling at week 13. GLP: Yes. Compliant with GLP standards of US EPA FIFRA, OECD, EU and MAFF (Japan). Rat, Fischer CDF®(F-344) CrlBr 50/sex/dose and 20/sex/dose for interim necropsy Reliability: 2	Proplant® 722 g/l (aquaeous formulation; 651 g/kg) 0, 2000, 5000, 12500, 15000 (interim sacrifice) ppm Equivalent to 0, 150, 368, 989, 1098 mg/kg bw/day in males and 0, 155, 392, 1022, 1195 mg/kg bw/day in females.	A NOAEL for chronic toxicity was not possible due to treatment-related histopathological findings in all treated groups (Vacuolar change, choroid plexus & lacrimal gland). The NOEL for carcinogenicity was 368 mg/kg bw/day,.	Anonymous; 2001; M-310604-01-1

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results	Reference
(Klimisch score)			
52-week oral dietary toxicity study with Proplant in Wistar ratseGuideline: EEC Directive 88302/EEC (1988); OECD No. 452, US EPA OPPTS 870.4100 (1998) DDeviations from currently accepted guidelines: Based on OECD Guideline 452 "Chronic toxicity studies", the following deviations were identified:-OECD Guideline 452 recommends replacing food at least weekly when rodents are used as the test animals. Although not entirely clear from the context of the report, it would appear that the food was replaced every two weeks during this study. A number of other protocol deviations were documented in this report. These were due to error variance and were of a nature and magnitude that were not considered to have adversely affected the integrity of the study. GLP: Yes. Compliant with GLP standards of US EPA FIFRA & TSCA and the OECD. Rat, Wistar Han, outbred, SPF quality 20/sex/dose Reliability: 2 (Klimisch score)	Propamocarb HCL 722 g/l 750.5 g/l (aqueous formulation; 691 g/kg) 0, 375, 1500, 6000 ppm (0, 21,84, 365 (m)/ 0, 29, 114, 476 (f) mg/kg bw)	Based on the incidence of vacuolation of the choroid plexus and of the lacrimal gland ducts in both sexes at the high dose and vacuolation of the choroid plexus in mid-dose females, an active ingredient NOEL of 375 ppm (29 mg/kg bw/day) is established for females The active ingredient NOEL for carcinogenicity was 6000 ppm (356 mg/kg bw/day in males and 476 mg/kg bw/day in female).	Anonymous; 2002; M-310609-01-1
Potential tumorigenicity to mice in dietary administration for 104 weeks. No guideline Mouse, CD-1 (Charles River) 60/sex/dose	Previcur N (SN 66 752) 76.1% SN 66 752 technical (corresponding to 70.2% pure SN 66 752) 0, 20, 100 and 500 ppm corresponding	.	. Anonymous; 1983; M-157604-01-1

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results	Reference
Deviations from currently accepted guidelines: Based on OECD Guideline 451 "Carcinogenicity studies", the following deviations were identified: Blood smears were not collected at 12 and 18 months; Tissue samples from the caecum and rectum were not preserved for histopathology; Clinical and pathological data relating to several individual rats was missing (appendix 3 to the study report). GLP: No. Although the in-life phase of the study commenced prior to the issuing of GLP regulations, such regulations as set forth in Title 21 of the US Code of Federal Regulations, Part 58 were implemented during the study. Overall the study was conducted according to the principles of GLP with a signed statement to this effect. Reliability: 2 (Klimisch score)	to active ingredient doses of 0, 14, 70 and 351 ppm	Taking in consideration body weight reduction in males at top dose, the NOAEL was set at 70 ppm active ingredient (equivalent to 6.8 mg/kg bw/day in males and 7.78 mg/kg bw/day in females).	

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results	Reference
Mouse dietary oncogenicity (18 months) study Mouse, CD-1 (Charles River) 50/sex/dose **Guidelines:** OECD Guideline for testing of chemicals, Section 4, Health effects, No. 451 Carcinogenicity Studies (1981); US EPA Pesticide Assessment Guideline 83-2 Oncogenicity Studies (1984); Japan MAFF SACI 59, NohSan No.4200 Oncogenicity Study (1985) **Deviations from currently accepted guidelines:** Based on OECD Guideline 451 "Carcinogenicity studies", no deviations were identified **GLP:** Yes. Reliability 1 (Klimisch score)	Propamocarb HCl liquid concentrate 71.2% w/w 0, 0, 75, 598 and 4785 ppm active ingredient	No treatment-related clinical signs of toxicity, mortalities, ocular effects or effects on food consumption, hematology, organ weight, gross pathological or histopathological findings. Female body weight was significantly decreased at the high dose from week 66 and at the mid dose from week 69. The decreases were not biologically significant. Overall female body weight gain was reduced by 12% and 15% in the mid and high-dose groups, respectively. Male body weight gain was unaffected by treatment. There was no evidence of a treatment-related carcinogenic effect. Since the effects on body weight and body weight gain were confined to one sex, occurred in the closing stages of treatment and were biologically insignificant, the NOAEL is 4785 ppm active ingredient (equivalent to 690 mg/kg bw/day in males and 883 mg/kg bw/day in females). The NOEL is 75 ppm active ingredient (equivalent to 11 mg/kg bw/day in males and 12 mg/kg bw/day in females).	. Anonymous; 1998; M-182006-01-1
18-month oral dietary carcino-genicity study with Proplant (Propamocarb HCl 722 g/l) in CD-1 mice Guidelines: OECD No. 451 (1981); US EPA OPPTS Guide-line 870.4200 (1998) **Deviations from currently accepted guidelines:** Based on OECD Guideline 451 "Carcinogenicity studies", the following deviations were identified:- • OECD Guideline 451 recommends replacing food at least weekly when rodents are used as the test animals. Although not entirely clear from the context of the report, it would appear that the food was replaced every two weeks during this study. • A number of other protocol deviations were documented in this	Propamocarb HCl 722 g/l 750.5 g/l (aqueous formulation; 691 g/kg)	The incidence of emaciation in females was increased in the high-dose group compared to controls. Body weight in both sexes was significantly reduced at the high-dose, the magnitude of the reduction never exceeding 10% of control values. Statistically significant decreases in body weight gain were recorded in high-dose males and females. Absolute heart weight was significantly decreased in both sexes at the high dose, the decrease in males being part of a dose-response relationship. The incidences of vacuolation of the choroids plexus of the brain and the lacrimal gland were such that no association with treatment could be made. There were no treatment-related neoplastic findings. Based on vacuolation of the	Anonymous; 2003; M-310623-01-1

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results	Reference
report. These were due to error variance and were of a nature and magnitude that were not considered to have adversely affected the integrity of the study. **GLP:** Yes. Compliant with GLP standards of US EPA FIFRA & TSCA and the OECD.Mouse, CRL:CD-1(ICR)BR, outbred, SPF-quality 50/sex/dose Reliability 2 (Klimisch score)		choroid plexus in the brain in the 52-week dietary study in rats (2002), an NOAEL of 1500 ppm (84 mg/kg bw/day) is established for males and a NOEL of 375 ppm (29 mg/kg bw/day) is established for females. There were no treatment-related neoplastic findings in mice at doses up to 1014 mg/kg bw/day for 78 weeks or in rats at doses up to 476 mg/kg bw/day for 52 weeks. The NOEL for carcinogenicity in mice was 6000 ppm (790 mg/kg bw/day in males and 1014 mg/kg bw/day in female).	

Table 50: Summary table of human data on carcinogenicity

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No human data available				

Table 51: Summary table of other studies relevant for carcinogenicity

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No other data available				

10.9.1 Short summary and overall relevance of the provided information on carcinogenicity

Three 2-year oral (dietary) combined chronic toxicity and oncogenicity studies in rats from 1983, 1998 and 2001 and a 52-week oral dietary toxicity study in rats (2002), and three oral dietary carcinogenicity studies in mice, a 24-month study from 1983 and two 18-month studies from 1998 and 2003, are available. The studies from 1998 to 2003 were GLP-compliant and did not deviate substantially from current guidelines. Although the in-life phase of the studies from 1983 commenced prior to the issuing of GLP regulations, such regulations as set forth in Title 21 of the US Code of Federal Regulations, Part 58 were implemented during the study. Overall the studies were conducted according to the principles of GLP with a signed statement to this effect. The 1983 studies were not conducted to any currently recognised guidelines.

In the 104-week rat combined chronic toxicity and carcinogenicity study from 1983, there were no treatment-related effects on body weight or body weight gain, food consumption or food conversion and water intake. No treatment-related ocular effects were recorded and there were no obvious treatment-

related effects on haematological, clinical biochemistry or urinalysis measurements. Organ weights were unaffected by treatment.

There were no remarkable macroscopic findings in males while in females a dose-dependent increase in the incidence of pale areas in the liver and enlarged haemorrhagic foci in the pituitary was of doubtful toxicological significance. Non-neoplastic histopathological findings were unremarkable. The NOAEL was 1000 ppm test material (equivalent to 36.5 mg/kg bw/day in males and 45.4 mg/kg bw/day in females). This corresponds to 702 ppm active ingredient (equivalent to 25.6 mg/kg bw/day in males and 31.9 mg/kg bw/day in females). The incidence of mammary gland fibro-adenoma in terminal sacrifice females was increased at the mid and high doses compared to controls. The frequencies were within the normal range for Charles River Sprague-Dawley female rats. This was a pre-guideline study and consequently a number of deviations from current guidelines were identified, e.g. the mortality rate exceeded 50% by 24-months ranging from 43 – 70 % (mean 58 %). In addition, the incidence of viral sialodacryo-adenitis was very high, especially in males with two distinct outbreaks during the course of the study. Therefore, this study is considered to be supplemental, but the negative oncogenicity findings of this study can be considered acceptable.

In the 104 week rat combined chronic toxicity and carcinogenicity study from 1998, no treatment-related effect on mortality occurred with the highest survival rates recorded at the high dose. Male and female body weight, body weight gain and food and water consumption were significantly reduced at the high dose throughout the treatment period. Body weight and body weight gain were also reduced in the mid-dose groups, though statistical and biological significance was not achieved. No treatment-related ocular effects were recorded. There is insufficient evidence of a treatment-related effect on hematological or clinical chemistry parameters. Increases in urine volume in high-dose females were recorded on months 3-18 coinciding with decreased specific gravity that may have been treatment-related. Perturbations in absolute and relative organ weights were not corroborated by gross pathological or histopathological findings. Gross pathology findings were unremarkable. Vacuolation of the ependymal cells of the choroid plexus of the brain was recorded in essentially all high-dose animals at both sacrifice times. The NOAEL was 1994 ppm active ingredient (equivalent to 84 mg/kg bw/day in males and 112 mg/kg bw/day in females). There was no evidence of a treatment-related carcinogenic effect. The NOEL for carcinogenicity is 15949 ppm active ingredient (equivalent to 682 mg/kg bw/day in males and 871 mg/kg bw/day in females).

A re-evaluation of choroid plexus cellular vacuolation led to the conclusion that this phenomenon could be due to either phospholipidosis or a direct localised effect on fluid homeostasis. However, staining of the choroid plexus for neutral fat (Sudan Black) or lipoprotein (Periodic Schiff) were negative in samples from control and high dose males while staining with Toluidine Blue did not indicate the presence of material within the ependymal cells. Vacuolation was not recorded in other tissues and no other histopathological findings were documented in the central nervous tissue or the ciliary body of the eye which is related to the choroid plexus. Since phospholipidosis stains strongly positive with Periodic Schiff stain, it was concluded that the observed vacuolation was likely the result of a species-specific localised effect on fluid homeostasis, i.e. accumulation of excess intracellular fluid.

In the 2001 study, the mortality rate did not differ significantly between control and treated groups. A number of non-specific clinical signs were increased in high-dose groups in terms of the total occurrence and the number of animals affected. These were considered to be indicative of a treatment effect. There was evidence of jaundice in high-dose females. The number of palpable masses did not differ significantly between each dose group. However, a dose-related increase in the proportion of masses that were hard was recorded in males.

Statistically significant reductions in body weight were recorded in both sexes in all treatment groups throughout the study. Toxicological significance (body weight decrease ≥ 10% of control) was achieved at the high dose and occasionally at the mid dose. Reductions in mean body weight at the low dose never exceeded 7% of control values. Reductions were also recorded in cumulative body weight gain, the magnitude of the reductions increasing, and the time of onset decreasing, with increasing dose. Statistically significant reductions in food consumption of up to 17% and 20% were recorded in high-dose males and females, respectively. Statistically significant reductions were also recorded at the mid dose during most periods and occasionally at the low dose. Increases in water consumption were recorded in mid- and high-dose males that occasionally reached statistical significance.

There was no indication of a test material-related ocular effect. Hematological findings were not considered to be toxicologically significant. Notable clinical biochemistry findings include increases in alkaline phosphatase and γ-glutamyl transpeptidase activities in high dose females that occasionally exceeded the historical control range. The increases on week 52 are indicative of hepatobiliary toxicity and coincide with decreased albumin, cholesterol and increased bilirubin. Evidence of jaundice was recorded in high-dose females while icterus was recorded in high-dose females found dead or prematurely sacrificed, but not at scheduled termination. Blood creatinine levels and creatine kinase activity were significantly reduced in high-dose males during week 104. This may be indicative of muscle wasting which could be a consequence of the decreased body weight and food consumption in high-dose males. Statistically significant increases in blood urea nitrogen and phosphorous in high-dose females were occasionally outside historical controls. While in conjunction with increased urine volume and the effects on alkaline phosphatase activity, these findings are indicative of kidney perturbations, no effects on plasma creatinine levels were recorded and there were no histopathological correlates.

The statistically significant differences in absolute and relative organ weights may have been related to the decreases in mean body weight and consequently were not considered to be toxicologically significant. Numerous gross pathological findings were reported, especially at the high dose. These were, for the most part, unremarkable. Many were consistent with findings commonly observed in aging rats. An increased incidence of icterus was recorded in females found dead or prematurely sacrificed which reflects the clinical signs of jaundice recorded. Body fat depletion in high-dose males may be a consequence of the decrease in

body weight while the incidence of ‘thin and watery blood’ was not corroborated by any haematological findings.

The principle non-neoplastic histopathological finding was a substantially increased incidence of intracytoplasmic vacuolation in the epithelial cells lining the choroid plexus of the brain and also the parenchyma of the lacrimal gland ducts in both sexes in all treated groups. The severity of the finding increased with dose. These observations were not corroborated by other findings, especially no neurological abnormalities were observed as consequence of the choroid plexus findings.

Peto analysis of control and high-dose groups identified statistically significant positive dose-responses for fatal/possibly fatal mononuclear cell leukaemias in the female haemolymphoreticular system ($p = 0.04$; table B.6.5.1-22). The significance of this finding was increased when the results for mononuclear cell leukaemias were pooled across the prevalence (animals with leukaemia but undetermined cause of death; $p = 0.03$) and death-rate analyses (includes animals with this tumour; $p = 0.04$).

The data were compared to spontaneous neoplasm rates determined for control F344 rats from two-year carcinogenicity studies carried out by the National Toxicology Program (NTP). Leukaemia is quite prevalent in aging rats. The incidence of mononuclear cell leukemia in untreated male and female F344 rats was 50.5% and 28.1%, respectively with a range of 32-74% and 14-52%, respectively. This compares with a control group incidence of 22% and a high-dose group incidence of 38% in the present study. However, the animals in the studies investigated in the NTP report were maintained on an NIH07 diet and were from sources other than the Charles River facility used in this study. The NTP report also suggests a link between body weight and tumour incidence in the F344 rat and clearly states that any meaningful utilization of the historical control database is dependent on the similarity with the body weight of control rats in a given study. However, the termination body weights for male and female rats investigated in the NTP database were 476 ± 19 and 343 ± 16 grams, respectively (mean ± SD). This compares with final control group body weights of 377 and 269 grams, respectively in this study. The NTP database contains information from studies conducted over a 7-year period. The SLI historical control incidence of mononuclear cell leukaemia is 69/265 animals or 26% (range 21-32%) for males and 56/265 animals or 21% (range 9-29%) for females. Therefore, the high-dose incidence of 38% in female rats in this study is far in excess of the historical control range maximum. The incidence of kidney neoplasms in males was 1/49, 0/50, 0/50 and 3/50 at 0, 150, 368 and 989 mg/kg bw/day, respectively. Peto analysis identified a statistically significant positive dose-response in this trend when control and all treated groups were compared ($p = 0.03$) although pair-wise comparisons were different from control. Statistical significance was lost when adenomas (4% incidence) and carcinomas (2% incidence) were analysed separately. On this basis, the notifier considered the findings to be toxicologically insignificant. However, the SLI historical control incidences given for kidney carcinoma

and adenoma in males were 1/90 animals (range 1.11-1.11%) and 1/175 animals (range 0-1.82%), respectively. Therefore, historical control incidences have been exceeded.

For females, Peto analysis of control and high-dose groups identified statistically significant positive dose-responses for fatal/possibly fatal mononuclear cell leukaemias in the female haemolymphoreticular system. Leukemias are not regarded as organ specific and, thus, are counted for the entire animal. Leukemias are very common in female F-344 rats with a mean incidence of 28 % and a range up to 52 % (Hasemann et al., 1998, see above). The incidence in the highest dose group of 38 % was within the range of the aforementioned published historical control incidence rates. Therefore, no toxicological significance was attributed to the statistical difference in the incidence of leukemias in the female rats. A NOAEL for chronic toxicity was not possible due to the histopathological findings in the choroid plexus in all treated groups. The NOEL for carcinogenicity was 368 mg/kg bw/day, active ingredient.

In the 52-week rat study from 2002, no treatment-related adverse ocular effects or significant effects on body weight or food consumption were observed. The incidence of alopecia was significantly increased in high-dose females only. The reduction in APTT in males at weeks 26 and 52 coincided with an increased resorption of calcium. While this is indicative of a possible perturbation in plasma calcium homeostasis, it is not substantiated by the clinical biochemistry data which recorded a very slight reduction in plasma calcium on week 13 only that was not associated with perturbations in total protein, inorganic phosphate, albumin or globulin levels. The increase in leukocyte count in high-dose males on weeks 13 and 52 were not recorded during week 26. Similarly, decreases in mid- and high-dose female haemoglobin concentration and haematocrit were recorded during week 13 only. The increase in alkaline phosphatase activity with dose in males on weeks 13 and 52 did not achieve statistical significance and was not recorded on week 26. The decrease in alanine aminotransferase and aspartate aminotransferase activities on week 52 was not substantiated by perturbations in other clinical biochemistry measurements and may have been artefactual. Whole brain cholinesterase activity was not affected by treatment. The decrease in urine electrolyte concentrations in males at 52 weeks possibly reflects increased absorption in the kidney. This coincided (at the high dose) with an increase in relative kidney weight. The toxicological significance of this is unknown. The decrease in absolute liver weight in females was not corroborated by histopathological findings while the increase in relative brain weight and was attributed to decreasing body weight at the mid and high dose.

Vacuolation of the choroid plexus was recorded in both sexes at the high dose and in mid dose females. The lesions were mostly moderate in nature with no evidence of epithelial cell degeneration. Vacuolation of the lacrimal gland ducts was recorded in both sexes at the high dose, especially in females. The vacuolation was mostly minimal in intensity and there was no evidence of epithelial cell degeneration.

There was no evidence of an oncogenic potential for the test material.

Based on the incidence of vacuolation of the choroid plexus and of the lacrimal gland ducts in both sexes at the high dose and vacuolation of the choroid plexus in mid-dose females, an active ingredient NOEL of 375 ppm (29 mg/kg bw/day) is established for females and an active ingredient NOAEL of 1500 ppm (84 mg/kg bw/day) is established for males. The active ingredient NOEL for carcinogenicity was 6000 ppm (356 mg/kg bw/day in males and 476 mg/kg bw/day in females).

In a 104-week mouse oncogenicity study, there were no treatment-related clinical signs of toxicity, mortalities, gross pathological findings, histopathological findings or effects on body weight, body weight gain, food consumption and food efficiency. There was no evidence of vacuolation in the brain or a treatment-related carcinogenic effect. The NOEL was 351 ppm active ingredient (equivalent to 36.5 mg/kg bw/day in males and 37.9 mg/kg bw/day in females).

In a 18-month mouse oncogenicity study, no treatment-related clinical signs of toxicity, mortalities, ocular effects or effects on food consumption, haematology, organ weight, gross pathological or histopathological findings were noted. Female body weight was significantly decreased at the high dose from week 66 and at the mid dose from week 69. The decreases were not biologically significant. Overall female body weight gain was reduced by 12% and 15% in the mid and high-dose groups, respectively. Male body weight gain was unaffected by treatment. There was no evidence of a treatment-related carcinogenic effect. Since the effects on body weight and body weight gain were confined to one sex, occurred in the closing stages of treatment and were biologically insignificant, the NOAEL is 4785 ppm

active ingredient (equivalent to 690 mg/kg bw/day in males and 883 mg/kg bw/day in females). The NOEL is 75 ppm active ingredient (equivalent to 11 mg/kg bw/day in males and 12 mg/kg bw/day in females).

In another 18-month mouse oncogenicity study, the incidence of emaciation in females was increased in the high-dose group compared to controls. Body weight in both sexes was significantly reduced at the high-dose, the magnitude of the reduction never exceeding 10 % of control values. Statistically significant decreases in body weight gain were recorded in high-dose males and females. Absolute heart weight was significantly decreased in both sexes at the high dose, the decrease in males being part of a dose-response relationship. Absolute kidney weight was also significantly decreased in high-dose females and in all male dose groups with a dose-relationship evident in males. In the absence of relevant historical control reference ranges and a clinical biochemistry evaluation, it was impossible to ascertain the significance of the perturbations in kidney weight. However, it should be noted that these findings were not corroborated by histopathological results. The incidences of vacuolation of the choroids plexus of the brain and the lacrimal gland were such that no association with treatment could be made. There were no treatment-related neoplastic findings.

Based on statistically significant decreases in body weight in both sexes at the high dose throughout most of the treatment period, a NOAEL of 840 ppm (106 mg/kg bw/day for males and 136 mg/kg bw/day for females) is established. Based on the absence of treatment-related neoplastic findings, a NOEL for carcinogenicity of 6000 ppm (790 mg/kg bw/day in males and 1014 mg/kg bw/day in female) is established.

Table 52: Compilation of factors to be taken into consideration in the hazard assessment

Species and strain	Tumour type and background incidence	Multi-site respon-ses	Progression of lesions to malignancy	Reduced tumour latency	Responses in single or both sexes	Confounding effect by excessive toxicity?	Route of exposure	MoA and relevance to humans
Rat, Sprague-Dawley	Mammary fibro-adenomas, adenomas and adenocarcinomas, not dose-related and within historical background incidences	No	Background-related incidence of benign and malignant tumors	No	Only females, no increased tumor incidences in males	No	Oral via diet	Normal strain- and age-related tumor oc-currence, not relevant to humans
Rat, Fischer CDF® (F-344) CrlBr	Mononuclear cell leukaemias in the female haemo-lymphoreticular system	Not organ specific, counted for the entire animal	Background-related incidence of benign and malignant tumors	No	Only females	High dose exceeded MTD	Oral via diet	Strain- and age-related tumor occurrence not relevant to humans
Rat, Fischer CDF®(F-344) CrlBr	Kidney neo-plasms in male rats: incidence in the current study within the range of published historical inci-dences for this strain and age (Haseman, et al, 1998)	No	Background-related incidence of benign and malignant tumors	No	Only males	High dose exceeded MTD	Oral via diet	Strain- and age-related tumor occurrence not relevant to humans

Species and strain	Tumour type and background incidence	Multi-site respon-ses	Progression of lesions to malignancy	Reduced tumour latency	Responses in single or both sexes	Confounding effect by excessive toxicity?	Route of exposure	MoA and relevance to humans
Mouse	No treatment-related increase of tumor incidences	-	-	-	-	-	-	-

10.9.2 Comparison with the CLP criteria

Propamocarb hydrochloride was extensively tested for a tumorigenic and carcinogenic potential. High dose levels of up to 22400 ppm of Propamocarb hydrochloride were used. At 22400 ppm body weight and body weight gain, food intake in both sexes and water intake in females were reduced. Incidences of vacuolation of the choroid plexus ependymal cells were increased in both sexes. In mice only body weight and food intake effects were observed. In these studies no compound-related deaths, major functional changes in the central or peripheral nervous system or in other organs, consistent changes in clinical biochemistry, hematology or urinalysis parameters that indicate severe organ dysfunction or severe organ damage noted in microscopic examination following autopsy were seen. The discussed mononuclear cell leukaemias in the female haemolymphoreticular system and kidney neoplasms in male rats at a dose beyond MTD are within historical control ranges and not treatment-related, therefore, no evidence of a tumorigenic or carcinogenic potential was evident in these studies with propamocarb hydrochloride.

10.9.3 Conclusion on classification and labelling for carcinogenicity

Propamocarb hydrochloride was extensively tested for a tumorigenic and carcinogenic potential. High dose levels of up to 22400 ppm of Propamocarb hydrochloride were used. Most importantly, no evidence of a tumorigenic or carcinogenic potential was evident in the studies. Therefore, the study results are conclusive and no carcinogenicity classification is justified.

10.10 Reproductive toxicity

10.10.1 Adverse effects on sexual function and fertility

Table 53: Summary table of animal studies on adverse effects on sexual function and fertility

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results	Reference
Rat Dietary Two-Generation Reproductive Toxicity Study Guidelines: USEPA (EPA) OPPTS 870.3800 (draft 1996). OECD 416 (1983). JMAFF NohSan no. 4200 (1985) Deviations: None GLP: Yes	Propamocarb Hydrochloride Liquid Concentrate 780g/L. 71.1% (100% pure for dose calculations) 0, 200, 1250, 8000 ppm	Parental =↓ in F_0, ♀ body weight and food consumption Reproductive = ↑ in gestation length, not relevant Development =↓ in ♂, ♀& mean pup weight in F_1 & F_2 offspring D14 & 21 lactation	Anonymous; 1998; M-183560-02-1

Method, guideline, deviations if any, species, strain, sex, no/group	**Test substance, dose levels duration of exposure**	**Results**	**Reference**
Rat, Sprague Dawley CRL: CD (SD) BR 30,sex/dose (F0 & F1) Reliability 1 (Klimisch score)			
Two-Generation Reproduction Toxicity Study in Rats with Proplant Guidelines: OECD guideline 416 (rev. draft 1999); US-EPA OPPTS 870.3800 (1998) Deviations: None GLP: Yes Rat, Sprague- Dawley CRL: CD (SD) IGS BR 28/sex/dose (F0, F1) Reliability 1 (Klimisch score)	Proplant, purity: 75.05% 0, 50, 200, 1000 mg/kg bw/day orally by gavage.	↓ in F0, F1 ♀ body weight gain ↓ food consumption in F0 ♀ , F1 ♂ Specific vacuolar changes in epithelial cells of the choroid plexus in F0, F1 ♂♀ ↓ Sperm concentration & count in F1 ♂epididymis ↓ F1 offspring pup Viability, mean pup weight and body weight at ♀ vaginal opening ↓ F2 pup viability	. Anonymous; 2002; M-310681-01-1

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results	Reference
See studies under 10.9 (carcinogenicity) and 10.12 (STOT-RE)	See 10.9 and 10.12	In other short- and long-term studies no evidence of a treatment-related effect on sperm parameters as would be indicated by histopathology or testes organ weight changes.	See 10.9 and 10.12

Table 54: Summary table of human data on adverse effects on sexual function and fertility

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No human data available				

Table 55: Summary table of other studies relevant for toxicity on sexual function and fertility

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No other data available				

10.10.2 Short summary and overall relevance of the provided information on adverse effects on sexual function and fertility

Propamocarb **hydrochloride** was tested in two reproduction toxicity studies. In a two-generation reproduction study, Sprague Dawley CD rats were exposed to dietary concentrations of 0, 200, 1250 and 8000 ppm of Propamocarb hydrochloride liquid concentrate. At 8000 ppm body weight gain and feed intake were reduced in the first (F0) generation in females. In the F1 generation, body weights of both sexes and feed intake in females during the pre-breeding, gestation and lactation periods were reduced at 8000 ppm. No other treatment-related effects, especially no effects on reproduction parameters were seen. The NOAEL for both, parental and developmental toxicity, was 1250 ppm of the liquid concentrate, corresponding to mean intakes of 58 and 90 mg/kg bw/day in males and females, respectively. The NOAEL for reproductive toxicity was 8000 ppm equivalent to 366.2 and 568.8 mg of propamocarb hydrochloride/kg bw/day for males and females, respectively.

In another two-generation reproduction study Sprague-Dawley rats were administered doses of 0, 50, 200 and 1000 mg/kg bw/day by gavage. Reduced body weight gains and food consumption, reduced survival, clinical signs and vacuolar changes in the epithelial cells of the choroid plexus were seen at ≥ 200 mg/kg bw. Only at the highest dose of 1000 mg/kg bw/day, changes in sperm parameters and decreased survival in F1 pups during lactation were noted. At this dose also a slightly decreased copulation index for F1 females was seen, with slight effects on this parameter also at 200 mg/kg bw. Therefore, the parental NOAEL was 50 mg/kg bw/day, equivalent to 37.5 mg active ingredient/kg bw/day. The reproductive NOAEL was 200 mg/kg bw/day, equivalent to 150.1 mg active/ ingredient/kg bw/day. The developmental NOAEL was 200 mg/kg bw/day, equivalent to 150.1 mg active ingredient/kg bw/day based on decreased pup viability at 1000 mg/kg bw/day.

This is discussed in detail in a position paper by J. Fowles M-256378-01-1). .

The changes in sperm parameters occurred only at the highest dose of 1000 mg/kg bw which caused severe clinical signs and distinct body weight and feed intake effects. Therefore, the sperm parameter changes are clearly the consequence of the general parental toxicity. Most importantly, the relevant reproduction parameters, like mating, female and male fertility index, did not show any impairment in any generation, even not at the highest dose. This shows that an evaluation of isolated sperm parameters is not reasonable, but that the male reproductive parameters have to be interpreted collectively, using a weight of evidence approach as recommended by USEPA and ECETOC (EPA, 1996 cited by ECETOC, 2002). Furthermore, the 2nd reproduction toxicity study did not confirm these sperm findings. Therefore, overall, based on the results of the two reproduction studies together, a classification is not justified.

Furthermore, no evidence of an effect of sperm parameters, testicular weight changes or other changes which are indicative of an effect on the male endocrine system were noted in the short- and long-term studies

10.10.3 Comparison with the CLP criteria

According to the CLP criteria, reproductive toxicity includes adverse effects on sexual function and fertility in adult males and females, as well as developmental toxicity in the offspring. The definitions presented in the CLP criteria are adapted from those agreed as working definitions in IPCS/EHC Document N°225, Principles for Evaluating Health Risks to Reproduction Associated with Exposure to Chemicals. In this classification system, reproductive toxicity is subdivided under two main headings:

- Adverse effects on sexual function and fertility;

- Adverse effects on development of the offspring.

Some reproductive toxic effects cannot be clearly assigned to either impairment of sexual function and fertility or to developmental toxicity. According to the CLP criteria, a ‘Suspected human reproductive toxicant’ is a substance which is classified in Category 2 for reproductive toxicity when there is some evidence from humans or experimental animals, possibly supplemented with other information, of an adverse effect on sexual function and fertility, or on development, and where the evidence is not sufficiently convincing to place the substance in Category 1. If deficiencies in the study make the quality of evidence less convincing, Category 2 could be the more appropriate classification.

Such effects shall have been observed in the absence of other toxic effects, or if occurring together with other toxic effects the adverse effect on reproduction is considered not to be a secondary non-specific consequence of the other toxic effects.

In one of the 2-generation rat studies parental toxicity occurred but no treatment-related effect on reproduction parameters.

In the other two-generation reproduction study, reduced body weight gains and food consumption, clinical signs and vacuolar changes in the epithelial cells of the choroid plexus were seen at ≥ 200 mg/kg bw. The changes in sperm parameters occurred only at the highest dose of 1000 mg/kg bw which caused severe clinical signs, reduced survival and distinct body weight and feed intake effects. Therefore, the sperm parameter changes are clearly the consequence of the severe parental toxicity and thus does not fulfil the CLP criterium of “Such effects shall have been observed in the absence of other toxic effects, or if occurring together with other toxic effects the adverse effect on reproduction is considered not to be a secondary non-specific consequence of the other toxic effects”.

Most importantly, the relevant reproduction parameters, like female and male fertility index, did not show any impairment in any generation, even not at the highest dose. Furthermore, the first reproduction toxicity study did not confirm these sperm findings. In addition, effects on sperm parameters were not seen in other short- and long-term studies with even higher doses and longer treatment durations.

Therefore, overall, based on the results of the two reproduction studies together, a classification is not justified. Therefore, the existing data for propamocarb hydrochloride are conclusive but do not warrant classification for adverse effects on sexual function and fertility

10.10.4 Adverse effects on development

Table 56: Summary table of animal studies on adverse effects on development

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results	Reference
Embryotoxicity including teratogenicity study in rats after daily intragastrical administration from Day 6 to Day 19 of gestation Guidelines: OECD, 1981 (C(81)30(Final)); USEPA (EPA) 83.3 (1978); JMAFF, 1984 **Deviations:** Dosing should be from Day 5, in this study dosing commenced on Day 6. Bodyweight should be conducted every 3 days from dosing, Body weight gain should be recorded every 3 day intervals. No food consumption measurements given. Food consumption should be measured every 3 days intervals to coincide with body weight measurements. Gravid uterus not weighed.	Previcur N (CP 604) 68% w/w Propamocarb HCL (ZK 66.752) 0, 68, 204, 680 or 2040 mg/kg bw Gestation days 6 - 19	The compound was maternally lethal and toxic, as evidenced by clinical signs, dam mortality rates greater than 10 %, markedly reduced (> 10%) body weight and body weight gain, decrease in the number of live foetuses and statistically significant increase in foetal deaths. It was also toxic to the embryofoetus causing an increased incidence of resorptions, reduced mean fetal weight and an increased incidence of variations such as retarded skeletal ossification and additional 14th ribs. Also at 680 mg/kg bw/day a slight body weight effect was seen, it was maternally lethal and embryofoetally toxic as evidenced by increased incidences of dead foetuses and retarded ossification and a statistically significant increase in the incidence of additional 14th rib. (NOAEL) for maternal toxicity: 204 mg/kg bw/day (corresponding to 1.0 mL of Previcur N/kg bw) NOAEL for developmental toxicity: 68 mg/kg bw propamocarb hydrochloride (corresponding to 0.1 mL of Previcur N/kg bw) propamocarb hydrochloride/kg (not corrected for density).	Anonymous; 1990; M-157608-02-1

Method, guideline, deviations if any, species, strain, sex, no/group	**Test substance, dose levels duration of exposure**	**Results**	**Reference**
GLP: Yes (Germany) Rat, Female Wistar Han Schering rats 25 females/dose group Reliability 2 (Klimisch score)			

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results	Reference
Embryotoxicity and terato-genicity study by dietary adminis-tration in female Wistar rats Guidelines: Dir. 87/302/ EEC, Annex V, part B (1988); OECD guideline 414 (1981); USEPA OPPTS 870.3700 (1998) Deviations: None GLP: Yes Rat, female Wistar rats Crl: (WI) BR (outbred, SPF-Quality) 24 females/dose Reliability 1 (Klimisch score)	Propamocarb HCL 691 g/kg (Corresponding to 750.5 g/L) Dietary: 0, 375, 1500, 6000 ppm (corresponding to 0, 31, 123 and 456 mg/kg body weight per day Gestation days 6 - 21	Maternal toxicity at 6000 ppm propamocarb consisted of a reduced body weight, body weight gain, corrected body weight gain, food consumption and relative food consumption during the treatment period. Foetal toxicity in 6000 ppm group consisted of reduced foetal weights and an increased incidence of small foetuses. Developmental effects at maternal-toxic dose: decreased foetal body weights, increased number of small foetuses and generalised retardation in ossification in foetuses. At 375 ppm and 1500 ppm, ossification parameters were essentially similar to those of the controls. Maternal and developmental NOAEL: 1500 ppm (123 mg substance/kg body weight/day) Reproductive NOAEL: 6000 ppm (456 mg substance/kg body weight/day).	Anonymous; 2001; M-310689-01-1
Embryotoxicity including teratogenicity study in rabbits after daily intragastrical administration from Day 6 to Day 18 of gestation Guidelines: Not stated but compliant with OECD guideline 414 (1981) and USEPA (EPA) 83-3 (1984)	Previcur N (CP 604) 0, 0.02, 0.06, 0.2, 0.4 or 0.8 ml/kg bw of Previcur N (equivalent to 0, 14, 42, 140, 280 or 560 mg/kg bw propamocarb hydrochloride (not corrected for density) Gestation days 6 - 18	Maternal toxicity at 560 mg/kg bw/day (equivalent 3.0 mL/kg of Previcur N), as evidenced by statistically significant markedly reduced (>10%) body weight gain compared to control animals. Up to 560 mg/kg bw/day (equivalent 3.0 mL/kg of Previcur N) no teratogenicity in pregnant rabbits. Increases in the incidence of post-implantation loss (due to increased resorptions at 560 mg/kg bw) and an increased trend in the incidence of variations such as additional 13th rib. Variations such as an additional 13th rib are reversible and secondary to maternal toxicity at 560 mg/kg bw/day. Thus, the foetal effects observed in this study occurred only at maternally toxic doses and are thus secondary. NOAEL: 280 mg/kg bw propamocarb hydrochloride.	. Anonymous; 1990; M-157597-02-1

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results	Reference
Deviations: Different animal strain used for preliminary study. Body weight should be recorded every 3 days from dosing. Body weight gain should be recorded every 3 day intervals. No food consumption measurements given. Food consumption should be measured every 3 days intervals to coincide with body weight measurements Rabbit, New Zealand White Rabbits 18-22 females/dose group Reliability 2 (Klimisch score)			

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, dose levels duration of exposure	Results	Reference
Embryotoxicity and terato-genicity study by dietary administration in female albino NZW rabbits Guidelines: Dir. 87/302/ EEC, Annex V, part B (1988); OECD 414 (1981); EPA-OPPTS 870.3700 (1998) Deviations: Temperature, outside guidelines range. Guidelines require 20 females with implantation sites at necropsy, group 2 only 16 females. Body weight and food consumption measurements were not taken at 3-day intervals as requested in the GL. **GLP:** Yes Rabbit, Female Albino rabbits, New Zealand strain 29-32 females/ dose Reliability 2 (Klimisch score)	Proplant (propamocarb HCl 722 g/l) 691 g/kg Propamocarb HCL (corresponding to 750.5 g/L propamocarb HCL) 0, 500, 2000, 8000 ppm PROPLANT (propamocarb HCL, 722 g/l) Gestation days 6 to Day 18	Maternal toxicity at 8000 ppm with reduced body weight, body weight gain and food consumption (corrected as well as uncorrected). No fetal or reproductive toxicity at any dose level and no treatment-related teratogenicity. Maternal NOAEL: 2000 ppm propamocarb hydrochloride (76 mg propamocarb-HCl/kg body weight/day). Fetal NOAEL: 8000 ppm propamocarb-HCl formulated as Proplant, (equivalent to 269 mg propamocarb-HCl/kg bw/ day).	. Anonymous; 2001; M-310689-01-1

Table 57: Summary table of human data on adverse effects on development

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No human data available				

Table 58: Summary table of other studies relevant for developmental toxicity

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No other data available				

10.10.5 Short summary and overall relevance of the provided information on adverse effects on development

In a rat developmental toxicity study, dose levels of 0, 0.1, 0.3, 1.0 and 3.0 mL/kg/day (equivalent to 0, 68, 204, 680 and 2040 mg/kg bw/day of propamocarb hydrochloride of Previcur N) were administered by gavage to mated Wistar-Han rats between Days 0 and 19 of gestation. Maternal toxic effects were seen at 680 mg/kg bw and higher, 2040 mg/kg bw caused maternal mortalities, clinical signs, body weight loss which persisted to termination. An increased incidence of post-implantation loss (due to early resorptions) and reduction in the mean number of live foetuses, further, reduced mean foetal weight, retarded ossification and an increased incidence of additional 14th ribs were seen at 2040 mg/kg bw. At 680 mg/kg bw increased incidences of dead foetuses, retarded ossification of the sternebrae and extra 14th ribs were seen. It was concluded that Previcur N was not teratogenic in rats, but was both maternally toxic and embryotoxic at relatively high dose levels. The NOAEL for maternal and developmental toxicity was 204 mg/kg bw/day of Propamocarb hydrochloride.

Dietary treatment of pregnant female Wistar rats with the product Proplant, containing 722 g/L propamocarb hydrochloride at dose levels of 375, 1500 or 6000 ppm during gestation days 6 to 21, caused reductions in maternal body weight and food consumption and in fetal body weight. Furthermore, decreased male to female ratio and general retardation of ossification were seen at 6000 ppm. A maternal and developmental NOAEL was established at 1500 ppm, equivalent to 123 mg/kg bw/day.

Mated New Zealand White rabbits received dose levels of 0, 0.02, 0.06, 0.2, 0.4 and 0.8 mL/kg Previcur N (equivalent to 0, 14, 42, 140, 280 and 560 mg/kg bw of propamocarb hydrochloride) by gavage between Days 6 and 18 of pregnancy. Maternal toxicity occurred at the two highest dose levels with stagnating body weight and loss of weight, respectively, during the dosing period. At these high doses also post-implantation loss (mainly dead foetuses at 280 mg/kg and early resorptions at 560 mg/kg) were seen, so that propamocarb hydrochloride was embryolethal only at maternal-toxic dose levels. The NOAEL for both maternal and developmental toxicity was 140 mg/kg bw/day of propamocarb hydrochloride (0.2 mL/kg of Previcur N). No evidence of teratogenicity was seen.

Dietary treatment of pregnant female albino NZW rabbits with Proplant (722 g/L propamocarb hydrochloride) at concentrations of 500, 2000 or 8000 ppm during gestation days 6 to 27 revealed reduced maternal body weight and food intake at 8000 ppm. No fetal or reproductive toxicity was observed at these dose levels. The maternal NOAEL was established at 2000 ppm (76 mg a.i./kg bw/day), the fetal and reproductive NOAEL at 8000 ppm (269 mg a.i./kg bw/day).

A position paper is available which provides arguments against R63 (H361d) labelling of the formulations Previcur Energy (Reg. No. 18-544) and Proplant (Reg. No. 361-1) in Denmark (M-425291-01-1).

Both formulations have been classified by Denmark based on findings in developmental toxicity studies conducted with the propamocarb hydrochloride-based straight formulations Previcur N and Proplant, both containing 722 g/L propamocarb hydrochloride.

It was alleged by Denmark that propamocarb hydrochloride showed developmental toxicity in non-maternally toxic doses in two rat studies. It is stated that the first study showed an increased incidence of 14th ribs from 204 mg /kg bw/day on, while from 680 mg/kg bw/day on increased mortality in the dams and increased number of dead fetuses were seen.

The second study allegedly showed an increased incidence of small fetuses and reduced weight of these, with a NOAEL for development at 31 mg/kg bw/day.

In the first study, the incidences (in %) for additional 14th ribs were 19, 27, 42, 40 and 30 for controls, 68, 204, 680 and 2040 mg/kg bw, respectively. Therefore, from the study results no dose relationship of the increase in additional 14th ribs can be derived. In addition to this, the relevance of the findings observed at 204 mg propamocarb hydrochloride/kg bw/day has to be questioned since no additional 14th ribs were observed at 456 mg/kg bw/day in the other study in the same strain of rats with administration on day 6 to 21 p.c. with Proplant (722 g/L propamocarb hydrochloride) (Anoyimous.; 2001; M-310689-01-1).

In this second rat developmental toxicity study (Anonymous.; 2001; M-310689-01-1) with dietary treatment of pregnant female Wistar rats with Proplant (propamocarb hydrochloride 722 g/L) at dose levels of 0, 375, 1500 or 6000 ppm during Days 6 to and including 21 post-coitum (equivalent to 0, 31, 123 and 456 mg Propamocarb hydrochloride/kg bw/day), decreases in body weight and food consumption were seen at 6000 ppm. Fetal toxicity was also observed at 6000 ppm with body weight reduction, increased number of 'small fetuses', decreased male to female ratio and general retardation of ossification. No reproductive toxicity was observed at these dose levels. An overview of the mean fetal weights together with historical data is given in the following table.

Overview of fetal body weights of the rat developmental toxicity study (Anonymous.; 2001; M-310689-01-1)

Parameters	**Dose level in ppm (mg/kg bw/d)**				**Historical data on fetal body weight (g)[#] mean ± SD**
	0	375 (71)	1500 (123)	6000 (456)	
Total no. of fetuses	335	302	325	322	5429
Mean body weight ± SD	5.2 ± 0.4	5.2 ± 0.4	5.1 ± 0.4**	4.8 ± 0.5**	5.3 ± 0.51
Male fetuses	183	146	156	146	2783
Mean body weight ± SD	5.4 ± 0.3	5.3 ± 0.4	5.3 ± 0.4*	4.9 ± 0.5**	5.4 ± 0.50
Female fetuses	152	156	169	176	2646
Mean body weight ± SD	5.1 ± 0.3	5.1 ± 0.3	5.0 ± 0.4	4.8 ± 0.4**	5.2 ± 0.48

[#] from Notox B.V. in Wistar rats between 1997 and 2005

As can be seen in this table, the slight decrease in fetal weight observed at 1500 ppm on individual basis cannot be considered as toxicologically relevant because it is well within the historical data from the Laboratory Notox B.V. which provided historical data from a total of 60 projects that had run between 1997 and 2005 in their laboratory. No historical data are available for the finding "small fetus" because

this parameter is very subjective. However the data on fetal weight as objective measurement are more relevant than the subjective data on 'small fetuses'.

The historical data of these studies conducted between 1997 and 2005 at the laboratory Notox B.V. show clearly that the mean fetal body weight of Wistar rats treated at 1500 ppm in the study reported by Anonymous.; 2001; M-310689-01-1 are in the same range as fetal body weights of historical control animals.

10.10.6 Comparison with the CLP criteria

In conclusion, the discussed effects on foetuses were observed at dose levels which caused also maternal toxicity in both studies so that there is no justification for a classification.

10.10.7 Adverse effects on or via lactation

No treatment-related effects on or via lactation were seen in the multi-generation studies.

Table 59: Summary table of animal studies on effects on or via lactation

Method, guideline, deviations if any, species, strain, sex, no/group	**Test substance, dose levels duration of exposure**	**Results**	**Reference**
No special studies on lactation available	-	-	-
Two-Generation Reproduction Toxicity Study in Rats with Proplant OECD guideline 416 (rev. draft 1999); US-EPA OPPTS 870.3800 (1998) Rat, Sprague-Dawley CRL: CD (SD) IGS BR 28/sex/dose (F0, F1)	Proplant, purity: 75.05% 0, 50, 200, 1000 mg/kg bw/day orally by gavage.	F1 offspring derived from the F0 generation showed a statistical decrease in pup viability and body weight decreased pup weight at the high dose level during Day 14 - 21 lactation including at female vaginal opening. These findings occurred at the highest dose which caused signs of general toxicity so that the findings during the lactation phase are secondary to this increased general toxicity.	. Anonymous; 2002; M-310681-01-1

Table 60: Summary table of human data on effects on or via lactation

Type of data/report	**Test substance**	**Relevant information about the study (as applicable)**	**Observations**	**Reference**
No human data available				

Table 61: Summary table of other studies relevant for effects on or via lactation

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No other studies on lactation available				

10.10.8 Short summary and overall relevance of the provided information on effects on or via lactation

The only finding in the lactation phase of one of the multi-generation rat studies was a statistical decrease in pup viability and body weight decreased pup weight in F1 offspring derived from the F0 generation at the high dose level during Day 14 - 21 lactation including the weight at female vaginal opening. These findings occurred at the highest dose which caused signs of general toxicity so that the findings during the lactation phase are secondary to this increased general toxicity.

10.10.9 Comparison with the CLP criteria

The only finding in the lactation phase of one of the multi-generation rat studies occurred at the highest dose which caused signs of general toxicity so that the findings during the lactation phase are not mediated by lactation but was the consequence of this increased general toxicity. Therefore, this finding is not sufficient to warrant classification.

10.10.10 Conclusion on classification and labelling for reproductive toxicity

Based on the results of the two reproduction studies together, the existing data for propamocarb are conclusive but do not warrant a reproduction classification.

The above discussed developmental effects on foetuses were observed at dose levels which caused also maternal toxicity in the developmental toxicity studies so that there is no justification for a classification.

The only finding in the lactation phase of one of the multi-generation rat studies occurred at the highest dose which caused signs of general toxicity so that the findings during the lactation phase are secondary to this increased general toxicity. Therefore, this finding is not sufficient to warrant classification.

Thus, based on the results of the multi-generation and the developmental toxicity studies, the data are conclusive, but do not warrant a reproductive toxicity classification.

10.11 Specific target organ toxicity-single exposure

Table 62: Summary table of animal studies on STOT SE

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, route of exposure, dose levels, duration of exposure	Results	Reference
See under 10.1 – 10.3	Acute oral, dermal and inhalation toxicity studies	No specific target organ toxicity, also no narcotic effects, which would fall under any STOT-SE criteria were noted in the acute toxicity studies.	See under 10.1 – 10.3
Rat acute oral neurotoxicity study	Previcur N SL 711 g/l propamocarb	Slight generalised toxicity was demonstrated by a temporary reduction in motor activity in females alone and an increased incidence of soiled coats in both sexes, on the day of dosing only.	. Anonymous; 1993; M-157666-01-1

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, route of exposure, dose levels, duration of exposure	Results	Reference
Guidelines: USEPA (=EPA) 81-8 and 82-7 (1991) GLP: Yes Rat, Sprague-Dawley, albino CD 10/sex/dose Reliability 1 (Klimisch score)	hydrochloride 0, 28.1, 281.0 and 2813.0 mg/kg bw (equivalent to 0, 20, 200 and 2000 mg/kg bw active substance)	The no observable adverse effect level (NOAEL) for neurotoxicity was 2813 mg/kg of Previcur N SL (corresponding to 2000 mg/kg propamocarb hydrochloride/day).	
Acute Neurotoxicity Study after Single Oral Dosing of Rats Guidelines: OECD guideline 424 (1997); US-EPA OPPTS 870.6200 (1998) GLP:Yes Rat, Wistar outbred (Crl:[WI]WU BR), albino 10/sex/dose Reliability 1 (Klimisch score)	Propamocarb HCl 69.1% (750.5 g/l) 0, 20, 200 and 2000 mg/kg bw by gavage	Specific neurotoxic effects of Proplant were not observed. The reversible effects on motor activity in the high dose males and females and mid dose males and the reduced body temperature in the high dose females were considered to originate from a generalized toxic effect of the test substance rather than a neurotoxic effect. Therefore, the NOAEL for neurotoxicity was 2000 mg/kg propamocarb hydrochloride/day.	Anonymous; 2002; M-310748-01-1

Table 63: Summary table of human data on STOT SE

Type of data/report	Test substance	Route of exposure Relevant information about the study (as applicable)	Observations	Reference
No human data				

Table 64: Summary table of other studies relevant for STOT SE

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No other data for STOT-SE				

10.11.1 Short summary and overall relevance of the provided information on specific target organ toxicity – single exposure

According to the ECHA Guidance a classification in STOT-SE Category 1 and also in 2 is not applicable. Also category 2 criteria are not fulfilled if non-lethal significant and/or severe toxic effects on target tissues/organs are not seen in acute toxicity studies up to the following guidance values:

Oral rat	2000 mg/kg bw
Dermal rat or rabbit	2000 mg/kg bw
Inhalation rat, dust / mist / fume	5 mg/l/4h

Furthermore, the ECHA Guidance specifies criteria that trigger a classification for STOT-SE Category 3. These criteria are generally independent from the aforementioned guidance values and include transient target organ effects, focusing on overt narcotic effects and respiratory tract irritation (respiratory tract irritation covers two different effects: 'sensory irritation' and 'local cytotoxic effects'). Specifically, the following examples for findings from single and repeated inhalation toxicity studies are mentioned as possible triggers for a STOT-SE Category 3 classification: clinical signs of toxicity (dyspnoea, rhinitis etc.) and histopathology (e.g. hyperemia, edema, minimal inflammation, thickened mucous layer) which are reversible.

Studies which can be used to evaluate potential STOT-SE effects, were already discussed under 10.1, 10.2 and 10.3. These studies on acute oral, dermal and inhalative toxicity demonstrated a low acute toxic potential of propamocarb with LD_{50} and LC_{50} values above the classification criteria.

In addition, acute neurotoxicity studies can be evaluated on potential STOT-SE effects. In one acute neurotoxicity study in rats, only slight generalised toxicity was demonstrated by a temporary reduction in motor activity in females alone and an increased incidence of soiled coats in both sexes, on the day of dosing only. The no observable adverse effect level (NOAEL) for neurotoxicity was 2813 mg/kg bw of Previcur N SL (corresponding to 2000 mg/kg bw propamocarb hydrochloride/day). In a second acute neurotoxicity study in rats specific neurotoxic effects of Proplant were not observed. The reversible effects on motor activity in the high dose males and females and mid dose males and the reduced body temperature in the high dose females were considered to originate from a generalized toxic effect of the test substance rather than a neurotoxic effect. Narcotic effects were not observed in the studies. Therefore, the NOAEL for neurotoxicity was 2000 mg/kg bw propamocarb hydrochloride/day.

In summary, the relevant acute toxicity studies conducted with propamocarb provide the following LOAELs and toxicological effects at the respective LOAELs:

Study	LOAEL Toxicological effects at LOAEL (Reference)
Acute oral rat	2000 mg/kg bw: No clinical signs, no mortalities
Acute dermal rat	2000, 5000 mg/kg bw: No clinical signs, no mortalities
Acute inhalation rat	5.54 mg/L/4h (highest tested dose): Wet fur, hunched posture and pilo-erection were common on the day of exposure. With the exception of one female who showed hunched posture and pilo-erection on Day 1 following exposure no further abnormalities were observed
Acute oral neuro-toxicity rat	In 2 acute neurotoxicity studies no neurotoxic potential and no narcotic effect was evident, the neurotoxicity NOAELs were 2000 mg/kg bw

According to the CLP criteria, also physicochemical properties, such as pH, physical form, solubility, vapour pressure, particle size, which can be important parameters in evaluating toxicity studies and in determining the most appropriate classification especially with respect to inhalation where physical form and particle size can have a significant impact on toxicity. For propamocarb none of these parameters indicate a potential to fall under STOT-SE.

10.11.2 Comparison with the CLP criteria

A comparison of these LOAELs and toxicological effects with the aforementioned classification criteria reveals that the criteria for STOT-SE Category 2 classification are not fulfilled.

Regarding a possible STOT-SE Category 3 classification for “overt narcotic effects”, the observed toxicological findings in all relevant studies do not indicate such effects; the reduced motor activity in one of the two acute neurotoxicity studies is seen as mild expression of general toxicity and not as a neuro-pharmaco-toxicological narcotic effect. Therefore, also criteria for a STOT-SE Category 3 classification are not fulfilled.

10.11.3 Conclusion on classification and labelling for STOT SE

A comparison of these toxicological effects in acute oral, dermal and inhalation toxicity studies, furthermore of effects in acute neurotoxicity rat studies with the aforementioned classification criteria reveals that the results are conclusive and that a STOT-SE Category 2 and 3 classification is not warranted.

10.12 Specific target organ toxicity-repeated exposure

Table 65: Summary table of animal studies on STOT RE

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, route of exposure, dose levels, duration of exposure	Results	Reference

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, route of exposure, dose levels, duration of exposure	Results	Reference
Subacute systemic tolerance study in rats with dietary administration over a period of 5 weeks Guidelines: Not applicable (only preliminary and explorative study design) but the study Substantially complies with OECD Guideline 407 (1995) Deviations from OECD 407 (1995): groups of 10 males and 10 females were used whereas groups of 5 of each sex are specified; high dose level was only minimally toxic; a few biochemical parameters were not measured (eg aspartate aminotransferase and γ-glutamyl transpeptidase) and only limited histopathology was conducted. But none of these omissions affect the scientific validity of the study **GLP:** No – conducted prior to GLP Rat, Wistar-Han-Schering SPF 10/sex/dose Reliability 3 (Klimisch score)	Previcur N 70.2 % SN 66.752 technical (corresponding to 64.3% of SN 66.752 0, 50, 500, 5000 ppm , corresponding to 0, 32, 322, 3215 mg/kg bw 5 weeks	Dietary administration of 50 to 5000 ppm of Previcur N to rats for 5 weeks induced a reduction in bone marrow lymphocytes and possible effects on serum total cholesterol (decreased) and sodium concentration (increased) in both sexes. Based on the minor nature of these findings and the absence of any evidence of organ damage at any dose level, the no observable adverse effect level (NOAEL) was the highest dose level, 5000 ppm of Previcur N, equivalent to 656 mg/kg/day in males and to 714 mg/kg bw/day in females. In terms of active substance, this dietary concentration corresponded to 3215 ppm and to mean daily intakes of 422 mg/kg bw/day in males and 459 mg/kg bw/day in females of propamocarb hydrochloride.	Anonymous; 1986; M-157580-01-1

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, route of exposure, dose levels, duration of exposure	Results	Reference
28-day range-finding (dietary) toxicity study in rats Guideline: Not applicable (only preliminary and explorative study design). **GLP:** Study was not performed under GLP, but the laboratory is GLP-certified Rat, Fischer CDF® (F-344) CrlBr 5/sex/dose Reliability 3 (Klimisch score)	Proplant® 67.04 % active ingredient 0, 2,500, 5,000, 12,500, 25,000 and 50,000 ppm of Proplant (propamocarb hydrochloride 722g/l SL) 28 days	At up to and including 12,500 ppm only weak effects seen, while higher concentrations led to significant toxic effects. Based on these results, the following dose levels were recommended for the two-year study: 12,500 ppm, 6,250 ppm and 3,125 ppm. The average consumption of test item at 12,500 ppm is approximately equivalent to this dosage limit. The brain histology revealed an intracytoplasmatic vacuolation of the epithelial cells of the choroids plexus of the brain, leading to a NOEL of 2500 ppm propamocarb hydrochloride, equivalent to 172 and 185 mg/kg bw/day in males and females respectively.	. Anonymous; 1997; M-310359-01-1
Preliminary 28-day oral (gavage) dose range-finding toxicity study in rats Guideline: Not applicable (only preliminary and explorative study design). **GLP:** Study was not performed under GLP, but the laboratory is GLP-certified Rat, Fischer CDF® (F-344) CrlBr 3/sex/dose Reliability 3 (Klimisch score)	Proplant® 72.94 % active ingredient S00.001.3437) 0, 20, 40, 100, 200, 500, 1000 mg/kg bw/day by gavage	Administration of Proplant® to Fischer rats by oral gavage for a period of 28 days at doses between 200 and 1000 mg/kg bw/day resulted in dose-dependent microscopic lesions in the choroid plexus of the brain and lacrimal glands. No such effects were noted in control, 20, 40 and 100 mg/kg bw/day groups. NOAEL: 100 mg/kg bw/day (expressed in terms of the active ingredient).	Anonymous; 2000; M-310378-01-1

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, route of exposure, dose levels, duration of exposure	Results	Reference
28-days toxicity feeding study (range finding) with repetitive administration to Beagle dogs Guidelines: Not applicable - no specific guidelines exist for such non-rodent range finding studies GLP: No Dog, Pedigreed Beagle 1/sex/dose Reliability 3 (Klimisch score)	Previcur N 68.4 % Propamocarb-HCl 0, 1000, 3000, 10000 ppm 28-days	Dietary administration of 10000 ppm of Previcur N to the Beagle dog for 28 days induced gross gastric mucosal lesions. NOAEL: 3000 ppm of Previcur N, equivalent to a mean daily intake of 119 mg/kg/day. In terms of active substance, this dietary concentration corresponded to 2052 ppm of propamocarb hydrochloride, equivalent to a mean daily intake of 81 mg/kg bw/day	Anonymous; 1982; M-157633-01-1

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, route of exposure, dose levels, duration of exposure	Results	Reference
Three month sub-chronic oral toxicity study in rats Guidelines: Japanese Guideline for Pesticide Regulation, of June 14, 1972. Substantially compliant with OECD 408 (1981) Deviations: groups of 30 males and 30 females were used rather than 10/sex as specified. Any other deviations were minor and did not affect the scientific validity of this study GLP: No Rat, SPF Wistar 30/sex/dose Reliability 2 (Klimisch score)	Previcur N 66.5 % active ingredient (Propamocarb-hydrochloride) 0, 200, 1000, 5000 ppm 3 months	No mortalities occurred in Wistar rats. A slight reduction in body weight in females (6.3%) and a minor reduction in food efficiency in both sexes (3% and 5% for males and females respectively) at 5000 ppm at the end of the study period. Relative brain weight was significantly increased in males at 5000 ppm and in females at 1000 and 5000. A statistically significant increase in relative kidney weights observed in male and female rats at 5,000 ppm Previcur N. However, no corroborating histopathological changes in the brain and kidney were recorded in the study report, and all changes were within normal limits. NOEL: 5000 ppm (equivalent to mean achieved intakes of 362 mg/kg/day for males and 396 mg/kg/day for females. In terms of the active substance, 5000 ppm corresponded to 3325 ppm of propamocarb hydrochloride and to mean daily intakes of 241 mg/kg/day and 263 mg/kg bw/day for males and females, respectively.	Anonymous; 1982; M-157612-01-1

Method, guideline, deviations if any, species, strain, sex, no/group	**Test substance, route of exposure, dose levels, duration of exposure**	**Results**	**Reference**
Rat dietary 90-day toxicity range finding study Guidelines: OECD 408 (1981); USEPA FIFRA: Subdivision F Serie 83-2 (1984); JMAFF 59 NohSan no.4200 (1985). Deviations: Not all tissues preserved were examined microscopically, but, according to the Notifier, this did not compromise the scientific validity of the study. GLP: Yes Rat, Sprague-Dawley Crl CD (SD) BR 10/sex/dose Reliability 1 (Klimisch score)	Propamocarb HCl 71.2% - 71.9% w/w Propamo-carb hydro-chloride 0, 7020, 14040 and 28080 ppm of propamocarb hydrochloride liquid concen-trate (71.2%-71.9% w/w propamocarb hydrochloride) (mean achieved dose 0, 447, 908 and 1915 mg/kg bw/day in males and 0, 510, 1005 and 2176 mg/kg bw/day in females) 90 days	A dose of 28080 ppm for 13 weeks resulted in reduced body weight, body weight gain, food consumption and food efficiency, particularly in females. A marked reduction in body weight (16% less than controls) and overall bodyweight gain (62% of controls) was also seen in females given 14040 ppm. NOEL: 7020 ppm, equivalent to overall mean intakes of 447 mg/kg/day for males and 510 mg/kg/day for females. In terms of the active substance, 7020 ppm corresponds to 5000 ppm of propamocarb hydrochloride and to mean daily intakes of 318 and 363 mg /kg bw/day in males and females, respectively.	Anonymous; 1998; M-168497-01-1

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, route of exposure, dose levels, duration of exposure	Results	Reference
90-day oral dietary toxicity study in Wistar rats, followed by a 28-day recovery period Guidelines: EU Directive 87/302/EEC (1988); OECD Guideline 408 (1998); US EPA 712-C-96-199, OPPTS 870.3100 (Draft 1996). GLP: Yes Rat, Hanlbm: Wistar rat, outbred, SPF quality 10/sex/dose Reliability 1 (Klimisch score)	Propamocarb HCl 722 g/L 0, 0 (recovery), 375, 1500, 6000, 6000 (recovery) ppm	No mortalities, reduced mean body weights (females only) and body weight gains (both sexes) at 6000 ppm from week 2 onwards, with evidence of slight recovery during 4-week recovery. Clinical pathology revealed a reversible reduced excretion of urinary sodium by males in the high dose group. Histopathologically vacuolation of the choroid plexus of the brain (in all animals) and of the lacrimal glands (some animals) at the high dose level (6000 ppm) seen. These morphological changes were simple in nature and did not appear to be associated with degenerative alterations in the affected epithelia. Following the recovery period, only the choroid plexus lesion remained, albeit diminished in severity, suggesting possible partial reversibility. No significant effects occurred in animals at the two other dose levels. NOEL: 1500 ppm, equivalent to an average daily dose of 104 or 130 mg/kg bw/day for males and females respectively.	Anonymous; 2001; M-310432-01-1

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, route of exposure, dose levels, duration of exposure	Results	Reference
Mouse dietary 90-day toxicity range finding study Guidelines: OECD 408 (1981); USEPA FIFRA: Subdivision F Serie 83-2 (1984); JMAFF 59 NohSan no. 4200 (1985) Deviations: No haematology, clinical chemistry or urinalysis investigations were conducted but, according to the Notifier, this did not affect the scientific validity of the study. GLP: Yes Mouse, Crl: CD-1 (1CR) BR strain 10/sex/dose Reliability 2 (Klimisch score)	Propamocarb HCl 71.2% - 71.9% w/w propamocarb hydrochloride 0, 1404, 2808, 5616, 11232 ppm (equivalent to 0, 1000, 2000, 4000, 8000 ppm active ingredient)	Dietary administration of propamocarb hydrochloride liquid concentrate at doses up to 11232 ppm had no toxicological effect on CD-1 mice. NOEL: 11232 ppm of propamocarb hydrochloride liquid concentrate, the highest dose tested (equivalent to achieved mean daily intakes of 1895 mg/kg bw/day in males and 2742 mg/kg bw/day in females). In terms of active substance, 11232 ppm of the liquid concentrate corresponded to 8000 ppm of propamocarb hydrochloride and to mean daily intakes of 1349 mg/kg bw/day for males and 1952 mg/kg bw/day for females.	Anonymous; 1998; M-168498-01-1

Method, guideline, deviations if any, species, strain, sex, no/group	**Test substance, route of exposure, dose levels, duration of exposure**	**Results**	**Reference**
Preliminary dose-ranging three-month oral (gavage) dose toxicity study in CD-1 mice Guidelines: Not applicable (only preliminary and explorative study design). GLP: Study was not performed under GLP, but the laboratory is GLP-certified. Mouse, Crl:CD-1®(ICR) BR mice 5/sex/dose Reliability 3 (Klimisch score)	Proplant® 70.63 % active ingredient 0, 10, 30, 100, 300, 1000 mg/kg bw by gavage	No mortalities and no meaningful toxicological effects were noted in any of the parameters assessed in mice dosed at 10, 30, 100, 300 and 1000 mg/kg for a period of 92 days. Histopathology of the choroid plexus of the mouse brain and lacrimal glands did not reveal lesions (vacuolation) which could be related to the test item. NOEL: 1000 mg/kg bw/day.	Anonymous; 2000; M-310427-01-1

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, route of exposure, dose levels, duration of exposure	Results	Reference
Sub-chronic (90-day) feeding study with ZK 17 296 in dogs Guidelines: Not stated. Deviations: from OECD guideline 409 (1998): purity of test substance, period of acclimatisation, frequency of clinical observations not stated. Ophthalmoscopy, platelet count, electrolytes and some other clinical chemistry parameters were not determined. Cholinesterase activity was measured and liver and kidney function tests were performed which are in excess of the guideline USEPA 83-1 (1984). GLP: No, study was conducted prior to GLP standards. Dog, Beagle, pure bred 4/sex/dose Reliability 2 (Klimisch score)	ZK 17 296 Purity not specified 0, 50, 100, 500, 1000 increased to 2000 ppm from week 7 on	Dietary administration of ZK 17.296 (Propamocarb) at doses up to 1000/2000 ppm for 90-days had no toxicological effect on Beagle dogs. NOEL: 1000/2000 ppm of ZK 17.296. 1000 ppm and 2000 ppm of ZK 17.296 are equivalent to mean daily intakes of approximately 40-48 or 80-95 mg/kg bw/day, respectively of propamocarb (free base).	Anonymous; 1990; M-157595-02-1

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, route of exposure, dose levels, duration of exposure	Results	Reference
90-day oral dietary toxicity study in male and female Beagle dogs Guidelines: EU Directive 87/302/EEC (1988); OECD Guideline 409 (1998); US EPA 712-C-98-200, OPPTS 870.3150 (1998) GLP: Yes Dog, Beagle, pure bred 4/sex/dose Reliability 1 (Klimisch score)	Propamocarb HCl 722 g/L 691g/kg Propamocarb HCl (corresponding to 750.5 g/L 0, 1000, 3000, 10000 ppm Propamocarb HCl)	No mortalities or clinical signs. Some evidence of dietary unpalatability at the highest dose group during the first 2 to 3 weeks of treatment. Thereafter however, the animals appeared to become accustomed to the taste and food intakes were similar to those of the control. Ophthalmoscopic examinations at 13 weeks revealed degeneration of the optic fundus and hyporeflectivity in animals receiving 10,000 ppm of test substance. Such tapetal lesions could be due to a deficiency in zinc, produced by the chelating properties of Propamocarb HCl. This finding is not relevant to man as there is no tapetum in man. Clinical pathology revealed only excretion of smaller volumes of more concentrated urine with a higher Cl by top-dose males and females. Histopathology revealed treatment related microscopic alterations in the trachea, oesophagus, stomach (fundus), salivary glands (sublingual and parotid), lacrimal glands, mandibular lymph nodes and in the lungs (bronchi/ submucosal glands), in form of vacuolar alteration, vacuolation or vacuoles in lymphoid. NOAEL: 1000 ppm Propamocarb hydrochloride, equivalent to an average daily dose of 45 or 51 mg/kg bw/day for males and females respectively.	Anonymous; 2001; M-310439-01-1
52-week oral dietary toxicity study with in male and female Beagle dogs Guidelines: EU Directive 87/302/EEC (1988); OECD Guideline 452 (1981); US EPA 712-C-98-210, OPPTS 870.4100 (1998) GLP: Yes Dog, Beagle, pure bred 4/sex/dose Reliability 1 (Klimisch score)	Proplant (Propamocarb HCl 722 g/L) 691g/kg Propamocarb HCl (corresponding to 750.5 g/L) 0, 1000, 2500, 10000 ppm Propamocarb HCl	No mortalities or clinical signs noted. At all doses, vacuolar alterations of epithelial cells in different organs and glands seen. The range of organs affected, and the incidence and/or severity usually increased in a dose related fashion, with the exception of vacuolation of the female adrenal cortex which reduced in incidence with increasing dose. Clinical pathology investigations demonstrated higher phospholipids levels in males at 2500 and 10000 ppm in weeks 13 and 26, and lower total protein levels in females at 2500 ppm (wk 26) and females at 10000 ppm (wk 26 and termination). In addition, the eyes of all 8 animals (both sexes) in the highest dose group (10000 ppm) and half of the males in the mid dose group (2500 ppm) displayed degeneration of the eye fundus and hyporeflectibility. These lesions could be due to a deficiency of zinc produced by chelating properties of Propamocarb HCl. Hyporeflectibility of the fundus is related to changes in the *tapetum lucidum* which are of no relevance for humans since no tapetum is present in humans. On the basis of the histopathological changes, a NOAEL cannot be determined since vacuolation was present in adrenals, duodenum, lungs, stomach-pylorus and trachea from 1,000 ppm Propamocarb hydrochloride on. This dietary concentration corresponds to 39 or 42 mg/kg bw/day in males and females respectively.	Anonymous; 2003; M-310442-01-1

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, route of exposure, dose levels, duration of exposure	Results	Reference
24-month oral (feeding) study with Previcur N in Beagle dogs Guidelines:US EPA 83-1 (1982) Deviations: Hearing tests were conducted after 3, 6, 9, 12, 18 and 24 months, a liver function test was performed after 24 months of treatment and electron microscopy of the eyes was conducted GLP: Yes Dog, Beagle, pure bred 6/sex/dose Reliability 1 (Klimisch score)	Previcur N Batch 3005073: 68.0% to 68.4% Batch 320072-75: 68.1% to 68.7% propamocarb hydrochloride 0, 1000, 3000, 10000 ppm (equivalent to 0, 682, 2046, 6820 ppm active ingredient Batch 320072-75: 68.1% to 68.7% propamocarb hydrochloride	Ocular changes in the *tapetum lucidum* and, possibly, renal glomerulosis in Beagle dogs was seen. In addition, the incidence of slight to moderate chronic erosive gastritis and/or acute gastric mucosal erosions was seen which was not considered related to treatment. NOAEL:3000 ppm Previcur N, equivalent to achieved mean daily intakes of 104 mg/kg/day in males and 107 mg/kg/day in females. In terms of active substance, 3000 ppm of Previcur N corresponded to 2046 ppm of propamocarb hydrochloride and to mean intakes of 71 mg/kg bw/day in males and 73 mg/kg bw/day in females. It should be noted that the ocular effects (upon which the NOAEL is primarily based), have no relevance to humans as they lack *a tapetum lucidum.*	Anonymous; 1985; M-157637-01-1
Rat 21-day dermal repeat dose study Guidelines: OECD Guideline 410 (1981); US EPA 82-2 (1984) Deviations: No indication of what was used as the control material (0 mg/kg dose level). GLP: Yes Rat, Sprague Dawley CRL:CD (SD) BR 5/sex/dose Reliability 2 (Klimisch score)	Previcur N (propamocarb HCl) 716.9 g/L Propamocarb HCl 0, 100, 500, 1000 mg/kg bw/day	Dermal application of Previcur N once daily to Sprague Dawley rats for a period of 21 days at doses up to 1000 mg/kg bw/day, did not result in any treatment-related systemic effects. Doses of 500 and 1000 mg/kg bw/day however, did result in a number of dermal effects manifest as scabbing at the treated skin site. At the microscopic level these changes were identified as ulcerative dermatitis comprising slight to severe acute dermatitis (acute inflammatory infiltration), slight to moderate epidermal hyperplasia, sloughing of the superficial tissues and eschar formation. NOAEL: 1000 mg/kg/day of Previcur N, equivalent to 717 mg/kg/day of active substance, propamocarb hydrochloride. The dermal NOAEL for irritancy was 100 mg/kg bw/day of Previcur N, equivalent to 71.7 mg/kg bw/day of propamocarb hydrochloride.	Anonymous; 1992; M-157653-01-1

Method, guideline, deviations if any, species, strain, sex, no/group	Test substance, route of exposure, dose levels, duration of exposure	Results	Reference
Repeated dose (28-days) dermal toxicity by daily exposure in the rat Guidelines: EU Directive 92/69/EEC (1992); OECD Guideline 410 (1981); US EPA 712-C-96-201, OPPTS 870.3200 (Draft 1996) GLP: Yes Rat, Wistar Crl:(Wl) BR (outbred, SPF-Quality) 10/sex/dose Reliability 1 (Klimisch score)	Proplant (propamocarb HCl 722 g/L) 691g/kg Propamocarb HCl (corresponding to 750.5 g/L) 0, 75, 300, 1200 mg/kg bw/day Propamocarb HCl)	Dermal application of Proplant® once daily to Wistar rats for a period of 28/29 days at doses of 75 or 300 mg/kg bw/day, did not result in any treatment-related effects. Doses as high as 1,200 mg/kg bw/day however, resulted in a number of dermal and systemic effects which were significantly more pronounced in females. They included reduced body weight gain, reduced absolute liver and thymus weights and decreased albumin and cholesterol levels (which may have been related to the decreased liver weights). Dermal effects included signs of skin irritation and correlating biochemical and histopathological changes. The irritation showed a dose response relationship with regard to incidence, severity and persistency of the effects. Some high dose females also showed increased white blood cell counts. These signs of irritation were less prominent in males (isolated scab formation was observed only in two males from the high dose group). Histopathological examinations revealed minimal to slight vacuolation of the choroid plexus of the brain in two high dose females but the findings were not associated with degenerative alterations in the affected epithelium. NOAEL: 300 mg/kg bw/day propamocarb hydrochloride.	. Anonymous; 2002; M-310445-01-1
28-day inhalat-ion toxicity study of propa-mocarb hydro-chloride in Sprague-Dawley rats Guidelines: OPPTS Guideline 870.3465, OECD Section 412 Deviations: None GLP: Yes Rat, Crl:CD (SD) 10/sex/dose Reliability 1 (Klimisch score)	Propamocarb hydrochloride 70.1 % 0, 100, 500, and 1000 mg/m^3	Exposure of Crl:CD(SD) rats to propamocarb hydrochloride via nose-only inhalation for 6 hours per day on a 5-day per week basis for 4 weeks at exposure concentrations of 0, 100, 500, and 1000 mg/m^3 was well tolerated. All animals survived until scheduled necropsy without clinical signs of physiologic dysfunction or physical impairment. Non-adverse test substance-related lower body weights and food consumption were noted in 1000 mg/m^3 group males. Therefore, the no-observed-effect concentration (NOEC) was 500 mg/m^3 and the no-observed-adverse-effect concentration (NOAEC) was 1000 mg/m^3, the highest concentration tested.	Anonymous; 2014; M-494160-01-1

Table 66: Summary table of human data on STOT RE

Type of data/report	Test substance	Route of exposure Relevant information about the study (as applicable)	Observations	Reference
No human data				

Table 67: Summary table of other studies relevant for STOT RE

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
Rat subchronic (3-month) dietary neurotoxicity study Guidelines: USEPA (=EPA) 81-8 and 82-7 (1991). Also stated that the study is compliant with USEPA (=EPA) 82-1 (1991) GLP: Yes 10/sex/dose Reliability 1 (Klimisch score)	Previcur N SL 711 g/l propamocarb hydrochloride 0, 281, 2813 and 28129 ppm	In addition to standard parameters, neurobehavioural observations, including motor activity, a functional observations battery and cholinesterase determination. Motor activity was measured and a functional observational battery was performed on all animals pretest and during weeks 5, 9 and 13 of treatment. Plasma and erythrocyte acetylcholinesterase were assayed for 5 animals/sex/ group during week 4 and at termination of the study. In addition, brain acetylcholinesterase was assayed for these same 5 animals/sex/group at study termination. All animals received a complete post-mortem examination after receiving the test material for at least 90 days. In addition, 5 rats of each sex from each dose group were perfused for neuropathology examinations.	Dietary administration of up to 28129 ppm of Previcur N SL had no effect on neuropathology, motor activity, general neurological condition as measured by a functional observation battery or acetyl cholinesterase activity. However, this high dose level reduced body weight and body weight gain in both sexes. NOAEL for neurotoxicity: 28129 ppm of Previcur N SL (20000 ppm of propamocarb hydrochloride) which equated to mean achieved intakes of test substance of 1858 mg/kg/day in males and 2089 mg/kg/day in females (1321 and 1485 mg/kg/day propamocarb hydrochloride in males and females, respectively).	Anonymous; 1993; M-157670-01-1
Subchronic (13-week) Neurotoxicity Study with propamocarb HCl in Rats: Neurobehavioural Observations and Automated Motor Activity Assessment Guidelines: OECD guideline 424 (1997); US-EPA OPPTS 870.6200 (1998) Rat, Wistar	propamocarb HCl 69.1% (750.5 g/L) 0, 375, 1500 and 6000 ppm	In addition to the standard parameters, neuro-behavioural screening including motor activity assessment (MAA) and a functional observation battery (FOB). MAA and FOB assessments were performed within one week prior to the start of treatment, during the first week of treatment and at the end of the first, second and third month of treatment. Neuropathological sampling and microscopic examination of 7/10 animals per group and sex took place. After completion of behavioural testing and selection for	No effect of the test substance was found on any of the parameters in either the autonomic, neuromuscular, sensorimotor and convulsive excitability and activity parameters. At the highest dose, effects on body weight and food consumption were seen. Based on the intra-epithelial vacuolation of the choroids plexus in the lateral, 3rd and 4th ventricles in cerebrum and cerebellum, the NOAEL for subchronic neurotoxicity in rat was set at 1500 ppm	Anonymous; 2002; M-310751-01-1

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
outbred (Crl:[WI]WU BR), albino 10/sex/dose Reliability 1 (Klimisch score)		neuropathological examination, the remaining animals were sacrificed and discarded after gross pathological examination. Gross macroscopic changes were recorded for all animals.	(±100 mg/kg bw propamocarb hydrochloride/day) for both sexes.	

10.12.1 Short summary and overall relevance of the provided information on specific target organ toxicity – repeated exposure

In rats, dietary administration of up to 5000 ppm of Previcur N (corresponding to 3215 ppm of propamocarb hydrochloride and to 422 and 459 mg/kg bw/day in males and females respectively) for 5 weeks had no significant effects. In a preliminary 28-day rat dietary study with Proplant, animals treated with 50000 ppm (5700-6430 mg/kg bw/day in males and females) were sacrificed due to overt toxicity. The main finding observed at 5000 ppm and above (425-457 mg/kg bw/day in males and females) was an intracytoplasmic vacuolation of the epithelial cells of the choroids plexus of the brain which also was seen together with vacuolation of the lacrimal glands in a second 28-day gavage study, starting at 200 mg/kg bw/day.

Three 90-day studies were conducted in rats. In one study, the highest dose level, 5000 ppm of Previcur N marginally led to a slightly reduced terminal body weight in the females and slightly reduced food efficiency in both sexes which started in females at 1000 ppm. A NOAEL was established at 5000 ppm propamocarb hydrochloride, equivalent to doses of 362 and 396 mg/kg bw/day for males and females, respectively.

In the second 90-day rat study with dose levels of 0, 7020, 14040 and 28080 ppm of propamocarb hydrochloride liquid concentrate, at dose levels of 14040 ppm and above female body weight, body weight gain, food consumption and food efficiency were reduced which were more marked at 28080 ppm in both sexes. No histopathological changes were observed. The NOAEL was 7020 ppm, equivalent to 5000 ppm of propamocarb hydrochloride, and to mean daily intakes of 318 and 363 mg/kg bw/day in males and females, respectively.

In the third 90-day rat study the maximum dose level of 6000 ppm of Proplant led to reduced body weight gain in both sexes and decreased urinary sodium concentration in males, further to a vacuolation of the choroids plexus of the brain in all and to vacuolation of the lacrimal glands in some animals. A NOAEL was established at 1500 ppm equivalent to 104 and 130 mg/kg bw/day in males and females, respectively.

In a 21-day dermal toxicity study in rats the highest dose of 1000 mg/kg of Previcur N did not cause any systemic toxicity, only local skin lesions due to irritancy at ≥ 500 mg/kg bw so that the NOAEL for systemic toxicity was1000 mg Previcur N/kg/day equivalent to 717 mg propamocarb hydrochloride/kg bw/day.

In another 28-day dermal study with Proplant, treatment-related findings were seen in females at 1200 mg/kg bw/day which included vacuolation of the choroid plexus of the brain, for which a NOAEL of 300 mg/kg bw/day was established.

Two 90-day studies in mice are available. In one study, dose levels of up to 11232 ppm of propamocarb hydrochloride liquid concentrate did not induce any toxicity so that this was the NOAEL which is equivalent to mean daily intakes of active substance of 1349 and 1952 mg/kg bw/day of propamocarb hydrochloride in males and females respectively. In the other study with doses of up to 1000 mg/kg bw/day by gavage, the maximum gavage dose of 1000 mg/kg bw/day, did not induce any toxicity and represented the NOAEL.

Several dog studies are available. In a 28-day study, dietary exposure of dogs to Previcur N, only led to gastric mucosal lesions at the highest dose level of 10000 ppm. The NOAEL for both sexes was 3000 ppm, equivalent to 81 mg propamocarb hydrochloride/kg bw/day.

In one of the 90-day dog studies, dietary administration of up to 1000/2000 ppm of propamocarb free base, equivalent to 48/95 mg propamocarb hydrochloride/kg bw/day did not cause any effect. In the other 90-day dog study with up to 10000 ppm Proplant, equivalent to 433/471 mg/kg bw/day in males and females no mortality or clinical signs were seen. Vacuolar alterations in some organs and glands occurred at 3000 and 10000 ppm and degenerative changes in the eyes of all animals at 10000 ppm. The NOAEL was established at 1000 ppm equating to 45 and 51 mg/kg bw/day in males and females, respectively.

In a one-year dog study with exposure to Proplant concentrations of 0, 1000, 2500 and 10000 ppm, vacuolar alterations were seen in adrenals, duodenum, lungs, stomach-pylorus and trachea at 1000 ppm, with additional degenerative changes in the eye of all animals at 2500 and 10000 ppm.

The only findings following two years of dietary administration of 0, 1000, 3000 and 10000 ppm of Previcur N to dogs were an increased incidence of renal glomerulosclerosis at the highest dose for which a treatment-relationship cannot be excluded and a loss of colour and reflectability of the ocular *tapetum lucidum* at 10000 ppm. In the other laboratory species rats and mice, which lack a *tapetum lucidum*, no effects were seen and since this tissue does not occur in humans, this dog finding is not relevant to humans. The NOAEL was set at 3000 ppm (equivalent to approximately 100 mg/kg bw). Based on the NOAELs or NOAELs (as mg/kg bw/day of propamocarb hydrochloride) in the short term studies the dog was the more sensitive species, however, no treatment-related deaths, no major functional changes in the central or peripheral nervous system or in other organs were seen and furthermore, no consistent changes in hematology, clinical chemistry or urinalysis parameters which could indicate severe organ dysfunctions or organ damage were noted in this species.

In summary, if results with propamocarb hydrochloride are compared with the CLP criteria, it can be stated that no treatment-related deaths occurred below 100 mg/kg bw in the conducted subchronic studies. No major functional changes in the central or peripheral nervous system or in other organs were seen. Also in the special subchronic neurotoxicity studies in rats no neurotoxic effects were demonstrated. Intracytoplasmic vacuolation of the epithelial cells of the choroids plexus of the brain which was seen in a 28-day study at 5000 ppm and above (425-457 mg/kg bw/day in males and females) was thus beyond the trigger dose for classification. In another 28-day rat study, this finding was seen at 200 mg/kg bw, but only very minimal and only in 1 rat of each sex so that the low-effect doses of the subchronic studies appear to be more relevant. In a 90-day rat study the maximum dose level of 6000 ppm of Proplant led to vacuolation of the choroid plexus of the brain which is above the trigger dose, but the NOAEL was established at 1500 ppm equivalent to 104 and 130 mg/kg bw/day in males and females, respectively.

Any consistent changes in clinical biochemistry, hematology or urinalysis parameters which could indicate severe organ dysfunctions or organ damage were not seen in the studies with propamocarb.

With regard to severe organ damage noted in microscopic examination following autopsy, the finding of intracytoplasmic vacuolation of the epithelial cells of the choroids plexus of the brain does not warrant classification since it occurred at higher doses and especially this did not cause any neurological abnormalities. An increased incidence of renal glomerulosclerosis at the highest dose of 10000 ppm tested in a 2-year dog study for which a treatment-relationship cannot be excluded occurred only at a higher dose than the trigger dose. In dogs vacuolation in the trachea, oesophagus, stomach, salivary and lacrimal glands, mandibular lymph nodes and in the lungs at higher doses were observed. The observed loss of color and reflectivity of the ocular *tapetum lucidum* of dogs at 10000 ppm is not relevant for humans since this tissue does not occur in humans.

In a 21-day dermal toxicity study in rats the highest dose of 1000 mg/kg of Previcur N did not cause any systemic toxicity, only local skin lesions due to irritancy at ≥ 500 mg/kg bw so that the NOAEL for systemic toxicity was 1000 mg Previcur N/kg/day equivalent to 717 mg propamocarb hydrochloride/kg bw/day. In a 28-day dermal study with Proplant, treatment-related findings were seen in females at 1200 mg/kg bw/day which included vacuolation of the choroid plexus of the brain.

Exposure of rats to propamocarb hydrochloride via nose-only inhalation for 6 hours per day on a 5-day per week basis for 4 weeks at exposure concentrations of 0, 100, 500, and 1000 mg/m^3 was well tolerated. Based on non-adverse test lower body weights and food consumption at 1000 mg/m^3 in males, the no-observed-effect concentration (NOEC) was 500 mg/m^3 and the no-observed-adverse-effect concentration (NOAEC) was 1000 mg/m^3, the highest concentration tested which is thus above the trigger dose of category 2.

Therefore, the available toxicity studies do not show significant or severe toxic effects at dose levels requiring classification as STOT-RE. Especially, the lowest doses at which first signs of choroid plexus vacuolization were seen were rather high with an isolated finding in one of the subacute rat studies at 200 mg/kg bw in 1 animal per sex only and with only minimal severity. It was clearly above the STOT-RE criteria with approximately more than 400 mg/kg bw/day in the more relevant subchronic toxicity and subchronic neurotoxicity studies in rats.

Extrapolation of equivalent effective dose for toxicity studies of greater or lesser duration than 90 days is not necessary.

Table 68: Extrapolation of equivalent effective dose for toxicity studies of greater or lesser duration than 90 days

Study reference	Effective dose (mg/kg/d)	Length of exposure	Extrapolated effective dose when extrapolated to 90-day exposure	Classification supported by the study
No extrapolation necessary				

10.12.2 Comparison with the CLP criteria

According to the ECHA Guidance a classification in STOT-RE Category 2 is not applicable, if significant toxic effects observed in 28-day, 90-day or 12-month repeated-dose studies conducted in experimental animals are not seen up to the following guidance values:

Exposure route species	28-day	90-day	12-month	>12-month
Oral rat	300 mg/kg bw/d	100 mg/kg bw/d	25 mg/kg bw/d	no guidance value provided
Dermal rat	600 mg/kg bw/d	200 mg/kg bw/d	no guidance value provided	no guidance value provided
Inhalation rat (dust/mist/fume)	600 mg/m^3	200 mg/m^3	no guidance value provided	no guidance value provided

It can be summarized from the study results in tables 65 and 67 that no treatment-related deaths or other significant effects below 100 mg/kg bw occurred. No major functional changes in the central or peripheral nervous system or in other organs were seen.

Intracytoplasmic vacuolation of the epithelial cells of the choroids plexus of the brain which was seen in 28-day studies only minimally at 200 mg/kg bw in one animal per sex, but mainly at 5000 ppm and above (425-457 mg/kg bw/day in males and females) and was thus beyond the trigger dose for classification in the more important subchronic studies. In a 90-day rat study the maximum dose level of 6000 ppm of Proplant led to vacuolation of the choroids plexus of the brain, but the NOAEL was established at 1500 ppm equivalent to 104 and 130 mg/kg bw/day in males and females, respectively which is above the trigger dose and also with regard to severity below the criteria since no neurological consequences were observed. Furthermore, since this finding was simple in nature, reversible as demonstrated in one study and especially was not associated with degenerative lesions in the affected

epithelia, it does not fulfill the criteria of STOT-RE category 2 of 'having the potential to be harmful to humans'.

Any consistent changes in clinical biochemistry, hematology or urinalysis parameters that indicate severe organ dysfunction were not seen.

Severe organ damage noted in microscopic examination following autopsy was not observed. The finding of intracytoplasmic vacuolation of the epithelial cells of the choroids plexus of the brain does not warrant classification since it was simple in nature, reversible, not associated with any secondary histopathological finding and did not cause any neurological effect. Also the lowest doses at which first signs of choroid plexus vacuolization were seen were high with an isolated and minimal effect in one of the subacute studies at 200 mg/kg bw in one animal per sex. In the more relevant subchronic toxicity and subchronic neurotoxicity studies in rats the doses were above the STOT-RE criteria with approximately more than 400 mg/kg bw/day. Most importantly, no subsequent neurological abnormalities were seen.

An increased incidence of renal glomerulosclerosis at the highest dose of 10000 ppm tested in a 2-year dog study for which a treatment-relationship cannot be excluded occurred only at a higher dose than the trigger dose. A loss of color and reflectivity of the ocular *tapetum lucidum* of dogs at 10000 ppm is not relevant for humans since humans do not have such a tissue.

In a 21-day dermal toxicity study in rats the highest dose of 1000 mg/kg of Previcur N did not cause any systemic toxicity, only local skin lesions due to irritancy at ≥ 500 mg/kg bw so that the NOAEL for systemic toxicity was 1000 mg Previcur N/kg/day equivalent to 717 mg propamocarb hydrochloride/kg bw/day. In a 28-day dermal study with Proplant, treatment-related findings were seen in females at 1200 mg/kg bw/day which included vacuolation of the choroid plexus of the brain.

Exposure of rats to propamocarb hydrochloride via nose-only inhalation for 6 hours per day on a 5-day per week basis for 4 weeks at exposure concentrations of 0, 100, 500, and 1000 mg/m^3 was well tolerated. Based on non-adverse lower body weights and food consumption at 1000 mg/m^3 in males, the no-observed-effect concentration (NOEC) was 500 mg/m^3 and the no-observed-adverse-effect concentration (NOAEC) was 1000 mg/m^3, the highest concentration tested which is thus above the trigger dose of category 2.

10.12.3 Conclusion on classification and labelling for STOT RE

The available toxicity studies with repeated oral, dermal and inhalative administration do not show significant or severe toxic effects at dose levels requiring classification, thus they are conclusive, but not sufficient to warrant a STOT-RE classification.

10.13 Aspiration hazard

Table 69: Summary table of evidence for aspiration hazard

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No specific studies on aspiration hazard are available. As propamocarb hydrochloride is not regarded a hydrocarbon (mineral oil) this point is not applicable.				

10.13.1 Short summary and overall relevance of the provided information on aspiration hazard

Not applicable.

10.13.2 Comparison with the CLP criteria

Not applicable.

10.13.3 Conclusion on classification and labelling for aspiration hazard

Not applicable.

11 EVALUATION OF ENVIRONMENTAL HAZARDS

Some studies conducted according current guidelines have been submitted. The assessments of those studies gave no indication of ecotoxicological hazards, therefore, gave no need for any ecotoxicological classification and labelling.

11.1 Rapid degradability of organic substances

Table 70 – Summary of relevant information on rapid degradability

Method	Results	Remarks	Reference
Ready biodegradability			
Carbon dioxide (CO2) evolution test (Modified Sturm Test) with Proplant Guidelines: OECD 301 B	The mean percentage of degradation on the basis of the difference in BOD for test substance and blank controls was determined to be 62.8% after 28 days of incubation. The reference compound was degraded and reached the level for ready biodegradability within 14 days of incubation, thus, indicating sufficient microbial activity of the test system. No toxicity of the test substance was observed in toxicity controls. The percentage of biodegradation between the duplicate samples/ in paralels with test item didn´t differ by more than 20% at the various time points of determination The oxygen consumption of the blank inoculum samples was ≤ 60 mg/L. Nitrite and nitrate were determined at the start and at the end of the study and the degradation data were corrected accordingly. However, this calculated correction was only applied on data of day 28.Therefore, the degradation data of the whole study duration was corrected for oxygen uptake for interference by nitrification. The nitrification of organic nitrogen contributed to 32.62 % to the measured BOD. The only source of nitrogen in the experiment, necessary for the process of nitrification, was the test item itself. Therefore, the nitrification rate of 32.62 % may overestimate the influence of nitrification on the BOD throughout the whole study duration. Using this correction, the reported BOD values in the study report were corrected to account for the percentage of nitrification by multiplying the BOD data by 0.67. The original data, as well as the corrected data reached the 60 % of the ThOD within the 28 day period of the experiment. The original data set passed the threshold within the 10-d-window, while the corrected was reached after 12 days. This circumstance would classify propamocarb as being not readily biodegradable due to the correction of the nitrification influence. However, the used correction approach is a worst case assumption as it may be expected that with real nitrification information throughout the whole study, the 10 d window would very likely be met. Therefore, it can be assumed, and propamocarb can be classified as readily biodegradable.	GLP: Yes Reliability score (Klimisch *et al.*,1997): 1	Desmares-Koopmans, M. J. E. (1999). *Propamocarb hydrochloride: Determination of ready biodegradability: Carbon dioxide (CO2) evolution test (Modified Sturm Test) with Proplant.* Report nº 247207 M-310925-01-1 KCA 7.2.2.1/01; 11.1.1 da RAR

Manometric Respirometry Test' in its essential parts being identical with conditions of OECD 301 F.

Guidelines: Council Directive 92/69/EEC Method C.4-D Manometric Respirometry Test (1992). This test method is in all essential parts identical with OECD Guideline 301 F.

The mean percentage of degradation on the basis of the difference in BOD for test substance and blank controls was determined to 62.8% after 28 days of incubation. The reference compound was degraded and reached the level for ready biodegradability within 14 days of incubation, thus, indicating sufficient microbial activity of the test system. No toxicity of the test substance was observed in toxicity controls. The percentage of biodegradation between the duplicate samples/ in paralels with test item didn´t differ by more than 20 percentage points at the various time points of determination (i.e. at the plateau, after the 10-day-window and at the end of incubation). The oxygen consumption of the blank inoculum samples was ≤ 60 mg/L. In cases where the degradation was ≤ 60 %, the pH value was between 6.0 and 8.5 at the end of the test (and, thus, poor degradation was not caused by the pH value). The mean percentage of propamocarb hydrochloride degradation, on the basis of the difference in BOD for test substance and blank controls was determined to 62.8% after 28 days of incubation. Propamocarb hydrochloride is considered to be "readily biodegradable".
According to the OECD guideline 301 F (adopted July, 1992), the results of the study need to be corrected for oxygen consumption by nitrification. Nitrite and nitrate were determined at the start and at the end of the study and the degradation data were corrected accordingly. However, this calculated correction was only applied on data of day 28, resulting in lower degradation on the last day than on the previous. Therefore, the degradation data of the whole study duration need to be corrected for oxygen uptake for interference by nitrification. The nitrification of organic nitrogen contributed by 32.62 % to the measured BOD. Using this correction, the reported BOD values in the study report were corrected to account for the percentage of nitrification by multiplying the BOD data with 0.67. Corrected BOD values and corrected degradation data are displayed in the table below.

Corrected degradation data:

Propamocarb OECD 301 /Corrected report data)					
	Test item degradation				
	BOD test item (mg O_2/L)		% degradation		
Time (day)	a1	a2	a1	a2	mean
0	0.00	0	0	0	0
1	1.88	1.15	0.58	0.58	0.86
2	2.22	1.36	0.78	0.78	1.07
3	1.55	0.95	0.37	0.37	0.66
4	9.09	5.55	0.95	0.95	3.25
5	38.91	23.75	15.12	15.12	19.44
6	44.22	27.00	26.42	26.42	26.71
7	51.63	31.52	32.18	32.18	31.85
8	64.75	39.53	39.53	39.53	39.53
9	70.88	43.27	43.27	43.27	43.27
10	78.28	47.79	47.38	47.38	47.59
11	88.11	53.79	51.33	51.33	52.56
12	90.47	55.23	56.46	56.46	55.85
13	91.88	56.09	58.97	58.97	57.53
14	92.55	56.50	60.20	60.20	58.35
15	93.36	57.00	60.70	60.70	58.85
16	95.65	58.40	62.50	62.50	60.45
17	97.13	59.30	63.41	63.41	61.35
18	98.48	60.12	63.41	63.41	61.76
19	98.55	60.16	64.27	64.27	62.22
20	98.95	60.41	64.52	64.52	62.46
21	99.69	60.86	64.56	64.56	62.71
22	99.08	60.49	65.01	65.01	62.75
23	99.22	60.57	64.68	64.68	62.63

The pass level for ready biodegradability according to OECD guideline 301 is 60 % of ThOD (theoretical oxygen demand) production for respirometric methods. This pass level needs to be reached 10 days after the degree of biodegradation has reached 10 %.

In view of the variable results obtained in the study Desmares-Koopman (1999), new data was generated in the study of Weyers (2008) following actual designs of OECD 301.

GLP: Yes.

Reliability score (Klimisch *et al*.,1997): 1

Weyers, A. (2008). *Biodegradation with propamocarb hydrochloride.* Report nº 2008/0004/01;

M-299907-02-1

KCA 7.2.2.1/03;

	The original data, as well as the corrected data reach the 60 % pass level within the 28 day period of the experiment. The original data set passes the threshold within the 10-d-window, while the corrected data narrowly fails as the value is reached after 12 days. This circumstance would classify propamocarb very close as being not readily biodegradable due to the correction of the nitrification influence. However, the used correction approach is a worst case assumption. The nitrification rate was determined based on the measured results of day 28 and it can be assumed that this rate is not representative for the whole duration of the experiment. The only source of nitrogen in the experiment, necessary for the process of nitrification, is the test item itself. Nitrification can, therefore, only occur, when the substance is already partly degraded and the nitrogen of the test item is released. With progressive degradation of the substance, the nitrification rate should increase as well. Therefore, the nitrification rate of 32.62 % may overestimate the influence of nitrification on the BOD throughout the whole study duration. Even by lowering the nitrification rate by only 1.92 % (to 30.7 %), the 10-d-window criterion is met. Therefore, it can be assumed, that with real nitrification information throughout the whole study, the 10 d window would very likely be met and propamocarb can be classified as readily biodegradable.		
<u>BOD5/COD</u>			
Guideline: Dutch G.2.	Propamocarb hydrochloride was "readily" degraded by microbial processes when sodium acetate was present while degradation was limited (< 10% after 35 days) in the absence of this additional carbon source. However and by its design, the existing test fulfilled key criteria according to the actual OECD Guideline 309, i.e., by diluting a 'mixed microbial population' from surface water (i.e. lake) in a mineral medium, to study the mineralization of the 14C-labeled active substance at 25°C in the dark for a maximum incubation period of 35 days. The test was performed in the presence and absence of an additional carbon source (acetate). However, the test concentration used in the study was 20 mg/L while tests to fully follow OECD 309 should be performed at 10 µg/L or lower. Consequently, this data was regarded as supplemental information.	Study evaluated as <u>supple-mental</u>. GLP: No Reliability score (Klimisch *et al*.,1997): 2	Iwan, J. (1983). *Microbial degradation of propamocarb hydrochloride in water.* Report nº R+S 13/83-PA 66752.73/2; A85467 M-157700-01-1 KCA 7.2.2.2/01;
Kinetic evaluation with the software KinGUI II, following FOCUS Kinetic guidance (2011). Guidelines: OECD Test Guideline No. 309. Commission Regulation (EU) No 283/2013 in accordance with Regulation (EC) No 1107/2009.	The overall biotransformation including mineralization of propamocarb-hydrochloride and its residues in non-sterile natural water was assessed.The mean material balances were 102.5% ±1.1% AR for low dose samples and 100.8 % ± 1.6 % for the high dose, demonstrating no significant losses of radioactivity from samples in the course of the test including processing till analysis. Formation of ^{14}C-carbon dioxide was observed as the sole major transformation product to account for 12.8 % AR (low dose) and 2.8 % (high dose) at the end of the study, day 60. Formation of other volatile components was negligible, amounting to 1.3 % AR (low dose) and 0.1 % (high dose) in maximum for the two concentrations tested. Biological activity of the test water was confirmed within 14 days of incubation. Biotransformation of ^{14}C-labeled propamocarb hydrochloride resulted in a decline from 101.1% AR at time zero to 87.7% after 60 days for the low dose and from 97.4% AR at time zero to 95.9% after 60 days for the high dose. No degradation of the active substance was observed in sterile controls after 60 days of incubation. A number of minor components was observed at trace level accounting in maximum for 2.2% (low dose, day 39) or 3.0% AR (high dose) each at day 39. The calculated DT_{50} value for propamocarb-hydrochloride in water was 296 days for the low dose (value derived from the SFO kinetic model as the best fits to the measured data). No DT_{50} value could be calculated for the high dose, due to the insignificant degradation observed. The overall biotransformation, including mineralization of propamocarb hydrochloride and its residues in non-sterile natural water, was moderate.	GLP: Yes Reliability score: (Klimisch *et al*.,1997): 1	Heinemann, O. & Kasel, D. (2015). *[1-14C]propamo-carb-hydrochlo-ride: Aerobic mineralization in surface water.* Report nº EnSa-14-0512 M-513451-01-1 KCA 7.2.2.2/02

Hydrolysis			
Guideline: OECD A 80/13; USEPA (=EPA): A 79-55	The hydrolysis rate constant at 25ºC for pH values 5, 7, and 9 was extrapolated using the results from 90ºC tests and the measured rate constant at pH 14 and 25ºC. The linear relationship between the rate of hydrolysis and the pH which was obtained in the tests performed at 90°C was used to extrapolate for degradation rates at pH 5, 7 and 9 at 25°C The additional experimental tests performed to check the extrapolations to lower pH values showed a decrease in propamocarb content over 5 days of no more than 8 %. Thus, the compound is considered to be hydrolytically stable at pH 5, 7, and 9.	GLP: Yes. Reliability score: (Klimisch et al.,1997): 1	Repenthin, W. (1976). *Determination of rates of hydrolysis of propamocarb base (SN 39 744) at pH 5, 7 and 9 - Including addendum to report APC 26/76.* M-157687-01-1 KCA 7.2.1.1/01; 2.9.1 and 7.2.1.1
Guideline(s): US EPA (=EPA) Subdivision N. Chemistry: Environmental Fate 161-1; European Union Guideline EC.C7	The rate of hydrolysis was examined in sterile aqueous buffers in the pH range of 4.0 to 9.0 over a five day period in the dark at 50□C under sterile conditions. Radiocarbon recoveries after 5 days ranged from 98.4% to 101.4% of the applied dose for all solutions. [14C]-propamocarb did not degrade at 50ºC over the five day period in any of the buffer systems tested indicating that it is stable to hydrolysis with a DT50 > 1 year.	GLP: Yes. Reliability score: (Klimisch et al.,1997): 1	Shepler, K. & McKemmie, T. (2001). *Hydrolysis of [14C]Propamo-carb at pH 4, 5, 7 and 9.* M-240450-01-1 KCA 7.2.1.1/02; 2.9.1 and 7.2.1.1
Guideline(s): OECD/GD(92)32 Commission Directive 92/69/EEC Method C7	Propamocarb hydrochloride has been found to undergo less than 10 % hydrolysis after 5 days at 50º C in pH 4, 7 and 9 buffer solutions. The estimated DT50 of PHC at 25º C was > 1 year.	GLP: Yes. Reliability score: (Klimisch et al.,1997): 1	Walker, A. J.; Mulle, D. M.; Barlett, A. J. (1995). *Propamocarb hydrochloride: determination of general physico-chemical properties* M-309665-01-1 KCA 7.2.1.1/03; 2.9.1 and 7.2.1.1
General conclusions from the studies on hydrolysis: Propamocarb hydrochloride was stable to abiotic hydrolysis.Therefore, no half-life was determined for the various values of pH investigated and no hydrolytic pathway was proposed. Abiotic hydrolysis is an insignificant process for the dissipation of propamocarb hydrochloride from the natural aquatic environment. This is true, in particular, when comparing the result of abiotic sterile hydrolysis with the results of tests in non-sterile natural water systems.			
Other convincing scientific evidence			
Field investigation and monitoring data			
Soil dissipation studies			
First order kinetic model for the estimation of field DT50 and DT90. Guideline(s):	Two field trials, conducted in California and Georgia, USA, to investigate the dissipation rate of propamocarb hydrochloride (PHC) indicated that the largest amount of PHC residues were observed in grass cuttings and thatch. In both trials, when PHC was applied to bare soil, it remained almost exclusively in the 0-15 cm layer of the soil profile. PHC residues concentrations in grass, thatch and bare soil continued to increase up until the final application and declined after the final application.	GLP/GEP: Yes. Reliability score: (Klimisch et al.,1997): 1	Willard, T. R. (2002). *Terrestrial field soil dissipation of propamocarb hydrochloride in turf.* M-310955-01-1

US-EPA Pesticide Assessment Guidelines, Subdivision N, Section 164-1; the study considered to meet the requirements outlined by SETAC-Europe: Procedures for Assessing the Environmental Fate and Ecotoxicity of Pesticides, Part 1, Section 2 (1995); Field Dissipation Studies for Terrestrial Uses	At the California trial site, DT50 (DT90) values for thatch and bare soil were 23.7 days (78.6 days) and 22.1 days (73.3 days), respectively. At the Georgia trial site, DT50 (DT90) values for thatch and bare soil were 17.4 days (57.7 days) and 17.6 days (58.6 days), respectively. In comparison with laboratory DT50 results, rates of dissipation in the field appear to match closely those determined in laboratory experiments, with the exception of soils that either have large clay content or low microbial biomass count.		KCA7.1.2.2.1/01;
Furthermore, there is information from additional field soil dissipation trials, four located in Canada and two in the USA. The locations were evaluated using the OECD ENASGIPS tool (Europe – North American Soil Geographic Information for Pesticide Studies) aiming to determine their representativeness throughout Europe based on climate and soil similarity. Three of the trial sites were found to be sufficiently representative for European conditions. For these, a kinetic evaluation for the determination of trigger endpoints was performed.			
Guideline(s): PMRA Environmental Chemistry and Fate Guideline 8.3.2	The dissipation of propamocarb hydrochloride in soil was similar for all three eastern Canadian soils. PHC residues remained relatively constant over the first 7 to 14 days, followed by a rapid decline. PHC residues remained, predominantly, in the 0-10 cm depth for these soils. Results from a first order kinetic model for the estimation of field DT50 and DT90 values revealed that PHC degraded rapidly in the New Brunswick, Ontario and Prince Edward Island soils dissipation values (DT50 and DT90) were obtained from the exponential plots of the data. With the exception of Manitoba, due to the presence of smectite clay minerals in this soil the curve fit was good (R2 = 0.87-0.93). The calculated DT50 and DT90 values were 22.5, 16.5 and 20.7 days and 74.8, 54.7 and 68.9 days, respectively, for the 3 soils. A calculated DT50 value of 630 days represents an overprediction for the Manitoba soil, as a result of an insignificant degradation in the year of application. However, sufficient degradation occurred in the year following the application and was observed a DT50 value of ~ 378 days for Manitoba. This period includes 5 months of winter.	GLP/GEP: Yes. Reliability score: (Klimisch et al.,1997): 1	Belyk, M. (1998). *The degradation and fate of propamocarb hydrochloride following an application to bare soils in Canada.* M-141261-01-1 KCA7.1.2.2.1/02
Analysis of propamocarb residues by gas chromatography. Guideline(s): US-EPA Pesticide Assessment Guidelines, Subdivision N, Section 164-1;	Field trials were conducted at two sites in the USA. Three applications of a liquid formulation of propamocarb hydrochloride were made to bare sandy loam soil with seven days between applications. Soil core samples were collected before the first application, immediately after three applications and further on at regular intervals up to 18 months after the final application The biphasic dissipation of propamocarb was similar for both sites. Over the first three to four weeks, the half-lives were 6 days at FSIL and 9 days at ARC sites. This very rapid early decline phase was followed by a slower decline phase with half-lives of 187 days and 132 days at ARC and FSIL, respectively. At trial site ARC, no evidence for leaching was observed, where typical rainfall conditions pertained. At this site, residues were only sporadically observed as low as the 15 cm to 30 cm horizon. At the FSIL trial site, the plot was subjected to rainfall which exceeded the 100 year maximum in the month following the final application. This saturated the test plot and led to PHC residues being observed as low as the 75 cm to 90 cm in isolated soil cores. However, the apparent penetration through the soil was not consistent. Estimation of field DT_{50} values, using a first order kinetic model for the biphasic dissipation of propamocarb, resulted in calculated DT_{50} of 9 and 6 days for the primary degradation phase and 187 and 132 days for	GLP/GEP: Yes. Reliability score: (Klimisch et al.,1997): 1	Cole M.G.(1995). *Dissipation of propamocarb.HCI in Soil Following Application of BANOL to Bare Plot, USA, 1993.* M-135484-01-1 KCA 7.1.2.2.1/03

the study considered to meet the requirements outlined by SETAC-Europe: Procedures for Assessing the Environmental Fate and Ecotoxicity of Pesticides, Part 1, Section 2 (1995); Field Dissipation Studies for Terrestrial Uses	the secondary degradation phase, at the ARC and FSIL sites, respectively.		
Conclusions: The field data were re-visited against the criteria given in actual guidance (FOCUS, 2011 and EFSA, 2014), being the reliability of existing field data assessed against the requirements. Major points included the time point of 10 mm rainfall after application to result in the availability of sufficient data points for kinetic evaluation (i.e. at least five), the availability of adequate weather data (i.e., daily data on rainfall, irrigation and sunshine hours) for normalisation and, the application to bare soil and the management of the treated soil plots in the following. Following application of the criteria, the existing field data didn´t qualify for a kinetic evaluation. The reasons included the non-availability of sufficient data points after each of the first three applications in view of the short spraying interval of 7 days. Formally, there were sufficient data points (i.e., five) after the last application. However, the residue level determined directly after last application was influenced by residues from previous applications resulting in no value at time zero for the kinetic evaluation. In addition, degradation was potentially influenced by enhanced microbial degradation after each repeated application. The design of the study, therefore, didn´t reflect a worst case situation, i.e., results should not be influenced by enhanced microbial degradation coming from adaptation to the test substance. Two further terrestrial field soil dissipation studies were performed to support the available data. These include field soil dissipation data originated from four trial sites in Canada and from two trial sites in the USA. According to the ecoregion crosswalk analysis, four root ecoregions representing three North American TFD trial sites are considered representative for European conditions. A kinetic evaluation according to FOCUS (2006, 2014) was performed for these three trial sites in order to determine trigger endpoints. A summary of the kinetic evaluation is provided below in KCA 7.1.2.2.1/05.			

OECD ENASGIPS tool v3.0 (Europe - North American Soil Geographic Information for Pesticide Studies) tool (PMRA, 2015), developed by the Pest Management Regulatory Agency - Health Canada and US EPA in collaboration with Agriculture and Agri-Food Canada and the European Commission's Joint Research Centre, as part of the OECD project "Harmonised International Guidance for Pesticide Terrestrial Field Dissipation Studies and Crosswalk of North American and European Ecoregions." The tool is recommended for conducting ecoregion crosswalks by the OECD Guidance (2016).	The fate and behaviour of propamocarb hydrochloride was investigated in three terrestrial field dissipation (TFD) studies in North America, covering in total eight trial sites, which were evaluated using the OECD ENASGIPS tool (Europe–North American Soil Geographic Information for Pesticide Studies) aiming to determine their representativeness throughout Europe based on climate and soil similarity. In addition to the holistic similarity approach, individual scores of soil and climate were evaluated in a refined assessment. While soil conditions (pH, OC content and texture) reached high scores in all ecoregions, individually and overall, temperature, as the main driving parameter for the degradation of pesticides among the climatic parameters (temperature and precipitation), reached low individual scores in one ecoregion (7% and 10%). This indicates pronounced differences in temperature conditions between compared ecoregions in North America and Europe. For the remaining four North American ecoregions, similarity of temperature conditions, i.e., an individual similarity score higher than 80% was reached for one or more European ecoregion. In summary, four root ecoregions representing three North American TFD trial sites are considered representative for European conditions.	Reliability score: (Klimisch et al.,1997): 1	van der Stouwe, F. (2020). *Propamocarb: Ecoregion Cross-walk for eight Terrestrial Field Dissipation Study Locations in North America.* M-753833-01-1 KCA 7.1.2.2.1/04
OECD ENASGIPS tool (Europe – North American Soil Geographic Information for Pesticide Studies) Generic Guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". EC Document Reference: None, version 1.1, 2014	<u>Study Results</u>: A kinetic evaluation of the three terrestrial field soil dissipation trials reported above was conducted. The field soil dissipation trials with sufficient similarity were subject to the kinetic evaluation. The degradation of propamocarb hydrocloride was well described assuming a SFO decay for all trial sites. The evaluation of the terrestrial field soil dissipation data resulted in non-normalised half-lives ranging from 8.4 to 23.1 days and DT_{90} values ranging from 28.0 to 76.8 days.	GLP/GEP: No. Reliability score: (Klimisch et al.,1997): 1	Porschewski, R. (2020). *Estimation of kinetic trigger endpoints for propamocarb from terrestrial field dissipation studies in the United States and Canada.* M-756746-01-1 KCA 7.1.2.2./05;

EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT50 values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014;12(5):3662			
Soil accumulation studies			
In case values of the $DisT_{50}$ in the field were higher than 1 year, two sites out of the set of available dissipation sites were identified to study the accumulation in the field for several successive years to reach the plateau concentration. According to the working document EU Commission 9188/VI/97 rev. 8 of 12.07.2000, modelling was regarded as adequate for the determination of maximum soil concentrations. In addition, the following triggers for the accumulation studies were not met: 15 out of 17 values of DT_{50} were far below the 3 months trigger for DT_{50} and the one year for DT_{90}. NER formation was below 70% and mineralisation was > 5% after 100 days. Modelling based on laboratory values are an acceptable surrogate for data. The data requirement resulting from EU triggers for accumulation can be adequately addressed by laboratory data. The geomean of aerobic soil degradation of PHC propamocarb hydrochloride in laboratory studies was 22.3 d. For calculations, the worst case lab DT50 of 136.7 d and the mixing (tillage) depth of 20 cm were used.			
Monitoring			
No formal monitoring program was requested or required to address this point for propamocarb-hydrochloride or its residues in soil and water in the EU.Moreover and specifically for the active substance and its salts, there aren´t available any published data from formal monitoring programs outside BCS that would indicate a specific concern or findings of PHC and its residues in remote environmental areas not being subject to the intended use.			
Inherent and enhanced ready biodegradation tests			
Not available.			
Water, water-sediment and soil degradation data (including simulation studies)			
Aerobic mineralisation in surface water (new data requirement)			
-	Please, refer to this study above in BOC_5/COD.	-	Iwan, J. (1983). *Microbial degradation of propamocarb hydrochloride in water*. M-157700-01-1 KCA 7.2.2.2/01;
	Please, refer to this study above in BOC_5/COD.		Heinemann, O. & Kasel, D. (2015).

			[1-14C]propamo-carb-hydrochlo-ride: Aerobic mineralization in surface water. Report nº EnSa-14-0512. M-513451-01-1 KCA 7.2.2.2/02
BBA Guideline, Part IV, 5-1, 1990	Under aerobic aquatic conditions, propamocarb hydrochloride (PHC) degraded readily in two water/sediment systems at 20 ºC. PHC The degradation in natural water and associated sediment was, principallymainly, through the action of micro-organisms resulting in mineralisation of ~ 70 % of the compound to CO2. Overall recoveries of radioactive material were good for both test systems, as PHC was mineralised, principally, to CO2 and NER. However, byBy the end of the study, non-extractable residuesNER represented less than 10 % of AR. No accumulation of intermediate degradation products wereas observed. In total, a maximum of eight minor metabolite peaks were observed during the incubation period. However, the concentration of these components was in all cases < 3.3 % of the AR. The proposed metabolites are transient in nature and progress to CO2. No further efforts were carried out to identify the metabolites. The sediment DT50 values of PHC propamocarb hydrochloride were higher than the water phase DT50 (26 days and 23 days in the MSP and IHS test systems, respectively). The total system (water/sediment) DT50 values were 21 (69) days and 16 (53) days in the MSP and IHS test systems, respectively. The DT50 values of propamocarb hydrochloridePHC for the water phase were calculated to be 10 days (MSP) and 15 days (IHS). The DT50 values of PHC estimated for the water phase and for the total system are also a function of PHC dissipation as well as degradation. The higher DT50 value for the MSP total system is likely to result from the higher clay and organic matter content of the sediment, binding the test substance to the sediment particles, thus, reducing availability to microbial attack.	GLP/GEP: Yes. Reliability score: (Klimisch et al.,1997): 1	1995; Allen, R. & Fordham, L.. *Propamocarb hydrochloride soluble concentrate 722 g/L (Code: CR18131) - Degradation in sediment/water microcosms.* M-157923-01-1 KCA 7.2.2.3/01;

Dutch Guideline for Registration of Pesticides, Section G 2.1: Details on the nature of conversion products and the rate at which they are formed, March 1995; German BBA Guidelines for the Official Examination of Plant Protection Agents, Part IV, Section 5-1 (December, 1990); European Economic Community (EEC), Commission directive 95/36/EC, amending Council Directive 91/414/EEC concerning the placing of plant protection products on the market, EEC Publication no. L172/8, July 1995; Society of Environmental Toxicology and Chemistry (SETAC), Procedures for assessing the environmental fate and ecotoxicity of pesticides, March 1995 (Dr. Mark R. Lynch).	Guidelines followed: Dutch Guideline for Registration of Pesticides, Section G 2.1: Details on the nature of conversion products and the rate at which they are formed, March 1995; German BBA Guidelines for the Official Examination of Plant Protection Agents, Part IV, Section 5-1 (December, 1990); European Economic Community (EEC), Commission directive 95/36/EC, amending Council Directive 91/414/EEC concerning the placing of plant protection products on the market, EEC Publication no. L172/8, July 1995; Society of Environmental Toxicology and Chemistry (SETAC), Procedures for assessing the environmental fate and ecotoxicity of pesticides, March 1995 (Dr. Mark R. Lynch). The route and rate of degradation of propamocarb hydrochloride was investigated in two natural water/sediment systems in a laboratory study. The water/sediment systems were kept incubated under aerobic conditions at 20 C in the dark (photoperiod of 8 h light 16 h dark at 300-350 Lux) for up to 104 days. Study results: Propamocarb hydrochloride PHC degraded readily in the two water/sediment systems. at 20□C. Overall recoveries of radioactive material was good for both test systems, as propamocarb hydrochloridePHC was mineralised principally to CO2 and NERnon-extractable residues. In total, a maximum of three minor metabolite peaks were observed during the incubation period, however, the concentration of these components was in all cases < 4 % AR. of the applied radioactivity. No further efforts were carried out to identify the metabolites. Based on literature, a degradation pathway for PHC was proposed for aerobic water/sediment system degradation: the active substance PHC progressed to Propyl-3-(dimethylamino) propylcarbamate, which could degrade to either N,N-Dimethylpropane-1, 3-diamine or, and in sequence, to propyl-3(methylamino) propylcarbamate and 1-pethyltetrahydro-1,3-diazin-2-one. In all cases, the proposed metabolites are transient in nature, progressing to carbon dioxide. The DT50 values of propamocarb hydrochloridePHC in the OVP and SW water/sediment systems were estimated to be 15.5 days and 15.9 days for the total system, respectively. The DT50 values of PHC for the water phase were calculated to be 11.6 days (OVP) and 12.0 days (SW).	GLP/GEP: Yes. Reliability score: (Klimisch et al.,1997): 1	de Vries, R. (1997). *Propamocarb hydrochloride: Degradation of propamocarb HCL in aerobic aquatic environment.* M-310804-01-1 KCA 7.2.2.3/02
Guideline(s):US EPA Pesticide Assessment Guidelines, Subdivision N, Guideline Section 162-3	The route and rate of degradation of Propamocarb hydrochloride was investigated in a natural water/sediment system under anaerobic conditions at 25°C in the dark for up to 419 days. Since this type of test was (and is) not a data requirement in the EU, the data were regarded as supplemental information.	Study performed in a nitrogen gas-flow incubation system, to maintain anaerobic conditions. The rate of degradation was determined using the kinetic model program (KIM 1.0).	Judge, D. N. (1998). *Code: AE B039744 - Degradation of [1-14C] propamocarb under laboratory anaerobic aquatic conditions propamocarb free base - Amendment to report number AV97E517.* M-167940-02-1. KCA 7.2.2.3/03

	Under anaerobic aquatic conditions propamocarb hydrochloride was observed to rapidly partition from the aqueous phase to the sediment phase. Significant degradation of propamocarb was observed through the mineralisation of the parent compound to CO2. Evidence of methane production from anaerobic methanogenic bacteria was also obtained from additional investigations. NER represented 20.1 %AR after 110 daysand 2.25%AR by the end of the study. Overall recoveries of radioactive material were good with a mean material balance of 93.4 % of AR. No accumulation of intermediate degradation products was observed. In total, a maximum of nine minor metabolite peaks were observed during the incubation period, however, the maximum concentration of one metabolite (unknown metabolite D) only reached 3.9 % and 0.9 % of the AR in the water and sediment phase, respectively. No further efforts were carried out to identify the metabolites. In all cases these proposed metabolites were transient in nature progressing to CO2 and methane. The DT50 and DT90 values for propamocarb hydrochloride in the aqueous phase under anaerobic conditions was calculated (k = 0.05747) to be 12.1 days and 40.1 days, respectively. For the sediment DT50 and DT90 values were estimated (k = 0.00745) to be 93.0 days and 309.1 days, respectively. Half-life estimation for sediment was determined after a hinge point representing the maximum amount of applied radioactivity reached on Day 54. For the total system DT50 (DT90) values were calculated(k = 0.00693) to be 100.0 (332.3) days.	GLP/GEP: Yes. Reliability score: (Klimisch et al.,1997): 1	
Kinetic re-evaluation of the data from the water/sediment tests KCA 7.2.2.3/01 and KCA 7.2.2.3/02 according to FOCUS guidance (2011)			
FOCUS 2006, FOCUS 2011, *Generic Guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration*. EC Document Reference: None, version 1.1, 2015 amending "*Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration".* Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference Sanco/10058/2005 version 2.0, 2006.	The kinetics of degradation and dissipation was evaluated for propamocarb-hydrochloride for four data sets resulting from two studies performed each with two differing water/sediment systems after application of the 14C-labeled active substance and incubation at 20°C. Kinetic evaluation of degradation in total systems and in the water phase gave acceptable to excellent fits to measured data by use of the SFO kinetic model for all data sets. Geometric mean $DegT_{50}$ of 20.5 days and $DisT_{50}$. of 12.6 days, respectively, were derived.. Level II evaluations were performed for all systems but revealed poor results regarding the statistical parameter (t-test) and the Fsed test and were therefore excluded. Kinetic evaluation of dissipation from the sediment as modelling endpoint gave good to excellent fits to measured data by use of the SFO kinetic model for all data sets. A geometric mean value for the $DisT_{50}$ of 22.2days was obtained. Level II evaluations were performed for all systems but revealed poor results regarding statistical parameter (t-test) and the Fsed test and were, therefore, excluded.	SFO kinetics with free optimisation of parameters, along with FOMC, DFOP and HS kinetics where appropriate. The kinetic evaluations and the statistical calculations were conducted with KinGUI (v2.0), using iteratively re-weighted least-squares (IRLS) optimisation. GLP/GEP: No. Reliability score: (Klimisch et al.,1997): 1	Oberdoerster, C.; Hoerold, C.; Boiselle, N. (2015a). *Kinetic evaluation of the aerobic aquatic metabolism of propamocarb-HCl in two water sediment laboratory studies.* M-541774-01-1 KCA 7.2.2.3/04
Irradiated water/sediment studies			

The degradation of propamocarb hydrochloride has been assessed under standard conditions of water/sediment testing.Within the existing water/sediment data submitted, the design of study KCA 7.2.2.3/02 included the influence of mixed light conditions on degradation by irradiation of samples for 8 hours at 300 to 350 Lux followed by a 16 hours dark interval. However, results on route and rate of degradation were found to be insignificantly different from data of study KCA 7.2.2.3/01 where samples were incubated in the dark only. This finding supported the overall limited potential of PHC to undergo direct or indirect photolytic degradation in aquatic media (KCA 7.2.1.2/01 to KCA 7.2.1.2/03 and KCA 7.2.1.3/01).
Consequently, the irradiated water/sediment study would not providebetter understanding of the behaviour of propamocarb and its residues in the aquatic environment. A new irradiated water/sediment study was, therefore, not performed or regarded as necessary.

Degradation in the saturated zone

The separate investigations on the degradation in the saturated zone are not regarded as necessary, since the risk assessment for the groundwater demonstrated no significant risk for a contamination of sub-soils or the saturated zone by the active substance and its metabolites when being applied according to good agricultural practice.

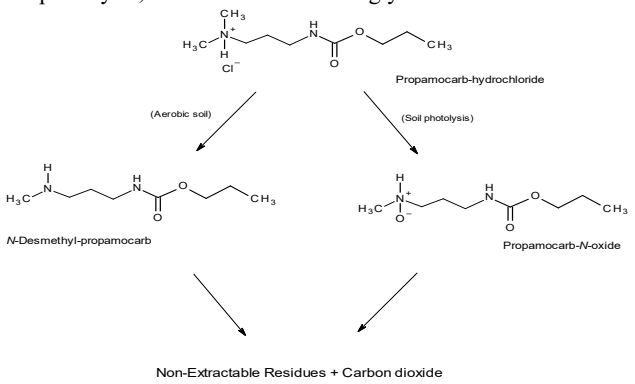
Degradation in the soil - Laboratory studies

Aerobic degradation in the soil

Analytical investigations were performed by Thin Layer Chromatography (TLC), autoradio-graphy and LSC as combustion of radioactive compounds.	The aerobic degradation at 15.ºC and 25.ºC of radiolabelled propamocarb hydrochloride was tested in different test studies and several soils at a test concentration corresponding to a field application rate of 150 kg a.s/ha, based on 5 cm depth and bulk density of 1.5 g/cm3. In all studies, propamocarb hydrochloride was metabolised quickly, readily mineralised under both temperatures. Lag phases were observed in the mechanics of propamocarb hydrochloride metabolism in two studies, which ranged from 5 to 21 days. Main products of metabolism were CO2 and non-extractable residues. Several unidentified metabolites were detected although individually none were present above 3% AR and were of transient nature. In the study KCA 7.1.1.1/01, ≈ 80% of the propamocarb hydrochloride was mineralised after two months. CO2 reached a maximum of 88.6 % of the applied radioactivity (AR). Bound residues reached a maximum of 13.1% at day 180. Three metabolites were detected in very low concentrations (< 2% of AR). In study KCA 7.1.1.1/02, more than 80% of propamocarb hydrochloride was mineralised to $^{14}CO_2$ after 90 days. CO2 reached a maximum of 88.5% of the AR. Bound residues reached a maximum of 12.4% at day 180 and then decreased to 11.3% by day 360. Three metabolites were detected in very low concentrations (< 1% of the AR). In study KCA 7.1.1.1/03, propamocarb hydrochloride was rapidly degraded after an initial lag phase of ≈ 3 weeks in German standard soil 2.2 (Neuhofen, loamy sand) and 2.3 (Hatzenbuehl, sandy loam). After 61 and 67 days greater than 63% and 94% of the PHC in the German standard soil 2.2 (Neuhofen, loamy sand) and 2.3 (Hatzenbuehl, sandy loam), respectively, were mineralized to $^{14}CO_2$. Bound residues in both soils reached a maximum of between 15.30 to 20.81% at day 32 and then decreased to 13.53 - 14.90 % by the last sampling day. Three metabolites were detected in very low concentrations (< 3% of AR) and other unkowns in minor concentrations (3.69% of AR). In study KCA 7.1.1.1/04, propamocarb hydrochloride was rapidly degraded under aerobic conditions. After 46 days greater than 75% of the PHC was minerialized to $^{14}CO_2$. Bound residues reached a maximum of 23.4% at day 13 and decreased thereafter to 14.55% by day 46. Three metabolites were detected in very low concentrations (< 2% of AR). In study KCA 7.1.1.1/05, propamocarb hydrochloride was applied twice, under aerobic conditions. After both applications, the test substance was rapidly degraded, however, after the first application an initial lag phase of approximately 5 days occurred. After the second application no lag phase was observed.. No degradation products other than $^{14}CO_2$ were detected in appreciable amounts (< 2% of AR) and bound residues reach a maximum of 7.5 % at day 59 but had declined to 5.0% of applied by day 87.	GLP/GEP: No. Reliability score: (Klimisch et al.,1997): 1	Bruehl, R. & Celerio, J. (1978) M-157704-01-1 KCA 7.1.1.1/01 Bruehl, R. (1979) M-157706-01-1 KCA 7.1.1.1/02 Bruehl, R. & Celorio, J. (1980) M-157708-01-1 KCA 7.1.1.1/03 Bruehl, R. & Celorio, J. (1980) M-157709-01-1 KCA 7.1.1.1/04 Bruehl, R. & Celorio, R. (1986) M-157783-01-2 KCA 7.1.1.1/05

Thin Layer Chromatography Guideline(s): SETAC-Europe, Procedures for Assessing the Environmental Fate and Ecotoxicity of Pesticides, Part 1, Section 1.1 (1995).	The route of degradation of propamocarb hydrochloride was investigated in a laboratory study at 20º C ± 2 ºC using four different soils (clat loam, loamy silt, loamy sand, and silty sand), under aerobic conditions at 40 % of their maximum water holding capacity in the dark for maximal 120 days. Propamocarb hydrochloride degraded readily in all but the clay loam soil where degradation was slower. CO2 was the main degradation product formed in all soils, except in the clay loam soil, reaching a maximum range of between 58.2% and 66.2%. In this soil, the maximum $^{14}CO2$ determined reached 22.8 % AR. Non-extractable residues accounted for a significant portion of the AR and reached a maximum of 21.4%, 20.0%, and 23.8% of AR in the loamy silt, loamy sand and silty sand soils. For the clay loam soil, large amounts of AR became associated with organic fractions bound to the soil, and accounted for 42.7% to 55.9% AR for the study duration. Under experimental conditions the clay loam soil was atypical, when compared to the other test soils.. Up to eight unidentified polar metabolites were observed during the study, however, the sum of the unknown metabolites never exceeded 8.1% of the AR and none single component exceeded 3.3% of AR at any sampling interval in any soil. For all metabolites observed in the study, no recognisable pattern of formation could be determined, indicating that the metabolites are transient in nature.	GLP/GEP: Yes Reliability score: (Klimisch et al.,1997): 1	Fent, G. & Hein, W. (2001). *Degradation and metabolism of propamocarb-HCL (AE B066752) in four different soils.* M-203298-01-1 KCA 7.1.1.1/06
OECD 1998, ENV/MC/CHEM (98) 17; EC Directive 95/36/EC. Active Substances, Section 7.1.1.2 (July 1995); SETAC Procedures for assessing the Environmental Fate and Ecotoxicity of Pesticides. Section 1.1 (March 1995), EPA, Subdivision N. Section 162-1 (October 1982); requirement for safety evaluation of agricultural chemicals published in 59NohSan No. 4200, Japanese Ministry of Agriculture Forestry and Fisheries (28 January 1985).	<u>Results of the study:</u> The aerobic degradation of propamocarb hydrochloride, applied at a rate of 250 mg/kg, corresponding to a field rate of 187.5 kg a.s/ha was investigated in four soils (2 sandy loam, and 2 clay loam soils). propamocarb hydrochloride degraded readily under the aerobic experimental conditions in the laboratory. CO2 and non-extractable residues were the main degradation products formed, reaching a maximum of 48.38 % and 47.45 % of the AR respectively. One of the metabolites formed was a polar component, which was observed at a maximum value of 7.3 % of the AR with a retention time of ~ 2.5 minutes. The attempts to identify the metabolite failed and could not be identified after further investigation (for further characterisation and identification, see study KCA 7.1.1.1/10). A further six unidentified transient degradation products were also formed over the duration of the experiment. These degradation components were only detected occasionally and individually did not exceed 2.03 % of the AR. Beside metabolite Unk 1, no other metabolite observed accounted for more than 5 % of the AR.	Liquid chromatography and mass spectrometry techniques GLP/GEP: Yes Reliability score: (Klimisch et al.,1997): 1	Schnoeder, F. (2003). *Amendment to final report - (14C)-propamocarb hydrochloride - Aerobic route and rate of soil degradation* M-310828-02-1 KCA 7.1.1.1/07
-	A mixed population of aerobic microorganisms capable of metabolizing [14C]-propamocarb hydrochloride was developed from Gerrnan Standard Soil 2.2. Following a lag-phase of about 24 hours, PHC was completely mineralized within 6 to 9 days as indicated by the evolution of respective quantities of $^{14}CO2$. No degradation products found in the culture medium were detected in appreciable amounts (< 4 %). Besides large quantities of $^{14}CO2$, radioactivity was also found in the pelleted tissue of the microorganisms (5.4 - 22.5 % of AR after 6 days). Although some of the detected radioactivity might have adhered to the surface of the microbial pellet in spite of washing, these data suggest that following oxidative metabolic processes C-1 or C-2 fragments from the carbon skeleton of the parent molecule had been introduced into natural anabolic pathways.	GLP/GEP: No. Reliability score: (Klimisch et al.,1997): 2	Iwan, J. (1979). R+S 38/79-PA 66 752.73/2, M-157719-01-1 KCA 7.1.1.1/08

	Fragments of the parent molecule seemed to be incorporated into the cells of the organisms which were partially identified as *Candida humicoia, Fusarium* sp. and 2 species of gram negative bacteria. Conclusion: The degradation of propamocarb hydrochloride in soil is, primarily, mediated by soil microorganisms. This study was performed in cultural media with microbial populations derived from soil rather than fully 'native', microbial active soil. Thus, the design and results were not comparable to a standard aerobic soil study.		
EPA guidelines.	To determine the impact of soil microorganisms on propamocarb hydrochloride degradation, tests were run with sterilized and non-sterilized German standard soil 2.2 according to current EPA guide-lines. After 14 days of incubation, recoverable propamocarb hydrochloride contents of sterilized samples remained constant (60% of applied material), the initial decrease being due to adsorption. After an initial period of adsorption to the soil, the percentage of applied propamocarb hydrochloride that was extractable from the sterilized soil remained constant at about 60 % of AR on days 14 and 31. In the non-sterile microbially active soil, extensive mineralisation occurred following a lag-phase of 7 days. Degradation of PHC under these conditions is best described by zero-order kinetics with a half-life of about 18 days. These data strongly suggest that soil degradation of PHC is mediated by microorganisms. A mixed culture of bacteria and fungi capable of degrading the pesticide was identified. Intermediate metabolic products didn´t accumulate in any of the samples investigated. The lack of degradation in soil after deactivation of an otherwise "metabolically" active soil by heat sterilization illustrates that the degradation of propamocarb hydrochloride in soil is primarily mediated by soil microorganisms. Major deficiencies: No day zero samples were investigated in combination with low total recove-ry below 90% AR for first sam-pling interval (day 1 after application).	GLP/GEP: No. Reliability score: (Klimisch et al.,1997): 2	Iwan, J. (1980). *Metabolism of propamocarb hydrochloride by soil microorganisms. Behaviour in sterilized and non-sterilized German standard soil 2.2 - Report of progress no. 2.* R+S 48/80-PA 66 752.73/2, M-157721-01-1. KCA 7.1.1.1/09
To fulfil actual data requirements of identification for minor components observed in the route of the aerobic degradation in soil, to characterise and, if possible, to identify the polar unknown radioactivity.			
OECD Test Guideline No. 307. Profiling of resi-dues in soil ex-tracts: additionnal HPLC methods developed. The polar unknown fraction of soil Woolverstone: characterized by HPLC using a Hypercarp column. The un-known compo-nent in soil Sarotti: identified by HPLC/MS/MS including fine mass determina-tion of the isolated HPLC fractions.	Samples were generated for characterisation and identification of unknown metabolites already observed in the two existing aerobic soil degradation studies KCA 7.1.1.1/07 and KCA 7.1.2.1.1/15. By its design as a metabolite identification study, no full material balances were established. Chromatographic investigations of extracted radioactivity showed extensive transformation. Total recoveries of extractable radioactivity declined from 95.3 (day zero) to 5.5% of AR (day 90) for soil Woolverstone (sandy loam) and from 70.3 (day zero) to 24.3% (day 29) for soil Sarotti (loamy silt), thus, underlining the extensive microbial transformation of the test substance in the two soils. Chromatographic analysis of soil extracts resulted in profiles of transformation products consisting of a number of metabolites, all occurring at trace level in the course of incubation. The patterns were, therefore, similar to those observed in earlier aerobic soil degradation studies conducted with the parent compound PHC, including the two unknown components observed (retention time in HPLC approx. 2.5 min, study KCA 7.1.1.1/07, and relative retention factor of approx. 0.33 to 0.36 in TLC, study KCA 7.1.2.1.1/15) in the existing tests at levels beyond the actual triggers set for identification. In soil Sarotti (loamy sand), an unknown component characterized by a relative retention factor of 0.33 to 0.36 in TLC was identified by HPLC analysis/fraction collection followed by HPLC/MS/MS and NMR spectroscopic investigations as oxo-propamocarb. The structure indicated one of the potential initial oxidative steps of microbial transformation in the route of degradation of the active substance in aerobic soil. The transient character is underlined by the fact that the compound was observed as a minor metabolite in tests performed at 10°C only, with no detection in tests at 20°C. In samples of the same soil Sarotti incubated at 20°C, the metabolite oxo-propamocarb was	GLP/GEP: Yes. Reliability score: (Klimisch et al.,1997): 1	Heinemann, O. & Kasel, D. (2015). *[1-^{14}C]propamo-carb-hydrochlo-ride: Characteri-sation of two unknown components observed in two aerobic soil metabolism studies*. M-529394-01-1 KCA 7.1.1.1/10.

Commission Regulation (EU) No 283/2013 in accordance with Regulation(EC) No 1107/2009. US EPA OCSPP Test Guideline No. 835.4100 / 835.4200.	observed at trace level below 3% AR (KCA 7.1.1.1/06). Incubation at 10°C, thus, resulted in slightly higher levels, just beyond 5% in the same soil, underlining the transient character with no trend for increase at later sampling intervals. Moreover, oxo-propamocarb occurred at trace level in other soils, in case of its formation at all. In view of its transient characteristics, oxo-propamocarb was therefore not defined as a residue for environmental risk assessment in soil, groundwater or surface water. For polar unknown radioactivity observed in soil Woolverstone, additional chromatographic investigations resulted in its separation into at least two components being each below the EU trigger for identification.		
Combustion/LSC, reversed phase HPLC , 14C-flow-through detection techniques, normal phase TLC, HPLC with authentic reference material, mass spectroscopic data. SFO kinetic model by the software GraphPadTM PRISM® using non-linear optimization. Guideline: US EPA Subdivision N, Section 162-1	Following incubation of radio-labeled propamocarb hydrochloride in two aerobic soils, extensive transformation was observed resulting in the metabolite N-desmethyl-propamocarb as transformation product. The overall basic processes of degradation were biotic in nature as demonstrated by de-methylation and the significant formation of 14C-CO2. Dependent on soil, the degradation of propamocarb hydrochloride was fast to moderate (half-life of 31.4 days for soil Porterville and 123 days for soil Aromas). Total recoveries of radioactivity ranged from 90.9 to 100.0% of AR for sandy loam soil Porterville and from 95.4 to 100.1% for sandy loam Aromas. The total extractable radioactivity decreased from 99.0% (soil Porterville) and 91.6% (soil Aromas) by day zero to 6.2% and 41.7% by day 119. The decrease of extractable radioactivity was accompanied by the formation of non-extractable residues (NER) to account for 14.8% (Porterville) and 17.8% (Aromas) after 119 days. As a result of microbiological degradation, mineralisation was extensive to account in maximum for 73.6% (Porterville) and 36.4% (Aromas) determined as ^{14}C-CO2 at the end of the study, day 119. Formation of other organic volatile components was insignificant (≤ 0.1% AR). Besides ^{14}C-CO2, formed as the predominant transformation product, the metabolite *N*-desmethyl-propamocarb was observed in Portervile, at 9.7% in maximum by day 30, while the metabolite was not detected in Aromas. Formation of unknown components was very low and at trace level (0.5% by day 30, soil Porterville) in the course of the study. The biotic character of degradation of [^{14}C]-PHC in aerobic soil was again confirmed by the formation of ^{14}C-CO2 as the major and terminal product of conversion along with the formation of non-extractable (bound) residues. The degradation data were kinetically re-evaluated under KCA 7.1.2.1.1/01 and KCA 7.1.2.1.2/01 for comparison with EU trigger endpoints and to derive input values for modelling in environmental exposure assessments. The degradation of [^{14}C]-PHC resulted in half-lives (DT_{50}) of 31.4 days for soil Porterville and 123 days for soil Aromas, associated with DT_{90} value of 104 days for soil Porterville and DT_{90} value of 409 days for soil Aromas. The proposed route of degradation of PHC in aerobic soil, including soil photolysis, was amended accordingly as illustrated below.  	GLP/GEP: Yes. Reliability score: (Klimisch et al.,1997): 2.	Desmarteau, D. A. (2006). *[^{14}C-propamocarb-hydrochloride]: Aerobic soil metabolism in two US soils.* M-270482-01-1 KCA 7.1.1.1/11

The existing and the new informations were evaluated kinetically according to actual FOCUS Guidance in order to derive values for the DT_{50} and DT_{90}, for comparison with trigger endpoints and half-lives for modeling endpoints. The re-evaluation, detailed in KCA 7.1.2.1.1/16, superseded the existing kinetic evaluations.			
SFO kinetic model and bi-phasic models FOMC or DFOP in case of unacceptable fits. Software KinGUI (v2.0) using iteratively re-weighted least-square (IRLS) optimization. FOCUS guidance [FOCUS, 2006, amended 2011]. Generic Guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". version 1.1, 2015 amending Report of the FOCUS on Degradation Kinetics. Sanco/ 10058/2005 version 2.0, 2006.	In the study KCA 7.1.2.1.1/15, the microbial biomass, at the start of the study (day 0), was 28.0 µg/g (dry basis) in the Porterville soil and 25.1 µg/g (dry basis) in the Aromas soil and, at the end of the study (day 119), was 25.9 µg/g (dry basis) in the Porterville soil and 12.3 µg/g (dry basis) in the Aromas soil. Therefore, both soils sustained their viability. Trigger endpoints: Non-normalised half-lives of PHC ranged from 7.9 days for German loamy sand soil (KCA 7.1.2.1.1/03) to 136.7 days for Minnesota clay loam soil (KCA 7.1.2.1.1/06), while values for the DT_{90} ranged from 26.1 days to 454.2 days for the same soils, respectively. Worst cased DT50 (days) = 136.7 days and DT90 (days) = 454.2 days. Modelling endpoints: Normalised (20°C, pF2) laboratory DT50 values for PHC was in the range of 8.4 – 149.1 days; the normalised geometric mean DT50 = 23.1 days.	GLP/GEP: No. Reliability score: (Klimisch et al.,1997): 1.	Oberdoerster, C., Boiselle, N., Hoerold, C. (2015b). *Kinetic evaluation of the degradation of propamocarb-hydrochloride and its metabolite N-desmethyl-propamocarb in soil under aerobic laboratory conditions.* M-541770-01-1 KCA 7.1.2.1.1/16
SETAC Procedures for Assessing the Environmental Fate and Ecotoxicity of Pesticides Part 1 1.1, March 1995.	Propamocarb hydrochloride, applied at a rate of 4.8 g/kg dry soil, corresponding to a field rate of 3.6 kg a.s./ha, degraded readily under aerobic experimental conditions at a temperature of 10º C. CO2 reached a maximum of 57.9% (or 59.8% of the average day 120 sampling point). Non-extractable residues also increased slightly, whilst the amount of radioactivity extracted from the soil decreased over time and consisted, principally, of the active substnce. In addition, up to six unidentified polar metabolites were observed, with one individual component of up to 5.5% (for characterisation and identification of component > 5% AR, see study KCA 7.1.1.1/10). No recognisable pattern of formation was determined for all the metabolites observed in the study, indicating that the metabolites are transient in nature. Similarly to the incubation at 20º C (study C012748 – AGR20), propamocarb hydrochloride showed rapid and nearly complete degradation at the lower test tem-perature of 10º C within the 120-day test period. Likewise, the major route of degradation resulted in the conversion to and release of $^{14}CO2$. No single metabolite was formed exceeding 5.5 % of the AR (for characterisation and identification, see study KCA 7.1.1.1/10), indicating that metabolites being formed at low temperatures still remained transient in nature.	GLP/GEP: Yes. Reliability score: (Klimisch et al.,1997): 1.	Fent, G. & Hein, W. (2001). *Degradation and metabolism of propamocarb-HCL (AE B066752) in one soil at 10 degrees C. M-203301-01-1 KCA 7.1.2.1.1/08;*
SETAC Procedures for Assessing the Environmental Fate and Ecotoxicity of Pesticides Part 1 1.1, March 1995. TLC, LSC, HPLC and TLC.	Propamocarb hydrochloride, applied at a rate of 0.48 mg/100 g dry soil, degraded under aerobic experimental conditions at depths of 20, 40, 60, and 90 cm at a temperature of 10º C. The degree of degradation was partially a function of soil depth. $^{14}CO2$ and non-extractable residues were the main degradation products formed. However, with increasing soil depth, the formation of $^{14}CO2$ decreased to amounts that were almost negligible and a greater portion of the test substance was non-extarctable. Up to nine unidentified polar metabolites were observed. The maximum value for a single component never exceeded 5.5% of the AR at two consecutive sampling intervals.	GLP/GEP: Yes. Reliability score: (Klimisch et al.,1997): 2.	Fent, G.& Hein, W. (2001). *Degradation and metabolism of propamocarb-HCl (AE B066752) in four subsoil horizons of one soil.* M-203303-01-1

<table>
<tr><td></td><td>The subsoils used for tests were in contrast to guideline requirements. This study is regarded as supplemental.</td><td></td><td>KCA 7.1.2.1.1/09</td></tr>
<tr><td colspan="4">The existing data of studies KCA 7.1.2.1.1/07 and KCA 7.1.2.1.1/08 were re-evaluated following actual FOCUS kinetic guidance [FOCUS, 2006, 2011], as reported in KCA 7.1.2.1.1/16., to derive values for the half-life and the DT90 in aerobic soil for trigger endpoints.</td></tr>
<tr><td>SFO kinetic model and bi-phasic models FOMC or DFOP, in case of unacceptable fits.
Software KinGUI (v2.0).
FOCUS guidance [FOCUS, 2006, amended 2011]. Generic Guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". version 1.1, 2015 amending Report of the FOCUS on Degradation Kinetics. Sanco/ 10058/2005 version 2.0, 2006.</td><td>Degradation data as referenced under KCA7.1.2.1.1/01 to KCA7.1.2.1.1/08 and KCA7.1.2.1.1/15 were kinetically evaluated according to actual FOCUS Guidance to derive values for the half-life and the DT90 in aerobic soil from studies performed at 15 to 25°C for modelling purposes.
Non-normalised half-lives of propamocarb hydrochloride at 10°C ranged from 0.5 days to 8.1 days while values for the DT_{90} ranged from 5.0 days to 87.1 days.
Comparison against EU triggers:
Kinetic evaluation of degradation for PHC in aerobic soil at 10°C in the laboratory are as follows.
<table>
<tr><th>Parameter</th><th>propamocarb-hydrochloride</th></tr>
<tr><td>10°C, Non-normalised DT_{50}, range (days)</td><td>25.3 – 47.2</td></tr>
<tr><td>Worst case DT_{50} (days)</td><td>47.2</td></tr>
<tr><td>10°C, Non-normalised DT_{90}, range (days)</td><td>84.2 – 156.9</td></tr>
<tr><td>Worst case DT_{90} (days)</td><td>156.9</td></tr>
</table>
Values of non-normalised half-lives at 10°C from best fits to measured data were 25.3 days for silt loam soil Sarotti and 47.2 days for sandy loam soil E (B6, Woolverstone). The corresponding DT_{90} were 84.2 days for soil Sarotti and 156.9 days for soil E (B6, Woolverstone).</td><td>GLP/GEP: No.

Reliability score: (Klimisch et al.,1997): 1.</td><td>Oberdoerster, C., Boiselle, N., Hoerold, C. (2015b). Kinetic evaluation of the degradation of propamocarb-hydrochloride and its metabolite N-desmethyl-propamocarb in soil under aerobic laboratory conditions.

M-541770-01-1

KCA 7.1.2.1.1/16</td></tr>
<tr><td>US EPA Subdivision N, Section 162-1</td><td>Besides the potential information on rate of degradation of metabolite N-desmethyl-propamocarb to be found in one soil of study KCA 7.1.2.1.2/01, additional degradation data were generated by dosing ^{14}C-labeled N-desmethyl-propamocarb separately to four soils (KCA 7.1.2.1.2/02). In addition, metabolite propamocarb-N-oxide was observed in the soil photolysis study KCA 7.1.1.3/01 at a maximum value of 8.7 % AR in irradiated samples after 30.66 days. Following actual data requirements of Commission Regulation (EU) No. 283/2013 amending Regulation (EC) No. 1107/2009, propamocarb-N-oxide was, thus, triggered for consideration in environmental risk assessment. Additional data on rate of degradation were, therefore, generated by dosing ^{14}C-labeled propamocarb-N-oxide separately to four soils (KCA 7.1.2.1.2/03). The kinetic evaluations were performed in KCA 7.1.2.1.2/04 and KCA 7.1.2.1.2/05 for N-desmethyl-propamocarb and in KCA 7.1.2.1.2/06 for propamocarb-N-oxide, in order to derive trigger and modeling endpoints for input into environmental risk assessments.</td><td>GLP/GEP: Yes.

Reliability score: (Klimisch et al.,1997): 1.</td><td>Desmarteau, D. A. (2006). [14C-Propamocarb-hydrochloride]: Aerobic soil metabolism in two US soils.

M-270482-01-1

KCA 7.1.2.1.2/01</td></tr>
<tr><td>SFO model

OECD Test Guideline No. 307
US EPA OPPTS Test Guideline No. 835.4100
Regulation (EC) No. 1107/2009 Commission Regulation (EU) No 283/2013.</td><td>Following application of 14C-N-desmethyl-propamocarb to four soils, degradation was rapid to form 14C-carbon dioxide and non-extractable residues as predominant transformation products underlining the biotic character of conversion of this compound in aerobic soil. Values for ^{14}C-N-desmethyl-propamocarb extractable from soil decreased from 100.6% (day zero) to 2.8% (day 7) in soil LS 2.2, from 98.3% to 2.5% in soil Laacher Hof AXXa, from 94.7% to 10.0% in soil Fraunhofer 06A and from 93.6% to 5.0% in soil Attenschwiller.
Best fit degradation kinetics to measured data were obtained by applying the SFO model for all soils. The resulting values for the DT_{50} and DT_{90} of N-desmethyl-propamocarb in aerobic soil are as follows:
<table>
<tr><th>Soil</th><th>DT_{50} [days]</th><th>DT_{90} [days]</th><th>Chi² error</th><th>Visual asses-sment</th><th>Kinetic model</th></tr>
<tr><td>LS2.2</td><td>1.40</td><td>4.63</td><td>12.72</td><td>A</td><td>SFO</td></tr>
<tr><td>Laacher Hof AXXa</td><td>0.78</td><td>2.61</td><td>4.64</td><td>A</td><td>SFO</td></tr>
</table></td><td>GLP/GEP: Yes.

Reliability score: (Klimisch et al.,1997): 1.</td><td>Walther, D. (2015a). [14C]N-desmethyl-propamocarb: Rate of degradation in four soils incubated under aerobic conditions.

M-530922-01-1

KCA 7.1.2.1.2/02</td></tr>
</table>

OECD Test Guideline No. 307 US EPA OPPTS Test Guideline No. 835.4100. Regulation (EC) No. 1107/2009. Commission Regulation (EU) No 283/2013.	Following application of 14C-propamocarb-N-oxide to four soils, degradation was rapid to form 14C-carbon dioxide and non-extractable residues as predominant transformation products underlining the biotic character of conversion of this compound in aerobic soil. Values for ^{14}C-propamocarb-N-oxide extractable from soil decreased from 95.0% (day zero) to 8.3% (day 10) in soil LS 2.2, from 93.7% to 1.9% in soil Laacher Hof AXXa, from 84.7% to 0.8% in soil Fraunhofer 06A and from 83.7% to 1.2% in soil Attenschwiller. The degradation resulted in half-lives of 0.78 to 3.40 days following best fits from SFO for two soils or the FOMC multi-compartment model for the other two.	GLP/GEP: Yes. Reliability score: (Klimisch et al.,1997): 1.	Walther, D. (2015b). *[14C]propamocarb-N-oxide: Rate of degradation in four soils incubated under aerobic conditions*. M-530457-01-1 KCA 7.1.2.1.2/03
FOCUS Guidance "Generic Guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". EC Document Reference: None, version 1.1, 2015 amending "Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference Sanco /10058/2005 version 2.0, 2006. SFO kinetic model and Bi-phasic models FOMC or DFOP, in case of unacceptable fits.	Trigger endpoints: The non-normalised half-life of *N*-desmethyl-propamocarb was 11.1 days for Porterville loamy sand soil while the value for the DT_{90} was 36.9 days for the same soil. Comparison against EU triggers - Summary of results of kinetic evaluation of degradation for N-desmethyl-propamocarb in aerobic soil in the laboratory: Modelling endpoints: The 'all-SFO' approach in combination with the active substance was confirmed as the visually and statistically best acceptable kinetic model for deriving the modelling endpoint. The overall mean normalised half-life of N-desmethyl propamocarb was estimated to be 11.2 days. Modelling endpoints: Normalised laboratory DT50 values for N-desmethyl propamocarb in aerobic soil for use as input in environmental exposure assessments: The evaluation of aerobic soil degradation data according to actual FOCUS kinetic guidance resulted in a non-normalised half-life of 11.1 days and a DT90 of 36.9 days for the metabolite N-desmethyl propamocarb for comparison with EU trigger endpoints. Degradation was found to be adequately described by SFO as kinetic model for all data sets to fit with experimental data. The approach for fitting with experimental data resulted in the use of the SFO kinetic model to derive non-normalised values for the DT50 then normalised for moisture (pF2) and temperature (20°C). The evaluation resulted in a normalized half-life of 11.1 days for use as modelling input parameter in environmental risk assessments. The value derived is regarded as suitable and reliable for use in environmental exposure assessments.	GLP/GEP: No. Reliability score: (Klimisch et al.,1997): 1.	KCA 7.1.2.1.2/04; Oberdoerster, C.; Boiselle, N.; Hoerold, C.; 2015a; M-541770-01-1 Kinetic evaluation of the degradation of propamocarb-hydrochloride and its metabolite N-desmethyl-propamocarb in soil under aerobic laboratory conditions

Fraunhofer 06A	3.40	11.3	2.45	A	SFO
Attenschwiller	1.81	6.02	11.61	A	SFO

Visual assessment of fit to be acceptable (A) or unacceptable (U)

Parameter	*N*-Desmethyl-propamocarb
20°C, Non-normalised DT_{50}, range (days)	11.1
Worst case DT_{50} (days)	11.1
20°C, Non-normalised DT_{90}, range (days)	36.9
Worst case DT_{90} (days)	36.9

Parameter	N-Desmethyl-propamocarb
Normalised (20°C, pF2) DT_{50}, range (days)	11.2
Geometric mean	n.a.

	Trigger endpoints: The non-normalised half-lives of *N*-desmethyl-propamocarb ranged from 0.76 days for Laacher Hof AXXa sandy loam soil to 3.19 days for Fraunhofer 06A soil while the corresponding values for the DT_{90} were from 3.22 days to 12.14 days for the same soils. Comparison against EU triggers: Summary of results of kinetic evaluation of degradation for N-desmethyl- propamocarb in aerobic soil in the laboratory: Parameter / *N*-Desmethyl-propamocarb 20°C, Non-normalised DT_{50}, range (days) / 0.76 – 3.19 Worst case DT_{50} (days) / 3.19 20°C, Non-normalised DT_{90}, range (days) / 3.22 – 12.14 Worst case DT_{90} (days) / 12.14 For completeness, includes values derived from active substance study Modelling endpoints: The kinetic model SFO was the visually and statistically best acceptable kinetic model for deriving the modelling endpoint for all soils. The values were normalised by comparison of study incubation conditions to reference conditions (20°C, pF2 moisture). For use as modelling endpoint and considering the results of a study performed with the active substance, the overall geometric mean normalised half-life of N-desmethyl propamocarb was estimated to 2.03 days. Parameter / N-Desmethyl-propamocarb Normalised (20°C, pF2) DT_{50}, range (days) / 0.67 – 2.36 Geometric mean / 1.32 Normalised (20°C, pF2) DT_{50}, range (days) / 0.67 – 11.1* Geometric mean / 2.03* *For completeness, includes value derived from active substance study Conclusion: For comparison with EU trigger endpoints the evaluation of aerobic soil degradation data according to actual FOCUS kinetic guidance resulted in non-normalised half-lives for metabolite N-desmethyl propamocarb to range from 0.76 days to 11.1 days and values of the DT90 of ranging from 2.52 days to 36.9 days. Degradation was found to be adequately described by SFO as kinetic model for all data sets to fit with experimental data. For use as modelling input parameter in environmental risk assessments the evaluation resulted in a normalized geometric mean half-life of 2.03 days for the total of data sets available. The approach for fitting with experimental data resulted in the use of the SFO kinetic model to derive non-normalised values for the DT50 then normalised for moisture (pF2) and temperature (20°C).	GLP/GEP: No. Reliability score: (Klimisch et al.,1997): 1.	Oberdoerster, C. & Hoerold, C. (2015a). *Kinetic evaluation of the degradation of N-desmethyl-propamocarb in soil under aerobic laboratory conditions.* M-541686-01-1 KCA 7.1.2.1.2/05

<table>
<tr>
<td>FOCUS Guidance “Generic Guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration”. EC Document Reference: None, version 1.1, 2015 amending “Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration”. Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference Sanco /10058/2005 version 2.0, 2006.

SFO kinetic model and Bi-phasic models FOMC or DFOP, in case of unacceptable fits.</td>
<td>Trigger endpoints: Non-normalised values of the DT_{50} and the DT_{90} were derived from an SFO best fit for one soil while use of FOMC (one soil) or DFOP (two soils) resulted in best fits to measured data.
The non-normalised half-lives of propamocarb-N-oxide ranged from 0.06 days for Fraunhofer silty clay soil to 2.37 days for the Speyer 2.2 loamy sand. The values for the DT_{90} were from 0.46 days to 9.14 days for the same soils.

<table>
<tr><td>Parameter</td><td>propamocarb-N-oxide</td></tr>
<tr><td>20°C, Non-normalised DT_{50}, range (days)</td><td>0.06 – 2.37</td></tr>
<tr><td>Worst case DT_{50} (days)</td><td>2.37</td></tr>
<tr><td>20°C, Non-normalised DT_{90}, range (days)</td><td>0.46 – 9.14</td></tr>
<tr><td>Worst case DT_{90} (days)</td><td>9.14</td></tr>
</table>

Modelling endpoints: Non-normalised values of the DT_{50} and the DT_{90} were derived from SFO best fits for two soils while use of FOMC (two soils) resulted in visually and statistically best acceptable kinetic models for deriving the modelling endpoint. The values were normalised by comparison of study incubation conditions to reference conditions (20°C, pF2 moisture).
For use as modelling endpoint, the geometric mean normalised half-life of propamocarb-N-oxide was estimated to 1.60 days.

<table>
<tr><td>Parameter</td><td>propamocarb-N-oxide</td></tr>
<tr><td>Normalised (20°C, pF2) DT_{50}, range (days)</td><td>0.12 – 2.55</td></tr>
<tr><td>Geometric mean</td><td>1.60</td></tr>
</table>

Conclusions:
For trigger endpoints the evaluation of aerobic soil degradation data according to actual FOCUS kinetic guidance resulted in non-normalised half-lives of metabolite propamocarb-N-oxide to range from 0.06 days to 2.37 days and values of the DT90 to range from 0.46 days to 9.14 days. Degradation was found to be adequately described by SFO as kinetic model for one soil while bi-phasic kinetic models showed best fits with experimental data for three soils.
For use as modelling input parameter in environmental risk assessments the evaluation of the total sets of data available resulted in a normalized geometric mean half-life of 0.71 days.
The approach for fitting with experimental data resulted in the use of the SFO kinetic model for two soils and bi-phasic kinetic models for another two soils to derive non-normalised values for the DT50 then normalised for moisture (pF2) and temperature (20°C).</td>
<td>GLP/GEP: No.

Reliability score: (Klimisch et al.,1997): 1.</td>
<td>Oberdoerster, C. & Hoerold, C. (2015b). Kinetic evaluation of the degradation of propamocarb-N-oxide in soil under aerobic laboratory conditions.

M-541685-01-1

KCA 7.1.2.1.2/06</td>
</tr>
<tr><td colspan="4">Anaerobic degradation in soil</td></tr>
<tr>
<td>-</td>
<td>In laboratory investigations, propamocarb hydrochloride slowly degraded representing 67.2% AR by day 180 under anaerobic conditions with only slight CO2 evolution from the test system (maximum of 7.7 %). Over the incubation period three unidentified metabolites were observed although none amounted to more than 2.0 % of the applied radioactivity.
Propamocarb hydrochloride degradation for the total system was described assuming first-order degradation of the active substance, described by linear regression. Using linear regression, the following equation was determined for propamocarb hydrochloride degradation (t in days):
Propamocarb hidrocloride was degraded slowly, with 67.2% of the AR attributed to PHC by day 180. PHC degradation for the total system was described assuming first-order degradation of the active substance, described by linear regression. Using linear regression, the following equation was determined for propamocarb hidrochloride degradation (t in days):
$y = 85.5x \cdot e^{-1.51\times10^{-3}t}$</td>
<td>GLP/GEP: No.

Reliability score: (Klimisch et al.,1997): 1.</td>
<td>Bruehl, R. (1979). Degradation of SN 66 752 in a loamy sand under anaerobic conditions.

M-157717-01-1

KCA 7.1.1.2/01</td>
</tr>
</table>

	The r^2 value was determined to be 0.76 and the DT_{50} was calculated to be 459.0 days. The DT_{90} value was calculated to be 1524.9 days. The persistence of propamocarb hydrochloridePHC under anaerobic soil conditions is considerably higher compared to aerobic conditions. The degradation of propamocarb hydrochloridePHC under anaerobic conditions is characterised by an estimated DT50 of 459.0 days (1.25 years). Metabolites were formed in low concentrations, none amounted to more than 2 % AR. Identification of the metabolites was not possible.		
EC Directive 95/3 6/EC, Active Substances, Section 7.1.1.1.2 (July 1995); SETAC Procedures for assessing the Environmental Fate and Ecotoxicity of Pesticides, Section 1.2 (March 1995), EPA, Subdivision N, Section 162-3 (October 1982) and The requirement for safety evaluation of agricultural chemicals published in 59 NohSan No. 4200, Japanese Ministry of Agriculture Forestry and Fisheries (28 January 1985).	Propamocarb hydrochloride degrades relatively slowly under anaerobic experimental conditions, in comparison to aerobic investigations. Observed CO_2 levels were negligible (< 2.0 % after 365 days) throughout the study, indicating that no significant mineralisation of the carbon in the labelled position was observed. Over 30 % of the AR remained in the soil as non-extractable by the end of the study. The most prominent metabolite formed was a polar component (with the same retention time as Unk 1 in study M-310828-02-1), which was observed in soil at a maximum value of 6.61 % of the AR at day 365. The metabolite had a retention time of ~2.5 minutes, but could not be identified (see study KCA7.1.1.1/10). A further six unidentified transient degradation products were also formed. These degradation components were only detected occasionally and were observed with usually ≤ 3.0% of AR. No metabolites were observed accounting for greater than 10% of the AR. The DT_{50} (DT_{90}) of the test item was calculated to be 308 (1024) days in the total system (1st order kinetic, r^2 =0.9815) for incubation group A. The DT_{50} (DT_{90}) of the test item for incubation group B was 66 (218) days in the total system (1st order kinetic, r^2 =0.9838). For different incubation groups, the DT_{50} of the test item was in the range of 308 /66 days (total system, 1st order kinetic).	GLP/GEP: Yes. Reliability score: (Klimisch et al.,1997): 1.	Schnoeder, F. (2002). *(14C)-Propamocarb hydrochloride: Anaerobic route and rate of soil degradation.* M-310969-01-1 KCA 7.1.1.2/02
EC Directive 95/3 6/EC, Active Substances, Section 7.1.1.1.2 (July 1995); SETAC Procedures for assessing the Environmental Fate and Ecotoxicity of Pesticides, Section 1.2 (March 1995), EPA, Subdivision N, Section 162-3 (October 1982) and The requirement for safety evaluation of agricultural chemicals published in 59 NohSan No. 4200, Japanese Ministry of Agriculture Forestry and Fisheries (28 January 1985)	The evaluations revealed that no metabolites were formed specific for the anaerobic conditions of the test. Moreover, it should be noted that propamocarb-hydrochloride is not intended for use in crops where anaerobic conditions in soil are prevalent. No further specific information is, therefore, required.	GLP/GEP: Yes. Reliability score: (Klimisch et al.,1997): 1.	Schnoeder, F. (2002). *(14C)-propamocarb hydrochloride: Anaerobic route and rate of soil degradation.* M-310969-01-1 KCA 7.1.2.1.4/02
Photochemical degradation Soil Photolysis			
US EPA Pesticide Assessment Guidelines, Subdivision N, Section 161-3 (1982)	The degradation of propamocarb hydrochloride was increased when applied only to the soil surface in comparison to the dark control. Under irradiated conditions, propamocarb hydrochloride was more readily degraded (54.6% of the AR after 30.66 days) relative to the dark control (97.6% of AR after 30.66 days). In both irradiated and non-irradiated experimental units an increase in NER was observed along with a concomitant decrease in radioactivity extractable from the soil samples, although these trends were more pronounced in the dark control samples. Propamocarb hydrochloride was the major constituent observed in both irradiated and non-irradiated soil samples during the incubation period. Three metabolites were observed. In additional experiments, the major photodegradation product (occurring at 8.7% of AR) was identified as N,N-dimethyl-N-(3-	GLP/GEP: No. Reliability score: (Klimisch et al.,1997): 1.	Tschampel, M. (1990).*The photodegradation of propamocarb hydrochloride (Schering Code ZK 66 752) on soil surfaces.* M-157828-01-1 KCA 7.1.1.3/01

	propoxycarbonylaminopropyl) amine N-oxide. Exposure to sunlight of the test compound at the soil surface appears to increase degradation of propamocarb hydrochloride relative to the dark control samples. Propamocarb hydrochloride was readily degraded under irradiated conditions on a loamy sand soil. DT_{50} value for propamocarb hydrochloride was estimated from the de-gradation rate k using the follow-ing equation: $DT_{50} = \frac{\ln 2}{k}$ Experimental first-order regression analysis indicated DT_{50} (DT_{90}) values of 35.4 (117.5) days, respectively, although the upper and lower limits of the 95% confidence intervals expanded the range to 20.6 and 123.8 days, respectively. DT50 and DT90 values determined for PHC under irradiated experimental conditions: DT50 (days) = 35.4 (20.6-123.8)[1)] ; DT90 (days) = 117.5 ; [1)] Limits of the 95 % confidence intervals. PHC was readily degraded under irradiated conditions on a loamy sand soil.		Tschampel, M. (1994).*Addendum to report APC 87/90 - The photodegradation of propamocarb hydrochloride (Schering Code ZK 66 752) on soil surfaces.* M-157830-01-1 KCA 7.1.1.3/02
SETAC-Europe, Procedures for Assessing the Environmental Fate and Ecotoxicity of Pesticides, Part 1, Section 2 (1995); US EPA Pesticide Assessment Guidelines, Subdivision N, Section 161-3 (1982) (see page 12).	Irradiation of propamocarb hydrochloridePHC didn´t augment or increase the rate at which PHC the substance was degraded on soil surface, instead the rate of degradation was limited, may be as a result of reduced local soil moisture content at the soil surface, due to drying effects of the light source. .The resulting DT50 of propamocarb hydrochloridePHC was 199.2 days. In contrast, propamocarb hydrochloridePHC degradation rate was increased in the dark control relative to the irradiated test soil, with a DT50 value of 103.1 days. In both irradiated and non-irradiated experimental units, an increase in NER non-extractable residues was observed along with a concomitant decrease in radioactivity extractable from the soil samples. Propamocarb hydrochloridePHC was the major constituent in both irradiated and non-irradiated soil samples during the incubation period. No significant production of photo-degradation metabolites occurred. Exposure to sunlight is not expected to increase the PHC degradation or lead to the formation of unique photo-degradates. PHC degradation was described assuming first-order degradation of the active substance, described by the regression equation $y = a \cdot e^{-k1 \cdot t}$	GLP/GEP: Yes. Reliability score: (Klimisch et al.,1997): 1.	Yeomans, P. (2001). (*14 C)-propamocarb hydrochloride: Photodegrada-tion on a soil surface.* M-310966-01-1 KCA 7.1.1.3/03
Aquatic systems – Direct photochemical degradation			
US EPA, Federal Register, 40, 26883, 25th June, 1975 (page 5).	The degradation of PHCpropamocarb hydrochloride, under irradiation for 92 hours at a wavelength (□) > 290 nm and at a light intensity of 2,250 J m-2 sec-1 in aqueous solution at a pH of between 5.5 and 6.0 and an initial concentration of 500 mg/L, was not greater than in a corresponding solution without irradiation. A slight decrease in the concentration of PHC was noted in both the photochemical and dark solutions. However, this was attributed to possible microbial degradation in solution. No photodegradates of propamocarb hydrochloridePHC were detected. Therefore, photodegradation was not considered a relevant pathway for propamocarb hydrochloridePHC in the aquatic environment.	GLP/GEP: No. Reliability score: (Klimisch et al.,1997): 1.	Klehr, M. (1978). *Photolysis of propamocarb. HCl (SN 66 752) in aqueous solution.* M-157849-01-1 KCA 7.2.1.2/01
Guideline(s): not specified	In study M-157698-01-1, the photolytic degradation of propamocarb hydrochloridePHC was investigated in a heat sterilised buffer solution at a pH of between 4 and 5. No significant difference was recorded in the PHC concentration after, approximately, 22 days (522.6 hours) of irradiation, with artificial sunlight. Therefore, photodegradation was not a relevant degradation pathway for propamocarb hydrochloride in the aquatic environment. No photodegradates of propamocarb hydrochloride were detected. Therefore, photodegradation was not considered a relevant pathway for propamocarb hydrochloride in the aquatic environment.	GLP/GEP: No. Reliability score: (Klimisch et al.,1997): 1.	Klehr, M. (1980). *Photolysis experiments with propamocarb HCL (SN 66 752) in heat sterilised aqueous solution.* M-157698-01-1 KCA 7.2.1.2/02

<table>
<tr>
<td>Guideline(s):

The Phototransformation of Chemicals in Water, ECETOC – Technical Report No. 12, Brussels 1984.</td>
<td>Propamocarb hydrochloride is not expected to photodegrade as absorption was noted in the λ max < 250 nm range. As energy is the prime requisite for a photochemical reaction, irradiation of propamocarb hydrochloride in the spectrum of λ > 290 nm is not expected to induce any photochemical transformation. The maximum molecular extinction coefficient and λmax were determined for NaOH at 261.0 dm3 mol-1 cm^{-1} and 217 nm, respectively. The maximum molecular extinction coefficient and λ max were determined for NaOH at 261.0 dm^3 mol^{-1} cm^{-1} and 217 nm, respectively. Propamocarb hydrochloride is unlikely to photodegradate owing to the low optical density of the test material at wavelengths greater than 290 nm.

Molecular extinction coefficients for non-labelled PHC at the λ max:
<table>
<tr><th>Solution matrix</th><th>Solution concentration (g/L)</th><th>Absorbance</th><th>λmax (nm)</th><th>ε (dm^3 mol^{-1} cm^{-1})</th></tr>
<tr><td>pH 7 buffer solution</td><td>1.17</td><td>1.1090</td><td>203</td><td>214</td></tr>
<tr><td>0.1M hydrochloride (pH <1)</td><td>1.20</td><td>1.2463</td><td>203</td><td>234</td></tr>
<tr><td>0.1M NaOH (pH > 13)</td><td>1.14</td><td>1.3236</td><td>217</td><td>261</td></tr>
</table>
</td>
<td>GLP/GEP: No.

Reliability score: (Klimisch et al.,1997): 1.</td>
<td>Mullee, D. M.; Bartlett, A. J. (1995). Propamocarb hydrochloride: Determination of photochemical degradation. M-310246-01-1

KCA 7.2.1.2/03</td>
</tr>
<tr><td colspan="4">Aquatic systems – Indirect photochemical degradation</td></tr>
<tr>
<td>The photolysis of 1-N-propyl-^{14}C-labeled PHC was investigated in sterile natural water.

Guideline(s):

JMAF: 13 Seisan No. 3986, October 10, 2001, 2-6-2, amended June 26, 2001, Nousan 8147. (Japan).</td>
<td>The data of this study are regarded as supplemental information.

The total irradiation time of four days (96 experimental hours) in maximum corresponded to 30.4 environmental days under light conditions of Tokyo, Japan from April to June to reflect a worst-case approach.
The mean recovered radioactivity ranged from 98.8 to 100.3% AR for irradiated samples and from 97.6 to 99.5% for dark controls. Volatile components including ^{14}C-carbon dioxide were not determined considering recoveries of > 97% AR in the test solutions. Formation of volatiles was, thus, expected to be insignificant. In irradiated samples, ^{14}C- propamocarb hydrochloride decreased from 99.0 % of AR at time zero to 91.6 % after 4 days of irradiation.
Irradiation resulted in formation of a number of minor photo-transformation products, occurring at 4.7 % after 3 days and 4 days in maximum, with none of the components exceeding 5 % of AR. In dark controls, no significant degradation (was negligible) of the ^{14}C-propamocarb hydrochloride was observed, as demonstrated by values of 99.0% AR at time zero to 97.5% after four days of incubation.
The experimental DT50 value for propamocarb hydrochloride in irradiated samples was calculated by applying a SFO kinetic model. No experimental DT50 value was calculated for dark controls considering the stability of the compound under the conditions of the test. The experimental DT50 was 40.9 days for irradiated samples and wasn´t corrected for biological degradation, due to the insignificant degradation observed in dark controls. When transferring this result to outdoor conditions, considering the (lower) light intensities of natural sunlight in Tokyo, Japan, the value for the DT50 was 310.8 days.
Therefore, indirect photolysis contribute in a negligible extent to the overall elimination of propamocarb hydrochloride from the aquatic environment. No major and distinct transformation products that require further assessment in environmental exposure assessments were, therefore, observed.</td>
<td>GLP/GEP: Yes.

Reliability score (Klimisch et al.,1997): 2.</td>
<td>Roohi, A. (2004). (14C)-propamocarb Hydrochloride: Aqueous photolysis in natural water. M-237606-01-1

KCA 7.2.1.3/01</td>
</tr>
</table>

11.1.1 Ready biodegradability

This data requirement was addressed under Point 7.2.1.3.1 of the Dossier submitted. Here is presented an overall summary of the reported test/study.

Report:	KCA 7.2.2.1/01; Desmares-Koopmans, M. J. E.; 1999; M-310925-01-1
Title:	Propamocarb hydrochloride: Determination of ready biodegradability: Carbon dioxide (CO2) evolution test (Modified Sturm Test) with Proplant
Report No.:	247207
Document No.:	M-310925-01-1
Guideline(s):	OECD 301 B
Guideline deviation(s):	not specified
GLP/GEP:	**yes**

Executive Summary

Three experiments were carried out in this study: in experiments 1 and 2, the test media were prepared using a stock solution of the test substance in purified water whereas, in experiment 3, the test substance was quantitatively added to the test media. In all experiments the test solutions were continuously stirred during the test. For some inoculations under the conditions of the modified Sturm test, Proplant had the potential to be readily biodegradable.

I. Material and Methods

A. Materials

1. Test Material: Proplant, aqueous formulation, containing 722 g/L propamocarb hydrochloride Density 1.0842g/mL

B. Study design

1. Experimental conditions: The test material Proplant, containing 722 g/L of propamocarb hydrochloride was mixed with inoculum from activated sludge freshly obtained from a sewage treatment plant in the Netherlands and added to a mineral medium. The target treatment rate was 64 mg per 2 litres of mineral medium, corresponding to 12 mg total organic carbon (TOC) per litre. The sludge was kept under continuous aeration prior to the experiment. The concentration of suspended solids was 3 – 4 g/L in the concentrated sludge for the three experiments. Before use, the sludge was allowed to settle for at least 30 minutes and the liquid decanted for use as inoculum at the amount of 10 mL/L of mineral medium.
The incubations lasted 28 days and were maintained under CO_2-free air. A mixture of oxygen (21%) and nitrogen (79%) was led through a bottle, containing 0.5 – 1 litre 0.0125M $Ba(OH)_2$ solution to trap CO_2 which might be present in small amounts. The CO_2-free air was sparged through the scrubbing solutions at a constant rate.
In addition to the test systems, blanks, positive controls and toxicity controls were prepared. The test suspension contained test substance and inoculum. The blanks contained only inoculum. The positive controls contained inoculum and approximately 40 mg/L of Natrium-acetate (equivalent to a total organic carbon of 12 mg/L). The toxicity control contained test substance, Natrium-acetate and inoculum together. The test substance and positive control were then added to incubation bottles containing the mineral medium. The volumes of suspensions were made up in all bottles by the addition of Milli-Q water previously aerated with CO_2-free air. Three CO_2 absorbers (bottles filled with 100 mL 0.0125M $Ba(OH)_2$) were connected in series to the exit air line of each test bottle. The test was started by bubbling CO_2-free air through the solution at a rate of approximately 1 – 2 bubbles per second (approximately 30 – 100 mL/min).
The CO_2 produced in each test bottle reacted with the barium hydroxide in the gas scrubbing bottle and precipitated out as barium carbonate. The amount of CO_2 produced was determined by titrating the remaining $Ba(OH)_2$ with 0.05M standarised hydrochloride. Titrations of CO_2 absorbers were made every second or third day for the first 10 days, then, at least, every fifth day until the end of incubation on Day 28. On the 28th day, the pH of the test suspensions was measured and 1 mL of concentrated

hydrochloride was added to each bottle. The bottles were aerated overnight to drive off CO_2 present in the test suspension. The final titration was made on Day 29.

2. Determination of theoretical CO_2 production: The theoretical CO_2 ($ThCO_2$) production was calculated from the molecular formula and the propamocarb hydrochloride content. $ThCO_2$, expressed as mg CO_2/mg test substance, that can be generated by a test substance was calculated as follows:

$$ThCO_2 = \frac{No.\,of\ carbon\ \ atoms\,in\,test\,substance \times MW\ CO_2}{MW\ test\ substance} \times 0.651$$

MW = molecular weight; PROPLANT is a formulation in water containing 651 g propamocarb hydrochloride per kg PROPLANT (active ingredient).

II. Results and Discussion

The theoretical CO_2 production ($ThCO_2$) of Proplant (MW = 188.3 g, propamocarb hydrochloride content: 651 g/kg) was calculated to be 1.37 mg CO_2/mg. Three experiments were conducted with the theoretical CO_2 production ($ThCO_2$) for test systems containing Proplant and inoculum being 87.7 mg, 88.2 mg and 88.1 mg per 2 litres for experiments 1, 2 and 3 respectively, assuming complete degradation. The results of the biodegradation test were considered to be valid if:
(a) the total CO_2 evolution in the inoculum blank at the end of the test did not normally exceed 40 mg/L;
(b) the difference of duplicate values for the % degradation of the test substance at the plateau, at the end of the test or at the end of the 10-day window, as appropriate, was less than 20;
(c) the percentage degradation of the reference substance reached the level for the ready biodegradability (60%) by 14 days.

The results of the biodegradation test for experiments 1, 2 and 3 are presented in Table 11.1.1-01. The results of each experiment are described as follows:
Experiment 1: Bottle A revealed no significant degradation of Proplant during the test period whereas bottle B revealed 68% degradation of Proplant as shown in Table 11.1.1-02. Furthermore, biodegradation of Proplant of approximately 60 % was reached within 10 days of biodegradation exceeding 10%.
In the toxicity control more than 25% degradation occurred within 14 days (based on $ThCO_2$). Therefore, the test substance was assumed to be not inhibitory. The cumulative CO_2 production of the toxicity control was comparable to the cumulative CO_2 production of the positive control substance. This indicated that there may be no additional CO_2 production originating from Proplant, which is comparable to test bottle A. In the first experiment the difference of duplicate values for % degradation of Proplant was more than 20. Therefore, a second experiment was performed.

CO_2 production and percentage biodegradation of Proplant in the modified Sturm test:

Day	Experiment 1		Experiment 2		Experiment 3	
	Cumulative CO_2 (mg/L)	Degradation (%)	Cumulative CO_2 (mg/L)	Degradation (%)	Cumulative CO_2 (mg/L)	Degradation (%)
CO_2 production and percentage biodegradation of the positive control substance						
2	10.7	12.5	14.1	16.4	1.2	1.4
5	33.3	38.9	33.1	38.5	27.6	32.2
7	46.6	54.4	44.2	51.4	40.1	46.8
9	56.4	65.8	47.4	55.1	47.7	55.7
14	62.8	73.3	54.9	63.8	52.0	60.7
19	66.5	77.6	57.2	66.5	57.6	67.2
23	68.8	80.3	57.9	67.3	60.7	70.8
27	70.6	82.4	58.8	68.4	62.5	72.9

Day	Experiment 1		Experiment 2		Experiment 3	
	Cumulative CO_2 (mg/L)	**Degradation (%)**	**Cumulative CO_2 (mg/L)**	**Degradation (%)**	**Cumulative CO_2 (mg/L)**	**Degradation (%)**
29	72.3	84.4	47.4	69.7	62.5	72.9
29	73.4	85.6	59.9	69.7	62.5	72.9
29	74.0	86.3	60.0	69.8	62.5	72.9
CO_2 production and percentage biodegradation of the test substance (bottle A)						
2	0.0	0.0	0.8	0.9	0.0	0.0
5	0.0	0.0	8.3	9.4	0.1	0.1
7	0.0	0.0	25.1	28.5	0.1	0.1
9	0.1	0.1	44.2	50.1	0.1	0.1
14	0.3	0.3	58.7	66.6	0.1	0.1
19	0.3	0.3	64.0	72.6	0.1	0.1
23	0.4	0.5	65.9	74.7	0.1	0.1
27	0.7	0.8	67.0	76.0	0.1	0.1
29	0.7	0.8	67.0	76.0	0.1	0.1
29	0.9	1.0	67.0	76.0	0.1	0.1
29	0.9	1.0	67.0	76.0	0.1	0.1
CO_2 production and percentage biodegradation of the test substance (bottle B)						
2	0.0	0.0	0.0	0.0	0.0	0.0
5	0.7	0.8	0.0	0.0	0.6	0.7
7	2.1	2.4	0.0	0.0	0.6	0.7
9	7.9	9.0	0.0	0.0	0.6	0.7

Day	Experiment 1		Experiment 2		Experiment 3	
	Cumulative CO_2 (mg/L)	Degradation (%)	Cumulative CO_2 (mg/L)	Degradation (%)	Cumulative CO_2 (mg/L)	Degradation (%)
14	36.8	42.0	0.6	0.7	1.0	1.1
19	51.3	58.5	0.6	0.7	1.0	1.1
23	57.4	65.5	0.6	0.7	1.2	1.4
27	58.7	66.9	0.8	0.9	2.0	2.3
29	59.2	67.5	0.8	0.9	2.0	2.3
29	59.8	68.2	0.8	0.9	2.3	2.6
29	60.0	68.4	0.8	0.9	2.3	2.6
CO_2 production and percentage biodegradation of the toxicity control						
2	11.4	6.6	12.9	7.4	11.3	6.5
5	35.2	20.3	30.5	17.5	36.6	21.0
7	48.5	28.0	39.6	22.7	60.6	34.7
9	57.1	32.9	58.3	33.4	71.3	40.9
14	63.3	36.5	96.7	55.5	98.9	56.7
19	68.5	39.5	122.7	70.4	112.5	64.5
23	71.9	41.5	136.3	78.2	121.5	69.6
27	72.1	41.6	142.2	81.6	129.1	74.0
29	72.8	42.0	145.9	83.7	134.0	76.8
29	73.1	42.2	145.9	83.7	135.2	77.5
29	73.2	42.2	145.9	83.7	135.2	77.5

CO_2 production and percentage biodegradation of Proplant in the modified Sturm test:

Day	Experiment 1		Experiment 2		Experiment 3	
	Cumulative CO_2 (mg/L)	Degradation (%)	Cumulative CO_2 (mg/L)	Degradation (%)	Cumulative CO_2 (mg/L)	Degradation (%)
CO_2 production in the blank						
2	1.4	-	1.9	-	1.4	-
5	4.3	-	4.5	-	4.7	-
7	6.8	-	7.4	-	8.3	-
9	9.3	-	10.0	-	11.6	-
14	11.6	-	12.4	-	14.3	-
19	15.0	-	16.5	-	18.2	-
23	18.2	-	21.1	-	23.4	-
27	22.4	-	25.3	-	27.6	-
29	26.5	-	29.2	-	32.3	-
29	29.5	-	32.1	-	34.5	-
29	29.8	-	33.2	-	35.1	-

Experiment 2: In test bottle A the relative degradation values calculated from the measurements performed during the test period revealed 76% degradation of Proplant. Furthermore, biodegradation of Proplant of at least 60% was reached within 10 days of biodegradation exceeding 10%. However, in test bottle B the relative degradation values calculated from the measurements performed during the test period revealed no significant degradation of Proplant.
In the toxicity control more than 25% degradation occurred within 14 days (based on $ThCO_2$). Therefore, the test substance was assumed to be not inhibitory. The cumulative CO_2 production of the toxicity control was 86 mg more than in the positive control bottle. This indicated that there may be CO_2 production originating from Proplant, which is comparable to test bottle A. In the second experiment the difference of duplicate values for percentage degradation was again more than 20, therefore, a third experiment was carried out.

Experiment 3: In the third experiment the relative degradation values calculated from the measurements performed during the test period revealed no significant degradation of Proplant in both test bottles. Thus, the difference of duplicate values for percentage degradation of Proplant was always less than 20. In the toxicity control more than 25% degradation occurred within 14 days (based on $ThCO_2$). Therefore, the test substance was assumed to be not inhibitory. The cumulative CO_2 production of the toxicity control was 73 mg more than in the positive control bottle. This indicated that there may be CO_2 production originating from Proplant, comparable to approximately 82% degradation. This was not found in test bottle A and B.

Degradation of Proplant:

Test bottle	Experiment 1	Experiment 2	Experiment 3
A	No	Yes	No
B	Yes	No	No
Toxicity control	No	Yes	Yes

In all experiments, the temperature recorded in a vessel with water in the same room varied between 20.5 °C and 22 °C. Table 11.1.1-04 shows the pH values of the different test media just before the start of the test and on Day 28.

pH values of the different test media just before the start of the test and on day 28:

Test medium	Experiment 1		Experiment 2		Experiment 3	
	Just before the start of the test	On Day 28	Just before the start of the test	On Day 28	Just before the start of the test	On Day 28
Blank control (A)	7.6	7.7	7.5	7.5	7.6	7.7
Blank control (B)	7.6	7.7	7.5	7.5	7.6	7.7
Positive control	7.6	8.2	7.6	7.8	7.6	8.1
PROPLANT (A)	7.6	7.8	7.5	7.3	7.6	7.7
PROPLANT (B)	7.6	7.7	7.5	7.5	7.6	7.7
Toxicity control	7.6	8.0	7.5	7.9	7.6	8.2

III. Conclusion

The evaluation revealed that, for some inoculations under the conditions of the modified Sturm tests, Proplant has the potential to be readily biodegradable/can be regarded as readily biodegradable. However, in some test vessels under the same conditions, no significant degradation of Proplant was observed, therefore, with results being variable. No explanation could be given for this variation.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

In view of the variable results obtained in the study presented above, on ready biodegradability, new data was generated, following actual designs of OECD 301. This data, which is presented below, was not evaluated at EU level so far.

Report:	KCA 7.2.2.1/03; Weyers, A.; 2008; M-299907-02-1
Title:	Biodegradation with Propamocarb-hydrochloride
Report No.:	2008/0004/01
Document No.:	M-299907-02-1
Guideline(s):	Council Directive 92/69/EEC Method C.4-D Manometric Respirometry Test (1992). This test method is in all essential parts identical with OECD Guideline 301 F.
Guideline deviation(s):	None
GLP/GEP:	**Yes**

Executive Summary

The ready biodegradability of non-labeled active substance propamocarb hydrochloride was investigated in a mineral medium inoculated by an activated sewage sludge at a test concentration of 100 mg a.s./L under conditions of a 'Manometric Respirometry Test' in its essential parts being identical with conditions of OECD 301 F. Samples were incubated at 22 ±1 C in the dark for 28 days in maximum.
Propamocarb hydrochloride is considered to be ready biodegradable, under the conditions of the test after fulfilling the criteria set according to OECD 301 F.

I. Material and Methods

A. Materials

1. Test Material: propamocarb-hydrochloride
Chemical purity: 74.8%
Sample ID: EK1C000096

2.Test system

The activated sludge used as origin for the inoculum in the test was collected from a wastewater treatment plant treating predominantly domestic sewage (i.e. wupper area water authority, treatment plant Odenthal, Germany).
The inoculum was prepared by diluting 30 mg sewage sludge in 1L water.

B. Study design

1. Experimental conditions: Samples of 250 mL mineral medium containing the inoculum were treated with the test substance to result in a test concentration of 100 mg a.s./L. The samples were incubated in the dark at 22±1°C for 28 days in maximum. Each sample was attached to an 'OxiTop' system for determination of carbon dioxide formed in the course of the test.
In addition, samples containing the reference substance sodium benzoate, untreated blank controls and toxicity controls were incubated under the same conditions and measured at the same time points.
2. Sampling and analytical procedures: The biological oxygen demand (BOD) in terms of mg O_2/L was determined on the basis of carbon dioxide formed for single (toxicity control), duplicate (test substance and reference substance) and triplicate samples (blank controls) daily for a maximum of 28 days.

3. Evaluation: The BOD of the test substance was compared with the BOD of blank controls to result in a corrected BOD for each sample at each day. Based on the known BOD of the test substance applied the percentage of degradation was determined correspondingly.

II. Results and Discussion

The temperature was maintained at 22 ± 1 during the test. Biological activity of the inoculated mineral medium was confirmed by the degradation of the reference substance.

The mean percentage of degradation on the basis of the difference in BOD for test substance and blank controls was determined to 62.8% after 28 days of incubation.

The reference compound was degraded and reached the level for ready biodegradability within 14 days of incubation thus indicating sufficient microbial activity of the test system.

No toxicity of the test substance was observed in toxicity controls.

The percentage of biodegradation between the duplicate samples/ in paralels with test item tested did not differ by more than 20 percentage points at the various time points of determination (i.e. at the plateau, after the 10-day-window and at the end of incubation).

The oxygen consumption of the blank inoculum samples was ≤ 60 mg/L.

In cases where the degradation was ≤ 60 %, the pH value was between 6.0 and 8.5 at the end of the test (and, thus, poor degradation was not caused by the pH value).

The mean percentage of propamocarb-hydrochloride degradation, on the basis of the difference in BOD for test substance and blank controls was determined to 62.8% after 28 days of incubation. Propamocarb-hydrochloride is considered to be "Readily Biodegradable".

In summary, the validity criteria of the test were, therefore, all met.

RESULTS (OXITOP SYSTEM)

BOD (mg O_2/L) after n days

	test item		blank			blank mean	reference compound		toxicity control
flask no.	15	16	1	2	3		4	5	17
code*	a1	a2	b1	b2	b3	bm	r1	r2	t1
time (d)									
0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
1	7.0	5.6	4.2	4.2	4.2	4.2	25.2	23.8	29.4
2	11.2	9.8	7.0	8.4	8.4	7.9	76.9	79.7	81.1
3	12.6	11.2	9.8	9.8	11.2	10.3	93.7	96.5	112.0
4	25.2	14.0	11.2	11.2	12.6	11.7	110.0	116.0	131.0
5	71.3	50.3	12.6	12.6	15.4	13.5	124.0	127.0	151.0
6	79.7	78.3	12.6	14.0	15.4	14.0	133.0	136.0	206.0
7	95.1	93.7	14.0	14.0	18.2	15.4	140.0	141.0	228.0
8	113.0	113.0	15.4	15.4	19.6	16.8	143.0	145.0	243.0
9	123.0	123.0	15.4	16.8	21.0	17.7	145.0	148.0	253.0
10	134.0	133.0	15.4	16.8	21.0	17.7	150.0	150.0	263.0
11	150.0	144.0	16.8	18.2	22.4	19.1	152.0	152.0	273.0
12	154.0	157.0	16.8	18.2	23.8	19.6	152.0	154.0	281.0
13	157.0	164.0	18.2	18.2	25.2	20.5	155.0	157.0	287.0
14	159.0	168.0	18.2	19.6	26.6	21.5	158.0	158.0	289.0
15	162.0	171.0	19.6	21.0	29.4	23.3	159.0	159.0	289.0
16	165.0	175.0	19.6	19.6	29.4	22.9	159.0	159.0	288.0
17	169.0	179.0	21.0	22.4	30.8	24.7	161.0	162.0	288.0
18	172.0	180.0	22.4	22.4	32.2	25.7	162.0	162.0	288.0
19	173.0	183.0	22.4	23.8	33.6	26.6	164.0	164.0	287.0
20	175.0	185.0	23.8	23.8	36.4	28.0	164.0	165.0	287.0
21	178.0	187.0	23.8	26.6	39.2	29.9	166.0	166.0	288.0
22	178.0	189.0	25.2	26.6	40.6	30.8	168.0	168.0	288.0
23	180.0	190.0	26.6	28.0	43.3	32.6	169.0	169.0	288.0
24	180.0	192.0	26.6	29.4	44.7	33.6	169.0	171.0	288.0
25	180.0	193.0	26.6	29.4	46.1	34.0	171.0	171.0	287.0
26	182.0	194.0	26.6	29.4	47.5	34.5	171.0	172.0	287.0
27	183.0	196.0	26.6	30.8	50.3	35.9	173.0	173.0	287.0
28	133.2	147.2	28.0	30.8	53.1	37.3	173.0	173.0	287.0

Comments: *Abbreviations according to test guideline.

The oxygen uptake by nitrification was determined (see Annex 1). The oxygen consumed by nitrification was 49.81 mg/L.

RESULTS (OXITOP SYSTEM)

Degradation of test item

Test concentration : 100 mg/L
Empirical formula : $C_9H_{21}ClN_2O_2$
Molecular weight : 224.7 g/mol
Theoretical oxygen demand : 1.638 mg O_2/mg

test item					
	corrected BOD test item (a-bm) (mg O_2/L)		% degradation		% degradation mean
time (d)	a1	a2	a1	a2	
0	0.0	0.0	0.0	0.0	0.0
1	2.8	1.4	1.7	0.9	1.3
2	3.3	1.9	2.0	1.1	1.6
3	2.3	0.9	1.4	0.6	1.0
4	13.5	2.3	8.3	1.4	4.8
5	57.8	36.8	35.3	22.4	28.9
6	65.7	64.3	40.1	39.3	39.7
7	79.7	78.3	48.7	47.8	48.2
8	96.2	96.2	58.7	58.7	58.7
9	105.3	105.3	64.3	64.3	64.3
10	116.3	115.3	71.0	70.4	70.7
11	130.9	124.9	79.9	76.2	78.1
12	134.4	137.4	82.1	83.9	83.0
13	136.5	143.5	83.3	87.6	85.4
14	137.5	146.5	84.0	89.5	86.7
15	138.7	147.7	84.7	90.2	87.4
16	142.1	152.1	86.8	92.9	89.8
17	144.3	154.3	88.1	94.2	91.1
18	146.3	154.3	89.3	94.2	91.8
19	146.4	156.4	89.4	95.5	92.4
20	147.0	157.0	89.7	95.8	92.8
21	148.1	157.1	90.4	95.9	93.2
22	147.2	158.2	89.9	96.6	93.2
23	147.4	157.4	90.0	96.1	93.0
24	146.4	158.4	89.4	96.7	93.1
25	146.0	159.0	89.1	97.0	93.1
26	147.5	159.5	90.0	97.4	93.7
27	147.1	160.1	89.8	97.7	93.8
28	95.9*	109.9*	58.5	67.1	62.8*

Comments: The oxygen uptake by nitrification was determined (see Annex 1). The oxygen consumed by nitrification was 49.81 mg/L. This value was subtracted from the respective 28 days measurements of the test item.

* After 28 days, nitrification of organic nitrogen (31 %) contributed significantly to the measured BOD. After 14 days (end of 10-day-window) degradation was 86.7 % and thus it is very likely that the 10-day-window criterion was met. The test item is considered to be readily biodegradable.

RESULTS (OXITOP SYSTEM)

Degradation of reference compound

Test concentration	:	100 mg/L
Empirical formula	:	$C_7 H_5 Na O_2$
Molecular weight	:	144.1 g/mol
Theoretical oxygen demand	:	1.665 mg O_2/mg

reference compound

time (d)	corrected BOD reference compound (r-bm) (mg O_2/L) r1	r2	% degradation r1	r2	% degradation mean
0	0.0	0.0	0.0	0.0	0.0
1	21.0	19.6	12.6	11.8	12.2
2	69.0	71.8	41.4	43.1	42.3
3	83.4	86.2	50.1	51.8	51.0
4	98.3	104.3	59.1	62.7	60.9
5	110.5	113.5	66.3	68.1	67.2
6	119.0	122.0	71.5	73.3	72.4
7	124.6	125.6	74.8	75.4	75.1
8	126.2	128.2	75.8	77.0	76.4
9	127.3	130.3	76.4	78.2	77.3
10	132.3	132.3	79.4	79.4	79.4
11	132.9	132.9	79.8	79.8	79.8
12	132.4	134.4	79.5	80.7	80.1
13	134.5	136.5	80.8	82.0	81.4
14	136.5	136.5	82.0	82.0	82.0
15	135.7	135.7	81.5	81.5	81.5
16	136.1	136.1	81.8	81.8	81.8
17	136.3	137.3	81.8	82.4	82.1
18	136.3	136.3	81.9	81.9	81.9
19	137.4	137.4	82.5	82.5	82.5
20	136.0	137.0	81.7	82.3	82.0
21	136.1	136.1	81.8	81.8	81.8
22	137.2	137.2	82.4	82.4	82.4
23	136.4	136.4	81.9	81.9	81.9
24	135.4	137.4	81.3	82.5	81.9
25	137.0	137.0	82.3	82.3	82.3
26	136.5	137.5	82.0	82.6	82.3
27	137.1	137.1	82.3	82.3	82.3
28	135.7	135.7	81.5	81.5	81.5

Comments: none

RESULTS (OXITOP SYSTEM)

Toxicity control

Test concentration test item : 100 mg/L
Theoretical oxygen demand test item : 1.638 mg O_2/mg
Test concentration reference compound : 100 mg/L
Theoretical oxygen demand reference compound : 1.665 mg O_2/mg

toxicity control		
time (d)	corrected BOD toxicity control (t-bm) (mg O_2/L) t1	% degradation t1
0	0.0	0.0
1	25.2	7.6
2	73.2	22.2
3	101.7	30.8
4	119.3	36.1
5	137.5	41.6
6	192.0	58.1
7	212.6	64.4
8	226.2	68.5
9	235.3	71.2
10	245.3	74.3
11	253.9	76.9
12	261.4	79.1
13	266.5	80.7
14	267.5	81.0
15	265.7	80.4
16	265.1	80.3
17	263.3	79.7
18	262.3	79.4
19	260.4	78.8
20	259.0	78.4
21	258.1	78.2
22	257.2	77.9
23	255.4	77.3
24	254.4	77.0
25	253.0	76.6
26	252.5	76.4
27	251.1	76.0
28	249.7	75.6

Comments: The used concentrations of the test item did not show toxic effects to bacteria.

The degradation curves are given in figure below.

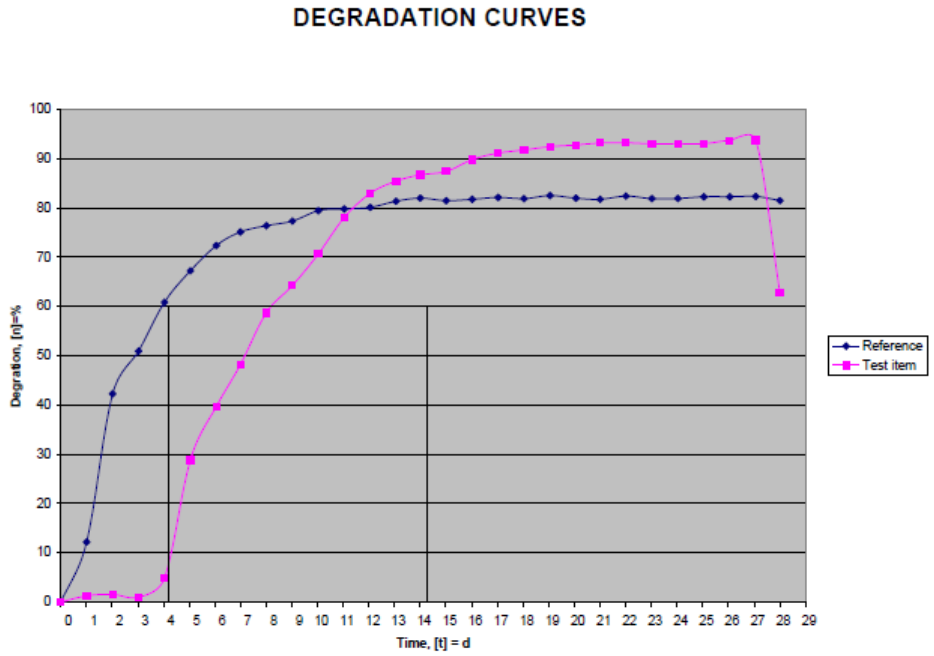


Fig. 1 Degradation curves of Propamocarb-hydrochloride and reference compound sodium benzoate.

III. Conclusion

Propamocarb-hydrochloride is considered to be ready biodegradable under the conditions of a Manometric Respirometry Test', thus, fulfilling the criteria set according to OECD 301 F.
The test item, propamocarb-hydrochloride, is an N-containing substance. According to the OECD guideline 301 F (adopted July, 1992), the results of the study need to be corrected for oxygen consumption by nitrification. Nitrite and nitrate were determined at the start and at the end of the study and the degradation data were corrected accordingly. However, this calculated correction was only applied on data of day 28, resulting in lower degradation on the last day than on the previous.
Therefore, the degradation data of the whole study duration need to be corrected for oxygen uptake for interference by nitrification.
As reported in the study, the share of oxygen uptake by nitrification of the measured BOD in the study was 49.81 mg/L. This value was used to correct the BOD values of day 28 in the report. To include the effects of nitrification not only on day 28, but on the whole study duration, the percentage share needs to be determined. The calculation of the contribution of nitrification of organic nitrogen is displayed in the table below.

Calculation of the nitrification rate:

	BOD test item (corrected)	**BOD test item (uncorrected)[a)]**	**% Nitrification[b)]**	**Mean % nitrification**
a1 28d	95.9	145.71	34.18	32.62
a2 28d	109.9	159.71	31.19	
[a)] Corrected value + 49.81 mg/L [b)] (49.81 / uncorrected value)*100				

Based on these results, the nitrification of organic nitrogen contributed by 32.62 % to the measured BOD. Using this correction, the reported BOD values in the study report are corrected to account for the

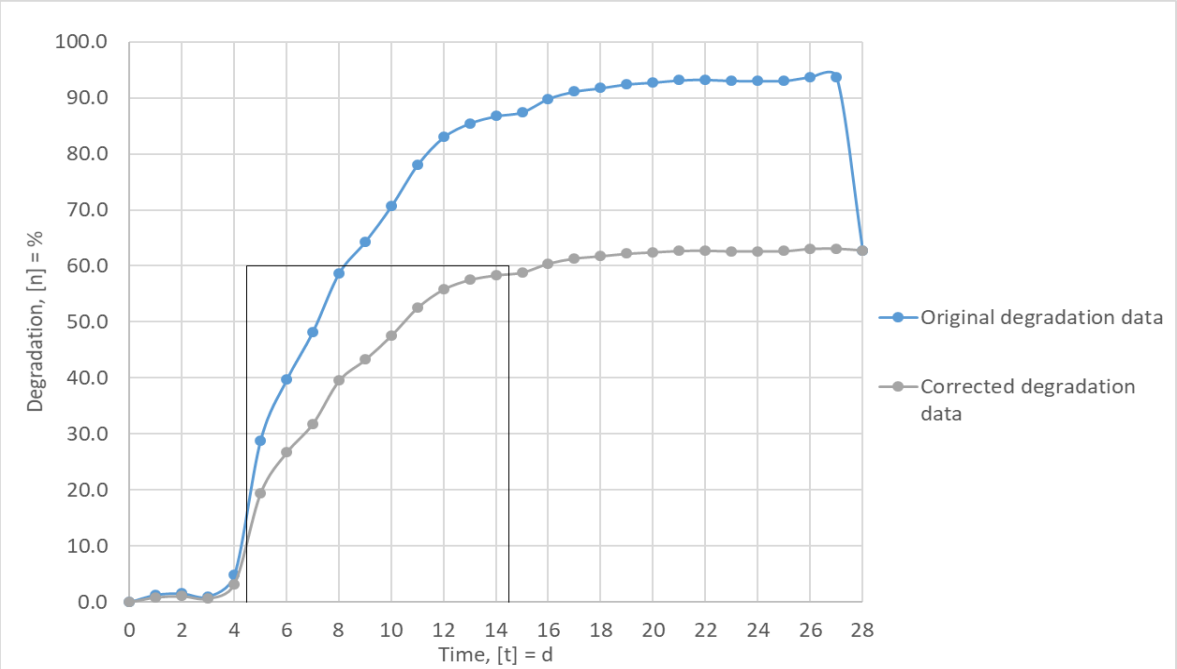
percentage of nitrification by multiplying the BOD data with 0.67. Corrected BOD values and corrected degradation data are displayed in the table below.

Corrected degradation data:

Propamocarb OECD 301 (Corrected report data)					
	Test item Degradation				
	BOD test item [mg O_2/L]		**% Degradation**		
time (d)	a1	a2	a1	a2	mean
0	0.00	0.00	0	0	0
1	1.88	0.94	1.15	0.58	0.86
2	2.22	1.28	1.36	0.78	1.07
3	1.55	0.61	0.95	0.37	0.66
4	9.09	1.55	5.55	0.95	3.25
5	38.91	24.77	23.75	15.12	19.44
6	44.22	43.28	27.00	26.42	26.71
7	51.63	52.71	31.52	32.18	31.85
8	64.75	64.75	39.53	39.53	39.53
9	70.88	70.88	43.27	43.27	43.27
10	78.28	77.61	47.79	47.38	47.59
11	88.11	84.07	53.79	51.33	52.56
12	90.47	92.49	55.23	56.46	55.85
13	91.88	96.59	56.09	58.97	57.53
14	92.55	98.61	56.50	60.20	58.35
15	93.36	99.42	57.00	60.70	58.85
16	95.65	102.38	58.40	62.50	60.45
17	97.13	103.86	59.30	63.41	61.35
18	98.48	103.86	60.12	63.41	61.76
19	98.55	105.28	60.16	64.27	62.22
20	98.95	105.68	60.41	64.52	62.46
21	99.69	105.75	60.86	64.56	62.71
22	99.08	106.49	60.49	65.01	62.75
23	99.22	105.95	60.57	64.68	62.63
24	98.55	106.62	60.16	65.09	62.63
25	98.28	107.03	60.00	65.34	62.67
26	99.29	107.36	60.61	65.55	63.08
27	99.02	107.77	60.45	65.79	63.12
28	95.90	109.09	58.50	67.10	62.80

The pass level for ready biodegradability according to OECD guideline 301 is 60 % of ThOD (theoretical oxygen demand) production for respirometric methods. This pass level needs to be reached 10 days after the degree of biodegradation has reached 10 %. Original degradation data, corrected degradation data and the 10-d-window are displayed in the figure below.

´Reported and corrected report degradation data of propamocarb´



The original data, as well as the corrected data reach the 60 % pass level within the 28 day period of the experiment. The original data set passes the threshold within the 10-d-window, while the corrected data narrowly fails as the value is reached after 12 days. This circumstance would classify propamocarb very close as being not readily biodegradable due to the correction of the nitrification influence. However, the used correction approach is a worst case assumption. The nitrification rate was determined based on the measured results of day 28 and it can be assumed, that this rate is not representative for the whole duration of the experiment.
The only source of nitrogen in the experiment, necessary for the process of nitrification, is the test item itself. Nitrification can, therefore, only occur, when the substance is already partly degraded and the nitrogen of the test item is released. With progressive degradation of the substance, the nitrification rate should increase as well.
Therefore, the nitrification rate of 32.62 % may overestimate the influence of nitrification on the BOD throughout the whole study duration. Even by lowering the nitrification rate by only 1.92 % (to 30.7 %), the 10-d-window criterion is met.
Therefore, it can be assumed, that with real nitrification information throughout the whole study, the 10-d-window would very likely be met and propamocarb can be classified as readily biodegradable.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al.*(1997).

11.1.2 BOD_5/COD

The following study (KCA 7.2.2.2/01; Iwan, J.; 1983; M-157700-01-1) was evaluated as SUPPLEMENTAL DATA.

Report:	KCA 7.2.2.2/01; Iwan, J.; 1983; M-157700-01-1
Title:	Microbial degradation of propamocarb hydrochloride in water
Report No.:	R+S 13/83-PA 66752.73/2; A85467
Document No.:	M-157700-01-1
Guideline(s):	Dutch G.2
Guideline deviation(s):	None
GLP/GEP:	**No**

The evaluation revealed that propamocarb-hydrochloride was 'readily' degraded by microbial processes when sodium acetate was present while degradation was limited (less than 10% after 35 days) in the absence of this additional carbon source.
However and by its design, the existing test fulfilled key criteria according to the actual OECD Guideline 309, i.e. by diluting a 'mixed microbial population' from surface water (i.e. lake) in a mineral medium, to study the mineralization of the 14C-labeled active substance at 25°C in the dark for a maximum incubation period of 35 days. The test was performed in the presence and absence of an additional carbon source (acetate). However, the test concentration used in the study was 20 mg/L while tests to fully follow OECD 309 should be performed at 10 µg/L or lower.
Consequently, this data was regarded as supplemental information.

In order to fulfill actual data requirements, a study, by Heinemann, O. & Kasel, D., (2015) was performed according to OECD Guideline 309.

Report:	KCA 7.2.2.2/02; Heinemann, O.; Kasel, D.; 2015; M-513451-01-1
Title:	[1-14C]propamocarb-hydrochloride: Aerobic mineralization in surface water
Report No.:	EnSa-14-0512
Document No.:	M-513451-01-1
Guideline(s):	OECD Test Guideline No. 309 Commission Regulation (EU) No 283/2013 in accordance with Regulation (EC) No 1107/2009
Guideline deviation(s):	None
GLP/GEP:	**Yes**

Executive Summary

The mineralisation of 1-*N*-propyl-^{14}C-labeled active substance propamocarb hydrochloride was investigated in non-sterile natural water at pH 8.2 at test concentrations of 10.0µg a.s./L (low dose) and 103.7 µg a.s./L (high dose). Samples were incubated at 20 ±2 C in the dark for 60 days in maximum. Microbial activity of the test water was demonstrated by incubation of phenyl-UL-^{14}C-labeled benzoic acid serving as reference.
The mean material balances were 102.5% ±1.1% AR for low dose samples and 100.8% ±1.6% for the high dose.
Values of the test substance in the test water decreased from 101.1% of AR for the low dose (97.4% for high dose) at time zero to 87.7% (95.9% for high dose) after 60 days of incubation.
Propamocarb-hydrochloride was bio-transformed to a number of minor components at trace level (≤ 3% AR) in the course of the study. Formation of other volatile components was negligible (≤ 1.3% AR in maximum for the two doses) while formation of carbon dioxide was significant to low amounting to 12.8% AR for the low dose and 2.8% for the high dose each after 60 days of incubation.
Best fits to measured data were obtained by following the simple first order (SFO) kinetic model for evaluation. The value of the DT_{50} of propamocarb hydrochloride under conditions of mineralization testing was calculated to be 296 days for the low dosed samples. No value of the DT_{50} was calculated for high dosed samples since degradation was insignificant under the conditions of the test.

I. Material and Methods

A. Materials

1. Test Material: [1-*N*-propyl-^{14}C]propamocarb-hydrochloride

Specific radioactivity:	8.44 MBq/mg (228.24 µCi/mg)
Radiochemical purity:	>99% (HPLC)

97.6% (TLC)
Sample ID: KML 9741

2. Test water

The natural water Wiehltalsperre used for the test was fresh collected from a reservoir serving as a source for drinking water at Reichshof, Northrhine-Westphalia, Germany.

Physico-chemical characteristics of test water:

Water	Wiehltalsperre
pH	8.2
Redox potential Eobs (mV)	205.1
Oxygen saturation (%)	100.7
Total organic carbon (TOC, mg/kg)	<2.0
Dissolved Organic Carbon (DOC, mg/L)	< 2.0
Biochemical oxygen demand (BOD5;mg/L)	n.a.*
Total nitrogen (mg/L)	2
Total phosphorus (mg/L)	<0.03

* not applicable due to low total organic carbon content

Before the start of incubation the test water was passed through a 0.063 mm sieve.

B. Study design

1. Experimental conditions: Samples of 100 mL test water each were filled into 250 mL Erlenmeyer glass flasks with baffles and pre-equilibrated four days prior to treatment at approximate study conditions (darkness, 20 C). The test was performed with 1-*N*-propyl-^{14}C-propamocarb-hydrochloride at initial concentrations of 10.0 µg/L (low dose) and 103.7 µg/L (high dose). Following application the samples were incubated in 'static' systems under gentle shaking and traps attached to collect ^{14}C-carbon dioxide and other volatiles, but being permeable to air. Samples were incubated at 20 ±2 C in the dark for 60 days in maximum.

In addition, samples containing biological controls were incubated under the same conditions and removed for analysis at selected time points. Biological controls contained the reference substance phenyl-UL-^{14}C-benzoic acid.

2. Sampling: Duplicate samples of each of the two test concentrations were removed for analysis after 0, 3, 8, 14, 21, 30, 39, 46 and 60 days of incubation.

Samples for determination of microbial activity (biological controls) were investigated after 0 and 2 days of incubation. Finally, sterile controls were removed for analysis after 60 days of incubation.

The complete samples were immediately processed and HPLC analysis was usually performed the same day. Therefore no additional investigations of storage stability were necessary.

The pH, oxygen concentration and the redox potential was determined at each sampling interval.

3. Analytical procedures: Aliquots of the samples were concentrated prior to analysis while the water of low dose samples was concentrated prior to analysis by rotary evaporation (max. 35°C, reduced pressure). The ^{14}C-material balance was established for each sample following analysis of the water and determination of volatile radioactivity in the traps. Following quantitation of radioactivity in water by LSC and concentration, analysis was performed by reversed phase HPLC and ^{14}C-flow-through detection techniques as the primary analytical method. Selected samples were analysed by TLC followed by ^{14}C-detection (phosphor imaging).

The LOQ of the primary analytical method was estimated to be 1.0% AR for a compound in low dose and high dose samples.

4. Kinetic evaluation: The kinetic evaluation was performed for the active substance propamocarb-hydrochloride with the software KinGUI II following FOCUS kinetic guidance (2011) to obtain best fits to the measured data.

II. Results and Discussion

The temperature was maintained at 22 ±1 C during the test. Biological activity of the test water was confirmed by the degradation of reference substance phenyl-UL-^{14}C-benzoic acid within 14 days of incubation. The pH, oxygen concentration and redox potential of the test water was shown to be within the same range for treated samples and for untreated controls.

The material balances and distribution of radioactivity (low dose and high dose) are summarized in the Table 11.1.2-02 (low dose) and Table 11.1.2-03 (high dose). The mean material balances were 102.5% ±1.1% AR for low dose samples and 100.8% ±1.6% for the high dose demonstrating no significant losses of radioactivity from samples in the course of the test including processing till analysis.
Formation of ^{14}C-carbon dioxide was observed as the sole major transformation product to account for 12.8% AR (low dose) and 2.8% (high dose) at the end of the study, day 60. Formation of other volatile components was negligible amounting to 1.3% AR (low dose) and 0.1% (high dose) in maximum for the two concentrations tested.
Biotransformation of ^{14}C-labeled propamocarb-hydrochloride resulted in a decline from 101.1% AR at time zero to 87.7% after 60 days for the low dose and from 97.4% AR at time zero to 95.9% after 60 days for the high dose. No degradation of active substance was observed in sterile controls as documented by a recovery of 103.0% AR for the active substance after 60 days of incubation.
A number of minor components was observed at trace level accounting in maximum for 2.2% (low dose, day 39) or 3.0% AR (high dose) each at day 39.
The observation of carbon dioxide indicated that the transformation of propamocarb-hydrochloride under the conditions of the test was clearly driven by microbial degradation.
The kinetic evaluation of the data resulted in DT_{50}-values of 296 days for the low dose. The value was derived from the SFO kinetic model as the best fits to measured data. No half-life could be calculated for the high dose due to the insignificant degradation observed under the conditions of the test. The results of kinetic evaluations are summarized below.

Low dose - Degradation of [1-*N*-propyl-^{14}C]propamocarb-hydrochloride in aerobic natural water (expressed as percentage of total applied radioactivity:

		Sampling interval (days)								
Component		**0**	**3**	**8**	**14**	**21**	**30**	**39**	**46**	**60**
Propamocarb-hydrochloride	Mean*	101.1	102.6	100.0	101.5	101.9	99.4	94.8	92.2	87.7
	SD	±2.5	±3.1	±0.1	±0.2	±2.4	±1.8	±2.9	±1.6	±0.6
Total of unknown radioactivity	Mean*	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	2.2	1.9	n.d.
	SD							±0.8	±0.0	
Total radioactivity in water	Mean*	101.1	102.6	100.0	101.5	101.9	99.4	96.9	94.0	87.7
	SD	±2.5	±3.1	±0.1	±0.2	±2.4	±1.8	±2.1	±0.3	±0.6
^{14}C-CO_2	Mean*	n.a.	0.4	0.9	2.1	0.9	2.3	4.9	9.3	12.8
	SD	n.a.	±0.1	±0.2	±0.1	±0.0	±1.3	±0.4	±0.2	±2.3
Other volatiles	Mean*	n.a.	1.3	0.9	0.1	0.1	0.1	0.1	0.1	0.2
	SD	n.a.	±1.2	±0.8	±0.0	±0.0	±0.0	±0.0	±0.0	±0.2
Total radioactivity (%)	Mean*	101.1	104.2	101.8	103.7	102.9	101.8	101.8	103.4	100.7
	SD	±2.5	±4.2	±1.1	±0.0	±2.4	±0.5	±1.7	±0.5	±3.1

Values given as percentages of initially applied radioactivity; SD = standard deviation; * Mean values of two replicates; n.a. = not analysed or not applicable; n.d. = not detected

High dose - Degradation of [1-*N*-propyl-^{14}C]propamocarb-hydrochloride in aerobic natural water, expressed as percentage of total applied radioactivity:

Component		Sampling interval (days)								
		0	**3**	**8**	**14**	**21**	**30**	**39**	**46**	**60**
Propamocarb-hydrochloride	Mean*	97.4	100.8	100.7	100.1	96.7	99.1	97.8	97.4	95.9
	SD	±0.9	±0.3	±0.1	±0.2	±0.4	±0.5	±3.8	±1.1	±0.4
Total of unknown radioactivity	Mean*	0.7	0.3	0.7	1.1	1.6	1.9	3.0	2.0	n.d.
	SD	±0.4	±0.0	±0.0	±0.2	±0.4	±0.0	±0.1	±0.3	
Total radioactivity in water	Mean*	98.1	101.1	101.4	101.2	98.3	101.0	100.8	99.4	95.9
	SD	±1.3	±0.3	±0.2	±0.0	±0.0	±0.5	±3.9	±1.4	±0.4
^{14}C-CO_2	Mean*	n.a.	0.2	0.2	1.2	0.4	1.0	1.1	1.3	2.8
	SD	n.a.	±0.0	±0.0	±0.6	±0.1	±0.2	±0.1	±0.0	±0.3
Other volatiles	Mean*	n.a.	<0.1	<0.1	0.1	<0.1	0.1	<0.1	<0.1	<0.1
	SD	n.a.	±0.0	±0.0	±0.0	±0.0	±0.1	±0.0	±0.0	±0.0
Total radioactivity (%)	Mean*	98.1	101.3	101.6	102.5	98.8	102.1	102.0	100.8	98.6
	SD	±1.3	±0.3	±0.1	±0.6	±0.1	±0.2	±3.9	±1.3	±0.7

Values given as percentages of initially applied radioactivity; SD = standard deviation; * Mean values of two replicates; n.a. = not analysed or not applicable; n.d. = not detected

Kinetic evaluation of degradation of [1-*N*-propyl-^{14}C]propamocarb-hydrochloride in aerobic natural water under conditions of OECD 309 testing:

Compound / Dose	Kinetic Model	DT_{50} (days)	DT_{90} (days)	Error for Chi^2	Visual assessment
Propamocarb-hydrochloride / Low	SFO	296	984	1.6	O
Propamocarb-hydrochloride / High	n.a.	n.a.	n.a.	n.a.	n.a.

SFO = simple first order; n.a. = not available due to insufficient degradation observed;
Visual assessment: + = good, O = moderate, - = bad

III. Conclusion

The overall biotransformation including mineralization of propamocarb-hydrochloride and its residues in non-sterile natural water was moderate under the 'pelagic' conditions of the test.
Besides ^{14}C-carbon dioxide, no major transformation products were observed that require consideration in environmental risk assessments.
The DT_{50} of propamocarb-hydrochloride in water under conditions of aerobic mineralisation testing was calculated to be 296 days.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

The results of the study above were in some contradiction to the behaviour and observations in existing water/sediment tests which indicate good degradability in the presence of sediment. When transferring this into outdoor conditions and considering the use of propamocarb in agricultural practice, water/sediment tests describes better the situation of a ditch adjacent to the agricultural field rather than the 'open water' underlying as principle for the tests according to OECD 309.

11.1.3 Hydrolysis

The abiotic hydrolysis of the active substance propamocarb-hydrochloride was investigated in three studies using, respectively:

- Sterile aqueous buffer solutions at pH 12 (90°C), 13 (70°C), and 14 (25°C, 70°C and 90°C) following application of non-labeled propamocarb base and extrapolation of hydrolysis rates to pH 5, 7 and 9, over a five day period in the dark at 50 C and under sterile conditions (KCA 7.2.1.1/01);
- Sterile aqueous buffer solutions at pH 4, 5, 7 and 9 following application of 1-*N*-propyl-^{14}C-labeled propamocarb base and incubation at 50°C in dark conditions (KCA 7.2.1.1/02);
- Aqueous buffer solutions at pH 4, 7 and 9 following application of non-labeled active substance and incubation over a five day period in the dark at 50°C (KCA 7.2.1.1/03).

Duplicate samples at each pH were analysed by radio HPLC immediately after dosing and 5 days later to determine whether propamocarb is susceptible to hydrolysis at any environmentally relevant pH values. Samples were analysed by HPLC on the day of collection.
For sterility assay, duplicate aliquots (100 µL) of the time 0 and day 5 pH 4, 5, 7 and 9 samples were taken at the time of sampling and cultured on plates of Trypticase Soy Agar (TSA) in an incubator at 35 C. After 48 hours, the cultures were evaluated for microbial growth. The concentration of [^{14}C]-propamocarb ranged from 8.7 mg/L at pH 4 and 5, to 9.5 mg/L at pH 7 and 9.9 mg/L at pH 9. The test solutions were analysed by high performance liquid chromatography (HPLC) with a flow-through radiodetector. Sterility was preserved throughout the study. Radiocarbon recoveries after 5 days ranged from 98.4 % to 101.4 % of the applied dose for all solutions.
In conclusion, [^{14}C]-propamocarb did not degrade at 50º C over the five day period in any of the buffer systems tested.

A summary of the studies submitted are presented below.

Report:	KCA 7.2.1.1/01; Repenthin, W.; 1976; M-157687-01-1
Title:	Determination of rates of hydrolysis of propamocarb base (SN 39 744) at pH 5, 7 and 9 - Including addendum to report APC 26/76
Report No.:	APC 26/76; A85458
Document No.:	M-157687-01-1
Guideline(s):	OECD A 80/13; USEPA (=EPA): A 79-55
Guideline deviation(s):	None
GLP/GEP:	**No**

Executive Summary

The hydrolysis of propamocarb was initially determined experimentally in aqueous buffer solutions at high pH values, since this was known to be the least stable pH range for carbamates. The pH and temperature conditions used were pH 12 at 90°C, pH 13 at 70°C and 90°C and pH 14 at 25°C, 70°C, and 90°C. A nominal concentration of non labelled 3 g propamocarb/L was used. Solutions were analysed by gas chromatography (GC) at time of dosing and at various intervals thereafter, up to a maximum of 412 hours.
Propamocarb is very stable towards hydrolysis. Even at pH 14 the DT_{50} is approximately 5 days. Extrapolation to pH 5, 7 and 9 at 25°C assuming a pure base catalysis results in very long DT_{50} values (thousands of years). Additional experimental tests carried out for 5 days at 50°C (pH 5, 7 and 9) and at 70°C (pH 5) confirmed the predicted hydrolytic stability at these lower pH values.

I. Material and Methods

A. Materials

1. Test Material: Common name: propamocarb hydrochloride
Chemical name: propyl 3-(dimethylamino)propylcarbamate hydrochloride

2. Test solution: Aqueous buffered solutions at pH 5, 7 and 9.

B. Study design

1. Experimental conditions: The hydrolysis rate constant at 25°C for pH values 5, 7, and 9 was extrapolated using the results from the 90 tests and the measured rate constant at pH 14 and 25°C.
In order to confirm predicted hydrolystic stability of propamocarb at the lower (environmentally relevant) pH values, the extent of its hydrolysis in pH 5, 7, and 9 aqueous buffer solutions was subsequently determined experimentally at 50°C (and also at 70°C for pH 5). A nominal concentration of C100 mg propamocarb/L was used and solutions were maintained at the required temperature for 5 days, with analysis at selected timepoints being performed by GC.

2. Analytical procedures: At predetermined time intervals samples were removed and analyzed with thymol as internal standard. The water solutions were injected directly into the gas chromatograph after a measured quantity of the internal standard was added.

II. Results and Discussion

A. Mass balance: Recoveries of propamocarb are shown below.

Recoveries of propamocarb at pH 5 and 50°C and 70°C:

Temperature	**50°C**		**70°C**	
Co (mg/5 mL) (determined by weight)	**0.4965**		**0.4932**	
Test No.	**1**	**2**	**1**	**2**
Co (mg/5 mL) (determined by extraction followed by GC)	-	-	0.4303 0.4718 0.4927 0.4928 0.5154 mean 0.4805 (96.8 % [1])	0.4511 0.4774 0.4826 0.5004 0.4794 mean 0.4782 (96.9 % [1])
C1 (mg/5 mL) t = 1 day	-	-	0.4468 0.4728 0.4892 0.5105 0.5059 mean 0.4850 (98.3 % [1])	0.4661 0.4726 0.4962 0.5024 mean 0.4843 (98.1 % [1])
C2 (mg/5 mL) t = 2 days	-	-	0.4733 0.4528 0.4603 0.4697 0.4780 mean 0.4668 (94.6 % [1])	0.4602 0.4626 0.4737 0.4762 0.4820 mean 0.4709 (95.5 % [1])
C3 (mg/5 mL) t = 3 days	-	-	0.4635 0.4842 0.4757 0.4716 0.4914 mean 0.4773 (96.8 % [1])	0.4676 0.4582 0.4752 0.4806 0.4947 mean 0.4753 (96.3 % [1])

C5 (mg/5 mL) t = 5 days	0.4654 0.4612 0.4610 0.4504 0.4707 mean 0.4617 (93.0 % [1])	0.4532 0.4746 0.4770 0.4440 0.4346 mean 0.4567 (92.0 % [1])	-	-

Note: [1] % of Co (determined by weight); - no data available

Recoveries of propamocarb at pH 7 and 9 at 50°C:

	pH 7				**pH 9**	
Co (mg/5 mL) (determined by weight)	**0.48901**		**0.48222**		**0.4686**	
Test No.	**1**	**2**	**1**	**2**	**1**	**2**
Co (mg/5 mL) (determined by extraction)	0.4366 0.4763 0.4877 0.4996 0.5143 mean 0.4829 (98.8 % [1])	0.4577 0.4861 0.5129 0.5202 0.5203 mean 0.4994 (102.1 % [1])	0.4125 0.4394 0.4679 0.4819 0.4791 0.4890 0.4993 mean 0.4670 (96.8 % [1])	0.4278 0.4425 0.4753 0.4725 0.4866 0.4939 0.4802 mean 0.4684 (97.1 % [1])	-	-
C5 (mg/5 mL) t = 5 days	0.4449 0.4526 0.4716 0.4714 0.4992 0.5026 0.5054 0.4960 mean 0.4805 (98.3 % [1])	0.4460 0.4684 0.4526 0.4819 0.4734 0.4880 mean 0.4684 (95.8 % [1])	0.4489 0.4758 0.4740 0.4779 0.4933 0.5000 mean 0.4783 (99.2 % [1])	0.4905 0.4587 0.4659 0.4847 0.4969 0.4980 0.5083 mean 0.4881 (101.2 % [1])	0.3820 0.4175 0.4186 0.5022 0.4444 mean 0.4329 (92.4 % [1])	0.4331 0.4482 0.4655 0.4718 0.4586 mean 0.4554 (97.2 % [1])

Note: [1] % of Co (determined by weight); - no data available; 1 Buffer 1; 2 Buffer 2

B. Transformation of test substance: propamocarb base is very stable towards hydrolysis reactions. The tests were initially run at high pH values and temperatures in order to obtain measurements within relatively short time intervals. From the linear function (–log k1 = f(pH)) which was measured at 90 °C for three different pH values (12, 13 and 14) one can assume a strong OH ion catalysis. Table CA-8.2.1.1-03 summarises rate constants and DT_{50} values measured at 90 °C.

Measured rate constants and DT_{50} values over the pH range 12, 13 and 14, measured at 90 °C:

pH	k1 (Min^{-1})	DT_{50} (Min)
12	1.68×10^{-4}	4,127
13	1.39×10^{-3}	496
14	1.68×10^{-2}	34

K1 is the pseudo first order rate constant for the hydrolysis at constant pH (K1 = KOH · (OH)

By dividing the measured k1 value by the corresponding OH ion concentration the second order rate constant is obtained as shown in Table 11.1.3-04.

kOH- = k1/OH-

Second-order rate constants at 90°C:

(OH-) (mol)	kOH- (min-1 . mol-1)
0.01	1.68×10^{-2}
0.1	1.39×10^{-2}
1.0	1.99×10^{-2}

mean kOH- = 0.0169 (min-1 . mol-1) at 90 °C

It was assumed that the specific base catalysis observed at 90 °C would also apply at room temperatures. A linear relationship was found between ln k1 (the natural log of the hydrolysis rate constants measured at 3 different temperatures (25, 70 and 90 °C) at pH 14) and the inverse of these three temperatures (in Kelvin) according to the Arrhenius equation: ln k1 = ln A – Ea/RT.
Thus, it is possible to extrapolate the rate constant for each temperature within the measured temperature range. The activation energy for alkaline hydrolysis of propamocarb was calculated from the slope of the Arrhenius line and was determined to be 17.57 kcal/mol. Extrapolation to pH 5, 7 and 9 at 25 °C assuming a pure base catalysis results in very long half-lives (thousands of years).
The linear relationship between the rate of hydrolysis and the pH which was obtained in the tests performed at 90°C makes it possible to calculate the values for k1 at pH 5, 7 and 9 at 25°C from the log10 of the hydrolysis rate constant k1, measured at 25°C for pH 14 and with a slope of -1 drawn through this point. The results are shown in Table 11.1.3-05.

k1 at pH 5, 7 and 9 and temperature 25°C:

pH	k1	DT_{50} (years)
5	1.05×10^{-13}	1.26×10^{7}
7	1.05×10^{-11}	1.26×10^{5}
9	1.05×10^{-9}	1.26×10^{3}

The additional experimental tests performed to check the extrapolations to lower pH values showed a decrease in propamocarb content over 5 days of no more than 8 %. Thus, the compound is considered to be hydrolytically stable at pH 5, 7, and 9.

III. Conclusion

Propamocarb is very stable towards hydrolysis. Even at a pH of 14 the DT_{50} is, approximately, 5 days.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Report:	KCA 7.2.1.1/02; Shepler, K.; McKemmie, T.; 2001; M-240450-01-1
Title:	Hydrolysis of [14C]propamocarb at pH 4, 5, 7 and 9
Report No.:	882 W-1; B003419
Document No.:	M-240450-01-1
Guideline(s):	US EPA (=EPA) Subdivision N. Chemistry: Environmental Fate 161-1; European Union Guideline EC.C7
Guideline deviation(s):	None
GLP/GEP:	**Yes**

Executive Summary

The rate of hydrolysis was examined in sterile aqueous buffers in the pH range of 4.0 to 9.0 over a five day period in the dark at 50°C under sterile conditions. The concentration of [^{14}C]-propamocarb ranged from 8.7 mg/L at pH 4 and 5, to 9.5 mg/L at pH 7 and 9.9 mg/L at pH 9. The test solutions were analysed by high performance liquid chromatography (HPLC) with a flow-through radiodetector. Sterility was preserved throughout the study. Radiocarbon recoveries after 5 days ranged from 98.4% to 101.4% of the applied dose for all solutions.

[^{14}C]-propamocarb did not degrade at 50°C over the five day period in any of the buffer systems tested indicating that it is stable to hydrolysis with a half-life greater than one year.

I. Material and Methods

A. Materials

1. Test Material: Common name: propamocarb hydrochloride
Chemical name: propyl 3-(dimethylamino)propylcarbamate hydrochloride
Radiolabelled purity: 99.4%
Batch # GAR2004/3
Specific activity 53.38 mCi/mmol

2. Test solution: Aqueous buffered solutions at pH 4, 5, 7 and 9.

B. Study design

1. Experimental conditions: In the definitive test, duplicate samples at each pH were analysed by radio HPLC immediately after dosing and 5 days later to determine whether propamocarb is susceptible to hydrolysis at any environmentally relevant pH values. Samples were analysed by HPLC on the day of collection.
Duplicate aliquots (100 µL) of the time 0 and Day 5 pH 4, 5, 7 and 9 samples were taken at the time of sampling and cultured on plates of Trypticase Soy Agar (TSA) in an incubator at 35°C for sterility assay. After 48 hours, the cultures were evaluated for microbial growth

2. Sampling: Duplicate samples of each pH test solution were collected at Time 0 and following 5 days incubation.

3. Analytical procedures: The pH of the sample was measured using an Orion pH meter. Aliquots were taken directly from the solutions (20 µL x 3) for radioassay by liquid scintillation counter (LSC) and for chromatographic analysis by high performance liquid chromatography (HPLC).

II. Results and Discussion

A. Mass balance: The material balance of radiocarbon was determined by Liquid Scintillation Counting (LSC) analysis of aliquots of the buffered solutions at the time of sampling. Recoveries, expressed as a percentage of the applied dose, for all samples are shown below. Recoveries following 5 days incubation at 50°C ranged from 98.4% to 101.4%.

Mass balance of radiocarbon following hydrolysis of [^{14}C]-propamocarb in pH 4, 5, 7 and 9 aqueous buffers at 50°C

	Percent of applied dose	Percent of applied dose
PH 4, Applied dose: (8.7 mg/L)		
Rep A	98.9	100.1
Rep B	98.6	100.9
PH 5, Applied dose: (8.7 mg/L)		
Rep A	98.2	98.4
Rep B	98.9	101.0
PH 7, Applied dose: (9.5 mg/L)		
Rep A	98.8	99.6
Rep B	98.2	100.9
PH 9, Applied dose: (9.9 mg/L)		
Rep A	97.3	101.4
Rep B	96.5	98.8

B. Transformation of test substance: The radiochemical purity of [^{14}C]-propamocarb was determined to be >99.9 % by HPLC prior to experiment. HPLC analysis of the time zero samples demonstrated that [^{14}C]-propamocarb was stable under conditions of administration. Aliquots of the dose solution taken before and after the dosing process showed that the dose solution was homogeneous during the application process (relative standard deviation of 1.2%).
In the preliminary test conducted to determine the possibility of sorption to the containers at all four pHs no significant sorption to the glass containers was observed for [^{14}C]-propamocarb in any of the solutions for up to 48 hours of incubation. Recoveries ranged from 97.41% to 100.55% for pH 4, 93.51% to 98.99% for pH 5, 93.34% to 99.56% for pH 7 and 95.05% to 99.12% for pH 9.
The pH of the samples was measured at each sampling time. The results for all four sets of samples showed that the pH of the buffer solutions did not change significantly during the study period. Sterility assays showed that sterile conditions were maintained during the study.

III. Conclusion

Propamocarb did not degrade at 50°C over the five day period in any of the buffer systems tested indicating that it is stable to hydrolysis (with a half-life greater than one year).

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

The “Abiotic Degradation Hydrolysis as a Function of pH” is also reported in the following physico-chemical study:

Report:	KCA 7.2.1.1/03; Walker, A. J.; Mulle, D. M.; Barlett, A. J.; 1995; M-309665-01-1
Title:	Propamocarb hydrochloride : Determination of general physico-chemical properties
Report No.:	722/013
Document No.:	M-309665-01-1
Guideline(s):	OECD/GD(92)32 Commission Directive 92/69/EEC Method C7
Guideline deviation(s):	not specified
GLP/GEP:	Yes

Executive Summary

The hydrolysis of propamocarb hydrochloride was studied in aqueous buffer solution at pH 4, 7, and 9, at a nominal concentration of 2.0 g/L. Propamocarb hydrochloride has been found to undergo less than 10 % hydrolysis after 5 days at 50°C in pH 4, 7 and 9 buffer solutions. The estimated half-life of propamocarb hydrochloride at 25°C, estimated from the above, is greater than 1 year.

I. Material and Methods

A. Materials

1. Test Material: Non-labelled propamocarb hydrochloride
99.1% purity
Reference dm/Oct.001.win

2. Test solution: pH4, potassium hydrogen phthalate, c = 0.05 M, pH 7, disodium hydrogen orthophosphate, c = 0.04 M, potassium dihydrogen orthophosphate, c = 0.03 M, pH 9, disodium tetraboarte 0.05, (pH adjusted with hydrochloride).

B. Study design

1. Experimental conditions: The solutions were maintained at 50 ± 0.5 °C for a period of 5 days.
2. Sampling: Duplicate aliquots of the sample solutions were removed at the following time intervals (hrs); 0, 2.4, 25 (27 in the case of pH 9) and 120 during the five day period.
3. Analytical procedures: All solutions were monitored by High Performance Liquid Chromatography (HPLC), the pH of each solution was also recorded.

II. Results and Discussion

The initial concentration and the concentration at various time intervals of propamocarb hydrochloride are shown below. Propamocarb hydrochloride has been found to undergo less than 10% hydrolysis after 5 days at 50°C in pH 4, 7 and 9 buffer solutions. The estimated half-life of propamocarb hydrochloride at 25°C, estimated from the above, is greater than 1 year.

Initial concentration and the concentration at the various time intervals of propamocarb hydrochloride. The pH values after 2.4, 25, 27, and 120 hours are expressed as a percent of the initial pH value:

Concentration of propamocarb hydrochloride	pH 4	pH 7	pH 9
As weighed (g/L)	2.01	2.08	2.01
Found initially (g/L)	2.01	2.05	1.97
After 2.4 hours (g/L)	1.98 (98.9)	2.05 (99.8)	1.98 (100)
After 25 hours (g/L)	2.02 (101)	2.10 (102)	-
After 27 hours (g/L)	-	-	2.02 (103)
After 120 hours (g/L)	2.06 (103)	2.15 (105)	2.06 (105)

Note: - No data available

III. Conclusion

Propamocarb hydrochloride has been found to undergo less than 10% hydrolysis after 5 days at 50 °C, which equates to a half-life of greater than 1 year at 25 °C.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Overall conclusions of the hydrolysis studies conducted and relied on:

Propamocarb hydrochloride was stable to abiotic hydrolysis. By consequence, no half-life value was determined for the various pH values investigated and no hydrolytic pathway was proposed.
It is concluded that abiotic hydrolysis is an insignificant process for the elimination of propamocarb hydrochloride from the natural aquatic environment. This is true, in particular, when comparing the result of abiotic sterile hydrolysis with the results of tests in non-sterile natural water systems.

11.1.4 Other convincing scientific evidence

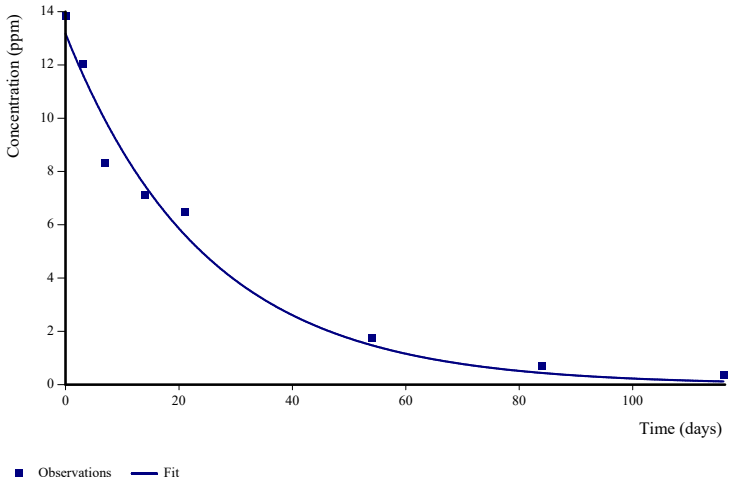
11.1.4.1 Field investigation and monitoring data (if relevant for C&L)

A) Field investigation

A.1) Soil dissipation studies

According to Commission Regulation No 283/2013, field dissipation studies shall be conducted when the DegT50lab for the active substance in one or more soils determined at 20°C and at a moisture content of the soil related to a pF value of 2 is greater than 60 days.
A field dissipation study (KCA 7.1.2.2.1/01; Willard, T.R., 2002) was submitted: two trials conducted in USA to investigate the dissipation rate of propamocarb hydrochloride. The trials were carried out on two cropped soils turf and on bare soils, following four foliar applications in California and Georgia. Propamocarb hydrochlorid degraded rapidly under field conditions: field DT50 values ranging from 17.4 to 23.7 days.
In view of changes made in regulatory practice and in the evaluation of degradation and mobility processes in soil, the assessment of behaviour of a compound in soil is regarded to be reliably performed on the basis of laboratory data only. By relying on laboratory data as the first Tier, this approach is regarded as the most conservative. Conclusively, the determination of half-lives of the dissipation of a compound, i.e. influenced by other processes than degradation only, would therefore not contribute to a more conservative assessment of the behaviour of residues in soil.
However, a crosswalk with ENSAGIPS shows, for California, a high and acceptable similarity score with southern EU regions (≥ 83%). A rough $DegT_{50}$ estimation according to EFSA guidance (2014; 12(5):3662) is performed. However, the evaluation is done with non-normalised values and no FOCUS value adaption. Seven days after the last application, 10 mm of rainfall was achieved (according to weather data given in report). The SFO fit after 10 mm of rainfall is visually and statistically reliable, with $\chi^2 = 9.1\%$ and a significant p-test ($k < 0.001$). The calculated degradation is fast, with a $DegT_{50}$ of 17.1 days.

SFO fit for Carlifornia soil after 10 mm of rainfall:



The exemplary roughly estimated $DegT_{50}$ is well below the used geomean modelling $DegT_{50}$ soil laboratory value of 22.33 days. This supports the defined strategy above that field dissipation half-lives would not contribute to a more conservative assessment of propamocarb hydrochloride in soil.

Report:	KCA 7.1.2.2.1/01; Willard, T. R.; 2002; M-310955-01-1
Title:	Terrestrial field soil dissipation of propamocarb hydrochloride in turf
Report No.:	AA010716
Document No.:	M-310955-01-1
Guideline(s):	US-EPA Pesticide Assessment Guidelines, Subdivision N, Section 164-1; the study considered to meet the requirements outlined by SETAC-Europe: Procedures for Assessing the Environmental Fate and Ecotoxicity of Pesticides, Part 1, Section 2 (1995); Field Dissipation Studies for Terrestrial Uses
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

Executive Summary

Two field trials were conducted in California and Georgia, USA, to investigate the dissipation rate of using the SL formulation of propamocarb hydrochloride (Proplant) at a nominal application rate of 9.10 to 9.35 kg a.s/ha and indicated that the largest propamocarb hydrochloride residues were observed in grass cuttings and thatch in both trials. It may be assumed that propamocarb hydrochloride is intercepted and retained by the grass and thatch layer. In both trials, when propamocarb hydrochloride was applied to bare soil it remained almost exclusively in the 0-15 cm layer of the soil profile. Propamocarb hydrochloride concentrations in grass, thatch, and bare soil continued to increase up until the final application. After the final application, propamocarb hydrochloride residues declined in bare soil, thatch, and grass cuttings. Results from storage stability studies indicate that propamocarb hydrochloride residues are stable in frozen grass and soil samples, this is further supported by good recoveries from field fortified grass and soil samples analysed after 188 to 254 days of storage. Dissipation in the environment was fairly rapid with field DT_{50} values ranging from 17.4 to 23.7 days. DT_{50} values determined for grass (between 13.2 and 18.1 days) indicate that propamocarb hydrochloride is readily dissipated when intercepted by a grass layer.

I. Material and Methods

A. Materials

1. Test Material: Common name: propamocarb hydrochloride

Chemical name: propyl 3-(dimethylamino)propylcarbamate hydrochloride
Preparation: Proplant SL
Nominal a.s. content 722 g a.s/L
Actual a.s. content 711.7 g a.s/L, lot # 41090

2. Test Sites: The soil and climate characteristics are presented Table 11.1.4.1-01.

Characterisation of soils and climate in field trials conducted to investigate the rate of propamocarb hydrochloride dissipation under field conditions:

	Location I		**Location II**	
Soil origin / experimental plot	**Georgia - USA / Bare soil plot**	**Georgia - USA / Turf plot**	**California - USA / Bare soil plot**	**California - USA / Turf plot**
Soil type (SCS soil classification)	**(Loamy sand-sandy clay loam)**	**(loamy sand-sandy clay loam)**	**(Sandy loam)**	**(Sandy loam – loam)**
Climate, Summer	Hot / Humid	Hot / Humid	Hot / Dry	Hot / Dry
Climate, Winter	Mild / Wet	Mild / Wet	Cool / Dry	Cool / Dry
Irrigation	As needed	As needed	As needed	As needed
US Textural analysis sand silt clay	 62-88 % 6-10 % 6-30 %	 49-83 % 6-10 % 7-45 %	 57-67 % 28-38 % 5-7 %	 47-61 % 32-46 % 5-9 %
pH value (depth)	5.7 (15cm) 5.9 (30cm) 6.1 (45cm) 5.7 (60cm) 5.6 (75cm) 5.6 (90cm)	5.9 (7 cm) 5.4 (15cm) 6.1 (30cm) 6.1 (45cm) 5.5 (60cm) 5.2 (75cm) 5.0 (90cm)	9.0 (15cm) 9.0 (30cm) 9.2 (45cm) 9.4 (60cm) 9.6 (75cm) 9.8 (90cm)	8.6 (7 cm) 8.5 (15cm) 8.8 (30cm) 8.7 (45cm) 9.0 (60cm) 9.3 (75cm) 9.4 (90cm)
Organic Matter % (depth)	0.8 (15cm) 0.6 (30cm) 0.4 (45cm) 0.3 (60cm) 0.3 (75cm) 0.3 (90cm)	1.1 (7 cm) 0.9 (15cm) 0.8 (30cm) 0.4 (45cm) 0.4 (60cm) 0.3 (75cm) 0.3 (90cm)	0.7 (15cm) 0.3 (30cm) 0.2 (45cm) 0.2 (60cm) 0.1 (75cm) 0.1 (90cm)	3.0 (7 cm) 1.2 (15cm) 0.7 (30cm) 0.5 (45cm) 0.3 (60cm) 0.3 (75cm) 0.3 (90cm)
Cation exchange capacity (meq/100 g)	3.6 – 6.1	4.3 – 7.6	10.0 – 12.1	10.6-13.5
Bulk density (g/mL)	1.26 – 1.46	1.11 – 1.43	1.11 – 1.25	0.98-1.11
Field capacity – 1/3 bar (depth)	5.5 (15cm) 5.9 (30cm) 10.0 (45cm) 13.7 (60cm) 16.0 (75cm) 16.5 (90cm)	7.2 (7 cm) 6.3 (15cm) 8.4 (30cm) 16.5 (45cm) 17.0 (60cm) 20.8 (75cm) 23.3 (90cm)	15.0 (15cm) 17.0 (30cm) 15.2 (45cm) 14.3 (60cm) 13.9 (75cm) 13.0 (90cm)	22.1 (7 cm) 15.4 (15cm) 17.2 (30cm) 20.8 (45cm) 21.4 (60cm) 20.9 (75cm) 20.2 (90cm)

B. Study design

1. Experimental conditions: Each test site consisted of three plots, an untreated plot covered in turf grass, a treated plot covered in turf grass, and a bare soil (no turf) treated plot. The treated plots were divided into three sampling subplots. Turf plots were cultured and maintained according to GAP.
2. Application verification: A soluble liquid (SL) formulation of propamocarb hydrochloride (Proplant SL) was applied to the trial plots, with a nominal content of 722 g a.s/L during the late summer/early autumn. Each trial involved four applications, at seven-day intervals, of propamocarb hydrochloride at a nominal rate of 9.10 to 9.35 kg a.s/ha. These rates are above the proposed maximum annual use rate. Applications of the active substance were made using spray equipment calibrated to deliver 914 to 957 L/ha. In order to verify the applied dose at each application, two pans of soil were distributed in each treated subplot and sampled immediately after application. The determined propamocarb Hydrochloride residues were then compared to the calculated amount applied to the test plots.

To determine the stability of propamocarb hydrochloride during the conditions of field sample handling, storage, and shipping, field soil and turf grass-clipping samples at each test site were fortified using spiking solutions. Soil and grass clippings were stored frozen for between 108 and 273 days, and between 93 and 199 days, respectively. Seven samples of each matrix (turf and soil) were prepared; three samples were fortified with 0.02 mg/L of propamocarb hydrochloride and three samples were prepared with 1.0 mg/L of propamocarb hydrochloride, and one sample served as an unfortified control.

3. Sampling and sample processing: Five soil core samples were collected prior to and following the first application. Following applications 2, 3, and 4 soil samples were collected at 1, 2, 3, 5, 7, 10, 14, 21, and 28 days after the fourth application, and at 2, 3 and 4 months after the fourth application. Five core samples were also collected from the control plot at each sampling event. Soil samples were collected using a two-stage hydraulic soil probe. The first stage collected a 0-15 cm core and the second stage collected a 15-90 cm core. Core samples from the turf plots (treated and control) were sectioned in the field sites into 0-7.5, 7.5-15, 15-30, 30-45, 45-60, 60-75, and 75-90 cm sections. Core samples from the bare soil plot were sectioned at the field site into 0-15, 15-30, 30-45, 45-60, 60-75, 75-90 cm sections. For the turf, control, and bare soil plots the same depth core segments from the same subplot were composited. This resulted in a total of 7 and 6 samples from each turf and bare soil plot, respectively. Soil cores were stored frozen at the test sites and whilst being shipped to the laboratory for analysis.

3. Irrigation and weather data: At the Georgia site rainfall was supplemented with irrigation as needed to provide total water input of at least 110 % of the 10-year average rainfall for the trial period

4. Analytical procedures: Residues of propamocarb hydrochloride in soil and grass were analysed using EN-CAS Analytical method ENC-4/02 and ENC-3/02, respectively, both of which have a lowest validated level of 0.02 mg/kg. Propamocarb hydrochloride was extracted from the matrix by shaking with MeOH/NaOH mixture in saturated NaCl. The extracted sample was then filtered and evaporated. The pH was then adjusted to 12-13 with NaOH and the analyte was partitioned two times with dichloromethane (DCM). DCM fractions were collected through a sodium sulphate pad, which was then rinsed with DCM, evaporated and reconstituted with MeOH. The sample was analysed for propamocarb hydrochloride using LC/MS.

C. Determination of degradation kinetics

Using the data from each field trial residue data in grass, thatch, and soil propamocarb hydrochloride dissipation was described assuming first-order kinetics. DT_{50} and DT_{90} values for propamocarb hydrochloride were estimated from the degradation rate k using the following equations:

$$DT_{50} = \frac{\ln 2}{k} \qquad DT_{90} = \frac{\ln 10}{k}$$

II. Results and Discussion

A. Mass accounting: Recoveries of propamocarb hydrochloride residues after storage in soil and grass clippings indicate good recovery. Average recoveries for propamocarb hydrochloride from fortified samples are provided below. Residues found at each storage interval were corrected for the for the freshly prepared recovery samples fortified at 0.02 and 0.20 mg/L. Adjusted recoveries from California grass samples were 95 % and 92 % after 92 and 212 days of frozen storage, respectively. The adjusted recoveries from California soil samples were 102 % and 87 % after 92 and 239 days of frozen storage, respectively. The adjusted recoveries from Georgia soil samples were 94 % and 71 % after 95 and 273 days of frozen storage, respectively.

Summary of average recoveries for propamocarb hydrochloride from fortified grass clippings and soil samples:

Location/fortification	Average recovery (%)
California/grass clippings	93 ± 11.2
California/soil	78 ± 9.4
Georgia/grass clippings	86 ± 8.5
Georgia/soil	78 ± 13.4

Results from tank mix analyses indicate that spray mixtures used in the application of Proplant SL to turf and bare soil were within the range of 96% to 113% of the nominal concentration of propamocarb hydrochloride. Overall, the measured concentrations of tank mixture samples collected pre- and post-application were 104% ± 5% and 105% ± 4% of the nominal concentration in California and Georgia samples, respectively.
Propamocarb hydrochloride residues in soil, and turf plot thatch and soil are provided below. Analysis of the turf plot thatch after the fourth application for both California (5.31 mg/kg) and Georgia (5.50 mg/kg) showed a steady increase in the amount of propamocarb hydrochloride in the thatch compared to residues after the first application. Residues increased in thatch in the Californian and Georgian trials, reaching maximum residues of 8.28 and 6.35 mg/kg, respectively, on Day 2 after the fourth application. In both trials propamocarb hydrochloride residues in thatch then began to decline steadily until reaching a minimum of 0.25 mg/kg (California) and 0.07 mg/kg (Georgia). Analysis of the bare soil after the fourth application for both California (15.22 mg/kg) and Georgia (10.66 mg/kg) showed a steady increase in the amount of propamocarb hydrochloride in the bare soil compared to residues after the first application. Residues decreased in soil in the Californian and Georgian trials after the fourth application. However, between day 2 and 3 in the Californian trial the propamocarb hydrochloride residue briefly increased from 10.77 to 13.23 mg/kg before declining again. In both trials propamocarb hydrochloride residues in bare soil declined reaching minimum values of 0.37 mg/kg (California) and 0.07 mg/kg (Georgia). All residues in the control plots were determined to be less than the LOQ (0.02 mg/kg).
For both trials, propamocarb hydrochloride residues in the turf plot soil below the thatch (7.5-15 and 15-30 cm) were insignificant in comparison to residues found in thatch samples. In the California trial the maximum average residue in the 7.5-15 cm and 15-30 cm layers were 0.51 mg/kg and 0.03 mg/kg, respectively. No residues greater than the LOQ were found in samples below 30 cm, except for one (0.024 mg/kg) in the 30-45 cm layer. In the Georgia trial the maximum average residue in the 7.5-15 cm layer was 0.17 mg/kg. No residues greater than the LOQ were found in samples below 15 cm.

Propamocarb hydrochloride residues in turf plot thatch and soil samples from field trials conducted in California and Georgia, USA:

Sampling Event	Average propamocarb hydrochloride residue (mg/kg)							
	California				Georgia			
	0-7.5 cm thatch		0-15 cm bare soil		0-7.5 cm thatch		0-15 cm bare soil	
	Measured	Adjusted 1)	Measured	Adjusted 1)	Measured	Adjusted 1)	Measured	Adjusted 1)
Days								
-1	<0.02	-	<0.02	-	<0.02	-	<0.02	-
0 appl. 1	1.93	2.48	3.61	4.63	0.44	0.57	2.26	2.89
0 appl. 2	3.48	4.46	6.11	7.84	1.45	1.85	3.95	5.07
0 appl. 3	2.61	3.35	9.61	12.33	4.04	5.18	7.89	10.11
0 appl. 4	4.14	5.31	11.87	15.22	4.29	5.50	8.31	10.66
1	5.15	6.60	10.04	12.87	3.87	4.96	6.76	8.67
2	6.46	8.28	8.40	10.77	4.95	6.35	5.02	6.44
3	4.82	6.18	10.32	13.23	3.80	4.87	4.99	6.40
5	4.19	5.38	10.17	13.04	3.38	4.33	2.46	3.15
7	4.68	6.00	10.80	13.84	4.35	5.58	1.90	2.44
10	4.03	5.17	9.39	12.04	1.82	2.33	1.15	1.47
14	2.37	3.04	6.49	8.32	0.50	0.64	0.43	0.55
21	1.51	1.93	5.56	7.13	0.31	0.39	0.14	0.19
28	1.00	1.28	5.04	6.47	0.26	0.34	0.23	0.29
Months								

2	0.58	0.74	1.36	1.75	0.08	0.10	0.08	0.10
3	0.24	0.31	0.54	0.69	0.06	0.07	0.07	0.08
4	0.20	0.25	0.29	0.37	0.05	0.07	0.06	0.07

Note: 1) Residue values were adjusted based on average recovery from soil field fortification samples from each site (California 78 %, Georgia 78 %); Appl. 1 = Application number 1 (of four)

Propamocarb hydrochloride residues in grass cutting samples are provided below. Residues of propamocarb hydrochloride in grass samples were greater after the fourth application than after the first application. Overall, the residues found in both trial sites were similar in both magnitude and dissipation rate. The maximum adjusted average propamocarb hydrochloride residues in grass samples were 831 mg/kg and 751 mg/kg for Georgia and California, respectively. By the final sampling point (4 months after the final application) residue levels had declined to 9.99 mg/kg and 1.48 mg/kg in the California and Georgia trials, respectively. Residues in all control plot samples from Georgia were significantly less than the LOQ, except for Day 1 after the fourth application in the Georgia trial (0.149 mg/kg). In the California trial residues in the control were less than the LOQ except for samples collected at Day 1 through to Day 10 after the fourth application. It is likely that turf in the control plot was contaminated during plot maintenance. Contamination appears to have been confined to the grass.

Propamocarb hydrochloride residues in turf plot thatch and soil samples from field trials conducted in California and Georgia, USA:

Sampling Event	Average propamocarb hydrochloride residue (mg/kg)			
	California		Georgia	
	Measured	Adjusted [1)]	Measured	Adjusted [1)]
Days				
-1	<0.02	-	<0.02	-
0 appl. 1	446.12	479.70	520.24	604.93
0 appl. 2	585.38	629.45	512.07	595.43
0 appl. 3	475.34	511.12	715.08	831.48
0 appl. 4	693.53	745.73	652.24	758.42
1	583.90	627.85	654.84	761.45
2	698.81	751.41	561.78	653.23
3	581.08	624.82	596.69	693.82
5	315.20	338.92	188.81	219.55
7	208.29	223.96	204.36	237.63
10	300.93	323.58	119.34	138.77
14	164.20	176.56	79.30	92.21
21	151.34	162.73	52.21	60.70
28	105.77	113.73	35.90	41.74
Months				
2	28.63	30.79	3.85	4.48
3	6.69	7.19	2.33	2.71
4	9.29	9.99	1.27	1.48

Note: 1) Residue values were adjusted based on average recovery from soil field fortification samples from each site (California 93 %, Georgia 86 %); Appl. 1 = Application number 1 (of four)

B. Kinetics: Results from a first order kinetic model for the estimation of field DT_{50} and DT_{90} values in thatch and bare soil are provided below. At the California trial site DT_{50} (DT_{90}) values for thatch and bare soil were 23.7 days (78.6 days) and 22.1 days (73.3 days), respectively. At the Georgia trial site DT_{50} (DT_{90}) values for thatch and bare soil were 17.4 days (57.7 days) and 17.6 days (58.6 days), respectively. In comparison with laboratory DT_{50} results, rates of dissipation in the field appear to match closely those determined in laboratory experiments with the exception of soils that either have large clay content or low microbial biomass count.
Results of a first order kinetic model for the estimation of field DT_{50} and DT_{90} values in grass samples are provided below. At the California trial site DT_{50} (DT_{90}) values for grass samples were 18.1 days (60.1 days). At the Georgia trial site DT_{50} (DT_{90}) values for grass samples were 13.2 days (43.9 days). DT_{50} and DT_{90} values determined for grass samples were lower than in thatch and bare soil samples.

First-order dissipation model parameters and estimated DT50 and DT90 values for propamocarb hydrochloride in turf plot thatch and bare soil from field trials conducted in California and Georgia, USA:

	California		Georgia	
	Thatch	**Bare soil**	**Thatch**	**Bare soil**
DT_{50} (days)	23.7	22.1	17.4	17.6
DT_{90} (days)	78.6	73.3	57.7	58.6
K	0.0293	0.0314	0.0399	0.0393
r^2	0.92	0.99	0.78	0.76

First-order dissipation model parameters and estimated DT50 and DT90 values for propamocarb hydrochloride in grass cutting samples from field trials conducted in California and Georgia, USA:

	California	Georgia
DT_{50} (days)	18.1	13.2
DT_{90} (days)	60.1	43.9
k	0.0383	0.0524
r^2	0.91	0.89

III. Conclusion

Propamocarb hydrochlorid rapidly degraded under field consitions with field DT_{50} values ranging from 17.4 to 23.7 days.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Furthermore, there is information available for four additional trial field soil dissipation trials located in Canada and two additional field soil dissipation trials located in the USA. The trials were carried out under field use conditions with three applications and seven days between applications. Summaries of the corresponding studies are included below (KCA 7.1.2.2.1/02 and KCA 7.1.2.2.1/03). The study locations were evaluated using the OECD ENASGIPS tool (Europe – North American Soil Geographic Information for Pesticide Studies) aiming to determine their representativeness throughout Europe based on climate and soil similarity. A summary of this evaluation is provided below (KCA 7.1.2.2.1/04). Three of the trial sites were found to be sufficiently representative for European conditions. For these trial sites a kinetic evaluation for the determination of trigger endpoints was performed and a summary of this evaluation is provided below (KCA 7.1.2.2.1/05).

Report:	7.1.2.2.1/02; Belyk, M.; 1998; M-141261-01-1
Title:	The degradation and fate of propamocarb hydrochloride following an application to bare soils in Canada
Report No.:	ACI97-48
Document No.:	M-141261-01-1
Guideline(s):	PMRA Environmental Chemistry and Fate Guideline 8.3.2
Guideline deviation(s):	not specified
GLP/GEP:	**yes**

Executive Summary

Field trials in Canada were conducted in Manitoba (Carberry), Ontario (Branchton), Prince Edward Island (New Glasgow) and New Brunswick (Richmond Corner) using a liquid formulation of propamocarb hydrochloride (Tattoo C®) at a nominal application rate of 1.0 kg a.s/ha. Three applications of Tattoo C® were made to bare soil with seven days between applications. Soil core samples were collected immediately after the first and second application, prior to the second and third application and further on at regular intervals up to 84 days after the final application (DAT). In

Manitoba, additional samples were collected in the following year (307 and 378 DAT). The sampling depth was 10 cm for samplings prior to the third application and 45 cm afterwards. Soil core samples were composited into 0-10, 10-20, 20-30 and 30-45 cm depths, where applicable. Propamocarb was extracted from soil and analysis was done by GC/TSD and GC/MS according to the validated Xenos laboratory procedure XAM-32.
The dissipation of propamocarb in soil was similar for all three eastern Canadian soils (Ontario, Prince Edward Island and New Brunswick). Propamocarb residues remained relatively constant over the first 7 to 14 days, followed by a rapid decline. Propamocarb residues remained predominantly in the 0-10 cm depth for these soils. Due to the presence of smectite-type clay minerals in the Manitoba soil, propamocarb was highly adsorbed at the 0-10 cm depth and unavailable for microbial degradation. As a result, residues were detected at the 0-10 cm depth into the following year. Propamocarb residues were also detected on DAT 0 at depths 10-20, 20-30 and 30-45 cm, respectively. These residue levels declined to less than the LOQ (<0.025 mg/kg) by 84 DAT.
Dissipation values (DT50 and DT90) were obtained from the exponential plots of the data. With the exception of Manitoba, the curve fit was good (R2 = 0.87-0.93). The calculated DT50 values were 22.5, 16.5 and 20.7 days and the DT90 values were 74.8, 54.7 and 68.9 days for the New Brunswick, Ontario and PEI soils, respectively. A DT50 value of approximately 378 days was observed for the Manitoba soil.
Overall, propamocarb is not expected to leach; residue in the soil was confined to the 0-10 cm depth as a result of rapid microbial degradation or clay adsorption.

I. Material and Methods

A. Materials

1. Test Material: Common name: propamocarb hydrochloride
Chemical name: propyl 3-(dimethylamino)propylcarbamate hydrochloride
Formulation: Tattoo C®, containing the active substance propamocarb and chlorothalonil (the latter was not analysed in the course of the study)
Nominal a.s. content 375 g a.s/L, lot # AR960519

2. Test Sites: The soil characteristics are presented below.

Characterisation of soils in field trials conducted to investigate the rate of propamocarb hydrochloride dissipation under field conditions:

	Location 1	Location 2	Location 3	Location 4
Soil location	**Carberry, Manitoba - Canada**	**Branchton, Ontario - Canada**	**Richmond Corner, New Brunswick - Canada**	**New Glasgow, Prince Edward Island (PEI) - Canada**
Soil type	**Loam**	**Silt Loam**	**Loam**	**Sandy Loam**
US Textural analysis				
sand	43-45 %	12-17 %	51 %	71 %
silt	32-34 %	70-75 %	35 %	22 %
clay	21-23 %	13-14 %	14 %	7 %
pH value (depth)	5.9 (0-10 cm) 6.4 (10-20 cm) 6.6 (20-30 cm) 6.9 (30-45 cm)	6.7 (0-10 cm) 7.0 (10-20 cm) 7.4 (20-30 cm) 7.8 (30-45 cm)	5.7 (0-30 cm)	5.8 (0-15 cm)
Organic Matter % (depth)	6.3 (0-10 cm) 4.9 (10-20 cm) 3.2 (20-30 cm) 2.3 (30-45 cm)	2.9 (0-10 cm) 2.7 (10-20 cm) 1.2 (20-30 cm) 0.6 (30-45 cm)	5.7 (0-30 cm)	4.2 (0-15 cm)
Cation exchange capacity (meq/100 g)	24.0 – 29.4	18.8 – 24.3	12.9	10.6
Bulk density (g/mL)	1.16 – 1.38	1.04 – 1.27	0.88	1.00
Field moisture holding capacity – 1/3 bar (depth)	0.23 (0-10 cm) 0.22 (10-20 cm) 0.19 (20-30 cm) 0.20 (30-45 cm)	23.9 (0-10 cm) 24.9 (10-20 cm) 26.2 (20-30 cm) 25.2 (30-45 cm)	40.0 (0-30 cm)	21.9 (0-15 cm)

B. Study design

1. Experimental conditions: Each test site consisted of three treated and three untreated soil plots. All plots were tilled and cleared of debris in spring prior to application of the test substance. Weed growth throughout the sampling period was controlled with approved nonselective herbicides

2. Weather data: Air temperature and precipitation data were recorded during the field soil dissipation trial at all sites. Maximum and minimum air temperatures at all sites have been typical when compared to the respective 30 year averages. Precipitation was in reasonable agreement with rainfall averages.

3. Application: A soluble liquid (SL) formulation of propamocarb hydrochloride (Tattoo C®) with a nominal content of 375 g a.s/L was applied to the trial plots at the end of June\beginning of July. Each trial involved three applications, at seven-day intervals, of propamocarb hydrochloride at a rate of 0.96 to 1.03 kg a.s/ha. These rates are close to the nominal application rate of 1 kg a.s/ha. Applications of the active substance were made using spray equipment at 220 L/ha. Application verification was not performed.

4. Sampling and sample processing:
Ten soil core samples per plot were collected by pressing a hydraulic core sampler or a hand-held coring device (minimum 3 cm diameter) into the ground at each sampling event. All ten samples were composited into a single sample. At all sites, samples were taken to a depth of 10 cm immediately after the first and second application and prior to the second and third application. Following the 3rd application samples were collected to a depth of 45 cm at 0, 3 (2 DAT for soil Manitoba), 7, 14, 28, 56 and 84 days after treatment (DAT). Additional samples were collected in the following year at Manitoba field site (307 and 378 DAT). All cores collected after the 3rd application were sectioned by depth (0-10, 10-20, 20-30, 30-45 cm).
Samples were also collected from 0-10 cm depth from the untreated plots immediately following the 1st application and on 0 and 14 DAT.
Prior to the conduct of the study, untreated soil (approximately 500 g each) from the 0-10, 10-20, 20-30 and 30-45 cm depths was collected from each field site. These samples were fortified with analytical standard in order to determine the efficiency of the analytical method.
All samples were transferred under chilled conditions from the test site area to a sample preparation area only when the expected travel time exceeded 2 hours. Once at the sample preparation area, all soils were weighed, thoroughly mixed divided into two subsamples, each representing no less than 400 g. All subsamples were stored in a deep freezer before and during shipping to the laboratory for the analysis.
An earlier study has shown that propamocarb hydrochloride (PHC) residues may be recovered in 77 % yield after 14 months of frozen storage. Since no treated samples were stored in frozen condition for longer than 8 months no correction factor for any possible losses during frozen storage has been applied to the reported concentrations.
5. Analytical procedures: Soil samples were analysed for PHC only. Propamocarb was extracted from the matrix by shaking the soil sample with acidified methanol. The extract was centrifuged, filtered and the methanol was removed using a rotary evaporator. The acidic extract was neutralized to pH 6 – 6.5 by addition of 10 N NaOH which results in the formation of a precipitate. The precipitate was removed by centrifuging, washed with water and the combined supernatant and water were transferred to a separatory funnel. After acidifying with 1 N HCl, the solution was extracted with dichloromethane and diisopropyl ether, the organic phases being discarded. The aqueous solution was basified with 10 N NaOH and the propamocarb was partitioned into dichloromethane. The dichloromethane extract was evaporated after adding aqueous HCl as a keeper. The aqueous concentrate was again basified and the propamocarb was partitioned into diisopropyl ether.
The diisopropyl ether extract was analyzed by GC/TSD or GC/Ion Trap MS. The overall mean recoveries and standard deviations of the analytical method were 89.3 ± 8.2 % and 108 ± 12.7 % by GC/TSD and GC/MS respectively. The limit of quantitation (LOQ) was 0.025 mg/kg.
Gravimetric moisture content was determined to correct the results of PHC determination for the soil moisture. Duplicate subsamples were weighed and dried in an oven at no less than 105 °C and the measured weight loss was divided by the final weight of the dried soil. An average moisture content was expressed as a percent.

C. Determination of degradation kinetics

DT_{50} and DT_{90} values for propamocarb hydrochloride were estimated from the exponential plots of the data using the following equations:

$$DT_{50} = \frac{\ln 2}{k} \qquad DT_{90} = \frac{\ln 10}{k}$$

II. Results and Discussion

A. Mass accounting: None of the untreated control samples from the four field sites contained any propamocarb residues greater than the LOQ. Average recoveries for PHC from fortified untreated control samples are provided below. The high % recoveries of propamocarb indicated an acceptable analytical method for all soil types. Residues found in the soil samples from treated plots were corrected for the mean recoveries of PHC from the respective fortified control samples and for the soil moisture content. Uncorrected residues determined to be below 0.025 mg/kg were reported as being below limit of quantification (<LOQ) with no correction factors for moisture content or recovery being applied.

Summary of average recoveries for PHC from fortified untreated soil samples:

Location	Fortification (µg/g)	No. of fortifications	Mean recovery, %
Carberry, Manitoba	0.025 to 1.0	21	77.8 ± 5.6
Branchton, Ontario	0.025 to 1.0	17	85.5 ± 14.9
Richmond Corner, New Brunswick	0.025 to 3.0	15	91.0 ± 11.5
New Glasgow, PEI	0.025 to 1.0	17	92.2 ± 14.2

PHC residues detected in soils from the four field sites are presented below.
The average residue levels of propamocarb found in the 0 – 10 cm layer of the soil from the Ontario field site after the first, second and third applications were 0.543 mg/kg (-14 DAT), 0.773 mg/kg (-7 DAT) and 0.899 mg/kg (0 DAT). Prior to the second and third sprays, the average levels were 0.281 and 0.689 mg/kg, respectively. In this layer, the residue levels appear to decline slowly over the first 7 to 14 days and then decline rapidly. With the exception of one replicate on 0 DAT, no PHC residues were detected in the Ontario soil collected below the 10 cm depth over the entire sampling period.

PHC residues at various depths in soil from the field site Branchton, Ontario (average values of the replicate measurements adjusted for daily recovery and moisture content are presented):

DAT	Replicate	Propamocarb, mg/kg			
		0-10 cm	10-20 cm	20-30 cm	30-45 cm
-14	A	0.583	-	-	-
	B	0.466	-	-	-
	C	0.579	-	-	-
	Mean	*0.543*	-	-	-
-7 (pre)	A	0.258	-	-	-
	B	0.297	-	-	-
	C	0.289	-	-	-
	Mean	*0.281*	-	-	-
-7	A	0.662	-	-	-
	B	0.810	-	-	-
	C	0.848	-	-	-
	Mean	*0.773*	-	-	-
0 (pre)	A	0.700	-	-	-
	B	0.672	-	-	-
	C	0.696	-	-	-
	Mean	*0.689*	-	-	-
0	A	0.757	*ND*	*ND*	*ND*

DAT	Replicate	Propamocarb, mg/kg			
		0-10 cm	10-20 cm	20-30 cm	30-45 cm
	B	0.814	*ND*	*ND*	*ND*
	C	1.127	*0.054*	*ND*	*ND*
	Mean	*0.899*	*0.054*	<LOQ	<LOQ
3	A	0.785	*ND*	*ND*	*ND*
	B	0.891	*ND*	*ND*	*ND*
	C	0.652	*ND*	*ND*	*ND*
	Mean	*0.776*	<LOQ	<LOQ	<LOQ
7	A	0.726	*ND*	*ND*	*ND*
	B	0.954	*ND*	*ND*	*ND*
	C	0.751	*ND*	*ND*	*ND*
	Mean	*0.810*	<LOQ	<LOQ	<LOQ
14	A	0.677	*ND*	*ND*	-
	B	0.912	*ND*	*ND*	-
	C	0.601	*ND*	*ND*	-
	Mean	*0.730*	<LOQ	<LOQ	<LOQ
28	A	0.259	*ND*	*ND*	*ND*
	B	0.134	*ND*	*ND*	*ND*
	C	0.164	*ND*	*ND*	*ND*
	Mean	*0.186*	<LOQ	<LOQ	<LOQ
56	A	0.079	*ND*	*ND*	*ND*
	B	0.057	*ND*	*ND*	*ND*
	C	0.047	*ND*	*ND*	*ND*
	Mean	*0.061*	<LOQ	<LOQ	<LOQ
84	A	0.039	*ND*	*ND*	-
	B	0.032	*ND*	*ND*	-
	C	0.037	*ND*	*ND*	-
	Mean	*0.036*	<LOQ	<LOQ	<LOQ

DAT = Days after treatment (third application); - = not sampled; Values calculated in the course in writing this summary are given in *italics*

The average residue levels of propamocarb found in the 0-10 cm layer of the soil from the New Brunswick field site after the first, second and third applications were 0.495 mg/kg (-14 DAT), 1.107 mg/kg (-7 DAT) and 1.001 mg/kg (0 DAT). Prior to the second and third sprays, the average levels were 0.327 and 1.339 mg/kg, respectively. Apart from anomalously high values from one replicate (3.01-3.49 mg/kg) on 7 DAT, the average values show little decline over the first 14 days after which degradation was rapid. No PHC residues were detected in the New Brunswick soil collected below the 10 cm depth over the entire sampling period.

Propamocarb residues at various depth in soil from the field site Richmond Corner, New Brunswick (average values of the replicate measurements adjusted for daily recovery and moisture content are presented):

DAT	Replicate	propamocarb, mg/kg			
		0-10 cm	10-20 cm	20-30 cm	30-45 cm
-14	A	0.596	-	-	-
	B	0.629	-	-	-
	C	0.259	-	-	-
	Mean	*0.495*	-	-	-
-7 (pre)	A	0.560	-	-	-
	B	0.215	-	-	-
	C	0.207	-	-	-
	Mean	*0.327*	-	-	-
-7	A	1.230	-	-	-
	B	1.353	-	-	-
	C	0.738	-	-	-
	Mean	*1.107*	-	-	-
0 (pre)	A	1.035	-	-	-
	B	1.741	-	-	-
	C	1.240	-	-	-
	Mean	*1.339*	-	-	-
0	A	1.018	ND	ND	ND
	B	0.755	ND	ND	ND
	C	1.230	ND	ND	ND
	Mean	*1.001*	*<LOQ*	*<LOQ*	*<LOQ*
3	A	0.835	ND	ND	ND
	B	0.819	ND	ND	ND
	C	1.412	ND	ND	ND
	Mean	*1.022*	*<LOQ*	*<LOQ*	*<LOQ*
7	A	1.698	ND	ND	ND
	B	3.009	ND	ND	ND
	C	1.100	ND	ND	ND
	D	1.840	-	-	-
	E	3.488	-	-	-
	F	1.509	-	-	-
	Mean	*2.107*	*<LOQ*	*<LOQ*	*<LOQ*
14	A	1.311	ND	ND	ND
	B	0.785	ND	ND	ND
	C	0.709	ND	ND	ND
	Mean	*0.935*	*<LOQ*	*<LOQ*	*<LOQ*
28	A	0.777	ND	ND	ND
	B	0.816	ND	ND	ND
	C	0.792	ND	ND	ND
	Mean	*0.795*	*<LOQ*	*<LOQ*	*<LOQ*
56	A	0.141	ND	ND	ND
	B	0.146	ND	ND	ND
	C	0.263	ND	ND	ND
	Mean	*0.183*	*<LOQ*	*<LOQ*	*<LOQ*
84	A	0.119	ND	ND	ND
	B	0.080	ND	ND	ND
	C	0.137	ND	ND	ND
	Mean	*0.112*	*<LOQ*	*<LOQ*	*<LOQ*

DAT = Days after treatment (third application); - = not sampled; Values calculated in the course in writing this summary are given in *italics*

The average residue levels of propamocarb found in the 0-10 cm layer of the soil from the PEI field site after the first, second and third applications were 0.396 mg/kg (-14 DAT), 0.915 mg/kg (-7 DAT) and 0.937 mg/kg (0 DAT). Before the second and third sprayings, the average levels were 0.474 and 0.832 mg/kg, respectively. In the 0-10 cm layer, the soil residue levels appear to decline slowly over the first 7 days and then decline rapidly. At the 10-20 cm depth, trace amounts of residues were detected only on 3 and 7 DAT. No propamocarb residues were detected in the PEI soil collected below the 20 cm depth over the entire sampling period.

Propamocarb residues at various depth in soil from the field site New Glasgow, PEI (average values of the replicate measurements adjusted for daily recovery and moisture content are presented):

DAT	Replicate	propamocarb, mg/kg			
		0-10 cm	10-20 cm	20-30 cm	30-45 cm
-14	*A*	*0.327*	-	-	-
	B	*0.424*	-	-	-
	C	*0.438*	-	-	-
	Mean	*0.396*	-	-	-
-7 (pre)	*A*	*0.589*	-	-	-
	B	*0.364*	-	-	-
	C	*0.468*	-	-	-
	Mean	*0.474*	-	-	-
-7	*A*	*1.010*	-	-	-
	B	*0.815*	-	-	-
	C	*0.921*	-	-	-
	Mean	*0.915*	-	-	-
0 (pre)	*A*	*0.855*	-	-	-
	B	*0.721*	-	-	-
	C	*0.624*	-	-	-
	D	*1*	-	-	-
	E	*0.789*	-	-	-
	F	*0.939*	-	-	-
	Mean	*0.832*	-	-	-
0	*A*	*0.886*	-	-	-
	B	*0.523*	-	-	-
	C	*0.61*	-	-	-
	D	*1*	*ND*	*ND*	*ND*
	E	*1*	*ND*	*ND*	*ND*
	F	*1*	*ND*	*ND*	*ND*
	Mean	*0.937*	*<LOQ*	*<LOQ*	*<LOQ*
3	*A*	*1*	*0.184*	*ND*	*ND*
	B	-	*0.107*	-	-
	C	*0.886*	*ND*	*ND*	*ND*
	D	*0.766*	*0.052*	*ND*	*ND*
	Mean	*0.891*	*0.114*	*<LOQ*	*<LOQ*
7	*A*	*0.884*	*ND*	*ND*	*ND*
	B	*0.861*	*0.039*	*ND*	*ND*
	C	*0.928*	*ND*	*ND*	*ND*
	Mean	*0.891*	*0.039*	*<LOQ*	*<LOQ*
14	*A*	*0.506*	*ND*	*ND*	*ND*
	B	*0.423*	*ND*	*ND*	*ND*

DAT	Replicate	propamocarb, mg/kg			
		0-10 cm	10-20 cm	20-30 cm	30-45 cm
	C	*0.463*	*ND*	*ND*	*ND*
	Mean	*0.464*	*<LOQ*	*<LOQ*	*<LOQ*
28	*A*	*0.533*	*ND*	*ND*	-
	B	*0.474*	*ND*	*ND*	-
	C	*0.451*	*ND*	*ND*	-
	Mean	*0.486*	*<LOQ*	*<LOQ*	*<LOQ*
56	*A*	*0.248*	*ND*	*ND*	-
	B	*0.098*	*ND*	*ND*	-
	C	*0.205*	*ND*	*ND*	-
	Mean	*0.184*	*<LOQ*	*<LOQ*	*<LOQ*
84	*A*	*0.055*	*ND*	*ND*	-
	B	*0.056*	*ND*	*ND*	-
	C	*0.037*	*ND*	*ND*	-
	Mean	*0.049*	*<LOQ*	*<LOQ*	*<LOQ*

DAT = Days after treatment (third application); - = not sampled; Values calculated in the course in writing this summary are given in *italics*

The average residue levels of propamocarb found in the 0-10 cm layer of the soil from the Manitoba field site after the first, second and third applications were 0.760 mg/kg (-14 DAT), 1.067 mg/kg (-7 DAT) and 1.275 mg/kg (0 DAT). Before the second and third sprayings, the average levels were 0.661 and 1.140 mg/kg, respectively. Based on the 0 and 307 DAT results (1.275 and 1.102 mg/kg, respectively), little degradation of propamocarb occurred during the first growing and winter seasons. By 378 DAT, the average level detected in the 0-10 cm depth declined to 0.573 mg/kg. This demonstrates that some degradation of propamocarb occurred during the second growing season.
Immediately after the third application (0 DAT), average propamocarb residue levels of 0.074, 0.062 and 0.050 mg/kg were detected at the 10-20, 20-30 and 30-45 cm depths. Presumably, the detection of sporadic residues in Manitoba was the result of loose, surface soil being dislodged and pulled down during the coring event. These residues disappear with time, none being detected at 84 DAT. No residues were detected below 10 cm following snowmelt infiltration in the year following the application.

Propamocarb residues at various depth in soil from the field site Carbery, Manitoba (average values of the replicate measurements adjusted for daily recovery and moisture content are presented):

DAT	Replicate	propamocarb, mg/kg			
		0-10 cm	10-20 cm	20-30 cm	30-45 cm
-14	A	0.807	-	-	-
	B	0.725	-	-	-
	C	0.749	-	-	-
	Mean	*0.760*	-	-	-
-7 (pre)	A	0.663	-	-	-
	B	0.608	-	-	-
	C	0.711	-	-	-
	Mean	*0.661*	-	-	-
-7	A	0.923	-	-	-
	B	1.082	-	-	-
	C	1.195	-	-	-
	Mean	*1.067*	-	-	-
0 (pre)	A	1.049	-	-	-
	B	1.131	-	-	-
	C	1.240	-	-	-
	Mean	*1.140*	-	-	-
0	A	1.353	0.08	0.054	0.056

DAT	Replicate	propamocarb, mg/kg			
		0-10 cm	10-20 cm	20-30 cm	30-45 cm
	B	1.238	0.076	0.074	0.049
	C	1.233	0.066	0.057	0.044
	Mean	*1.275*	*0.074*	*0.062*	*0.050*
2	A	1.103	0.056	0.048	0.053
	B	0.850	0.071	0.074	0.07
	C	1.073	0.063	0.054	0.05
	Mean	*1.009*	*0.063*	*0.059*	*0.058*
7	A	1.142	0.041	0.038	0.047
	B	1.388	0.064	0.061	0.058
	C	1.214	0.064	0.061	0.072
	Mean	*1.248*	*0.056*	*0.053*	*0.059*
14	A	1.036	0.047	0.04	0.039
	B	1.179	0.043	0.035	0.042
	C	1.320	0.057	0.034	0.043
	Mean	*1.178*	*0.049*	*0.036*	*0.041*
28	A	1.042	ND	0.033	0.034
	B	0.668	0.037	ND	ND
	C	1.506	0.037	0.036	0.036
	Mean	*1.072*	*0.037*	*0.035*	*0.035*
56	A	0.980	0.042	0.041	0.047
	B	0.885	0.033	0.035	0.035
	C	0.822	0.034	0.043	0.045
	Mean	*0.896*	*0.036*	*0.040*	*0.042*
84	A	1.154	ND	ND	-
	B	0.809	ND	ND	-
	C	1.162	ND	ND	-
	D	1.171	-	-	-
	E	0.800	-	-	-
	F	1.197	-	-	-
	G	1.149	-	-	-
	H	0.853	-	-	-
	I	1.205	-	-	-
	Mean	*1.056*	*<LOQ*	*<LOQ*	*<LOQ*
307	A	0.978	ND	ND	ND
	B	1.170	ND	ND	ND
	C	1.159	ND	ND	ND
	Mean	*1.102*	*<LOQ*	*<LOQ*	*<LOQ*
378	A	0.567	ND	ND	ND
	B	0.612	ND	ND	ND
	C	0.539	ND	ND	ND
	Mean	*0.573*	*<LOQ*	*<LOQ*	*<LOQ*

DAT = Days after treatment (third application); - = not sampled; Values calculated in the course in writing this summary are given in *italics*

B. Kinetics: Results from a first order kinetic model for the estimation of field DT_{50} and DT_{90} values in soils from the four Canadian field sites are provided in Table Table 11.1.4.1-13. Propamocarb degraded rapidly in the New Brunswick, Ontario and Prince Edward Island soils. Calculated DT_{50} and DT_{90} values were 16.5 to 22.5 days and 54.7 to 74.8 days, respectively, for the 3 eastern Canadian soils. A calculated DT_{50} value of 630 days represents an overprediction for the Manitoba soil as a result of an insignificant degradation in the year of application. However, sufficient degradation of propamocarb occurred in the

year following the application to provide an observed DT_{50} value of approximately 378 days. This period includes 5 months of winter.

First-order dissipation model parameters and observed and estimated DT50 and DT_{90} values for propamocarb dissipation in Canada

	Field Site			
	Branchton, Ontario	**Richmond Corner, New Brunswick**	**New Glasgow, Prince Edward Island (PEI)**	**Carberry, Manitoba**
DT_{50} (days) observed	14-28	28-56	14-28	~ 378
DT_{90} (days) observed	56-84	56-84	56-84	-
DT_{50} (days)	16.5	22.5	20.7	630
DT_{90} (days)	54.7	74.8	68.9	-
k	0.0421	0.0308	0.0334	0.0011
r^2	0.93	0.87	0.92	0.30

III. Conclusion

The field dissipation of propamocarb was very rapid (calculated DT_{50} = 16.5 to 22.5 days) in soils tested in Ontario, New Brunswick and Prince Edward Island, The dissipation of propamocarb was substantially slower in Manitoba (observed DT_{50} ~ 378 days) due to the presence of smectite clay minerals in the Manitoba soil. Presumably, propamocarb was tightly bound to this clay type resulting in carry over into the following year. Overall, propamocarb is not expected to leach; residue in the soil was confined to the 0-10 cm depth as a result of rapid microbial degradation or clay adsorption.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Report:	KCA 7.1.2.2.1/03; Cole M. G.; 1995; M-135484-01-1
Title:	Dissipation of propamocarb.HCI in Soil Following Application of BANOL to Bare Plot, USA, 1993
Report No.:	AV-93R-01
Document No.:	M-135484-01-1
Guideline(s):	US-EPA Pesticide Assessment Guidelines, Subdivision N, Section 164-1; the study considered to meet the requirements outlined by SETAC-Europe: Procedures for Assessing the Environmental Fate and Ecotoxicity of Pesticides, Part 1, Section 2 (1995); Field Dissipation Studies for Terrestrial Uses
Guideline deviation(s):	not specified
GLP/GEP:	yes

Executive Summary

Field trials were conducted at two sites in the USA, AgrEvo Illinois Field Research Station (FSIL), Wonder Lake IL and the AgrEvo Research Center (ARC), Pikeville, NC, using a liquid formulation of propamocarb hydrochloride (BANOL®). Three applications of BANOL® were made to bare sandy loam soil with seven days between applications. Soil core samples were collected before the first application, immediately after three applications and further on at regular intervals up to 18 months after the final application. Samples were cut into 0–7.5, 7.5–15, 15–30, 30–45, 45–60, 60–75 and 75–90 cm horizons. Analysis of propamocarb residues was performed by gas chromatography.

The biphasic dissipation of propamocarb was similar for both sites. Over the first three to four weeks the half-lives were 6 days at FSIL and 9 days at ARC. This rapid decline was followed by a slower decline phase with half-lives of 187 days and 132 days respectively at ARC and FSIL.

No evidence for leaching was observed at trial site ARC where typical rainfall conditions pertained. At this site, residues were only sporadically observed as low as the 15 cm to 30 cm horizon. At trial site FSIL, the plot was subjected to rainfall which exceeded the 100 year maximum in the month following

the final application. This saturated the test plot and led to propamocarb residues being observed as low as the 75 cm to 90 cm in isolated soil cores. Residues observed below 30 cm were at least two orders of magnitude below those in the surface horizons.

I. Materials and Methods

A. Materials

1. Test Material: Common name: propamocarb hydrochloride
Chemical name: propyl 3-(dimethylamino)propylcarbamate monohydrochloride
Preparation: BANOL
A.s. content 66.5 %, lot # 13402804

2. Test Sites: The soil characteristics are presented below.

Characterisation of soils in field trials conducted to investigate the rate of propamocarb hydrochloride dissipation under field conditions:

	Location 1	Location 2
Soil location	**AgrEvo Research Center (ARC), Pikeville, NC - USA**	**Illinois Field Research Station (FSIL), Richmond, IL - USA**
Soil type	**Sandy loam**	**Sandy loam**
US Textural analysis sand silt clay	 52 – 72 % 16 – 22 % 8 – 32 %	 48 – 63 % 21 – 34 % 14 – 25 %
pH value (depths)	5.7 (7.5 cm) 5.9 (15 cm) 5.8 (30 cm) 5.3 (45 cm) 5.3 (60 cm) 5.2 (75 cm) 5.0 (90 cm)	6.3 (7.5 cm) 6.4 (15 cm) 6.5 (30 cm) 6.6 (45 cm) 6.8 (60 cm) 6.8 (75 cm) 6.6 (90 cm)
Organic Matter, % (depths)	1.5 (7.5 cm) 1.5 (15 cm) 1.8 (30 cm) 2.6 (45 cm) 2.3 (60 cm) 2.2 (75 cm) 2.1 (90 cm)	3.7 (7.5 cm) 4.6 (15 cm) 3.7 (30 cm) 1.9 (45 cm) 1.6 (60 cm) 1.7 (75 cm) 1.6 (90 cm)
Cation exchange capacity, meq/100 g	2.9 – 3.7	1.3 – 27.0
Field moisture holding capacity at 1/3 bar	8.4 (7.5 cm) 8.0 (15 cm) 10.0 (30 cm) 17.3 (45 cm) 17.1 (60 cm) 17.7 (75 cm) 16.7 (90 cm)	3.9 (7.5 cm) 5.1 (15 cm) 4.5 (30 cm) 3.6 (45 cm) 3.6 (60 cm) 2.5 (75 cm) 2.7 (90 cm)

B. Study design

1. Experimental conditions: Each test site consisted of one treated and one untreated soil plot. The plots were kept bare for the duration of the trial by the use of pre-approved herbicides. During periods when the total rainfall on the plots fell below the average the plots were irrigated with pond water (ARC site) or creek water (FSIL site).

2. Weather data: Air temperatures at both sites have been typical throughout the trials to when compared to the ten year average at each location. The site in Illinois received much heavier than normal rainfall in June of 1993. However the total rainfall plus irrigation during the trial was close to the ten year average.

3. Application: A soluble liquid (SL) formulation of propamocarb hydrochloride (BANOL®) with a nominal content of 66.5 % of a.s. was applied to the trial plots in May (FSIL plot) or September (ARC plot) using spray equipment. Each trial involved three applications of propamocarb hydrochloride at seven-day intervals at a rate of 9.0 to 9.2 kg a.s/ha in the first two applications, and 4.6 to 4.9 kg a.s./ha – in the third (final) application.

4. Sampling and sample processing: Prior to the start of experimental work each plot was divided into 64 subplots. Each subplot was sufficiently large to allow five cores, separated by one meter from each other, to be taken. At each time point three random subplots were sampled from the treated plot to the depth of 90 cm. The 0-15 cm segment of the core was taken separately to minimize the risk of contamination of the lower horizons. A small excavation to a depth of 15 cm was then dug near the site of the original core and the 15-90 cm segment of the core was taken from the bottom of the excavation. Samples from treated plots were taken prior to the first application and immediately after each application at both test sites. Following the final application samples from treated plots were collected at 1, 7, 14, 21, 28, 48, 58, 124, 181, 273, 315, 358, 449 and 546 days at ARC site and at 1, 6, 14, 22, 28, 42, 64, 122, 184, 294, 365, 450 and 548 days at FSIL site.

The untreated control plots were sampled less frequently than the treated plots, namely before the first application of propamocarb, at 1, 28, 181, 358 and 546 days at ARC site and at 1, 28, 184, 365 and 548 days at FSIL site. The core was taken from the surface to 90 cm in one segment during sampling of the control plot.

All samples were cut into subcores from 0-7.5, 7.5-15, 15-30, 30-45, 45-60, 60-75 and 75-90 cm horizons. Each five subcores from the same horizon of the same subplot were mixed into a composite sample and homogenized. FSIL samples were frozen before being shipped to the AgrEvo Research Center (ARC) by freezer truck. ARC samples were taken directly to a deep-freeze storage from the field. An earlier study has shown that propamocarb residues may be recovered in 77 % yield after 14 months of frozen storage (Wrede-Rucke, 1992). Since no treated samples were stored in frozen condition for longer than 11 months no correction factor for any possible losses during frozen storage has been applied to the reported concentrations.

5. Analytical procedures: Soil samples were analysed for Propamocarb which was extracted from the matrix by shaking the soil sample with acidified acetone. The extract was centrifuged, filtered and the acetone was removed using a rotary evaporator. The aqueous extract remaining was basified and propamocarb residues partitioned into dichloromethane, the aqueous phase then being discarded. A little aqueous hydrochloric acid was added, to the dichloromethane, as a keeper and the organic solvent removed by rotary evaporation. The aqueous concentrate was then treated with sodium chloride and rendered basic by the addition of aqueous sodium hydroxide solution. Propamocarb residues were partitioned into a known volume of di-propylether for quantification by gas chromatography. Detection of propamocarb was by mass selective detection or nitrogen phosphorus detection.

Gravimetric moisture content (GMC) was determined to correct the results of propamocarb determination for the soil moisture. A small subsample of soil was weighed and dried in an oven. The gravimetric moisture content (GMC) was calculated by dividing the weight loss by the final weight of the dried soil and the resulting value was expressed as a percent.

C. Determination of degradation kinetics

The half-life determinations were based on the average residues observed in all horizons, which were calculated according to the following equation:

$$Average\ residue\ (all\ horizons), mg/kg = \sum \frac{Corrected\ residue\ in\ horizon,\ mg/kg}{Length\ of\ each\ horizon,\ cm/90}$$

DT_{50} values for propamocarb hydrochloride (PHC) were estimated from the exponential plots of the data using the following equation:

$$DT_{50} = \frac{\ln 2}{k}$$

II. Results and Discussion

A. Mass accounting: The efficiency of the method was tested by including one unfortified and at least one fortified control sample from the untreated plot with each set of samples analysed. The fortification range was between 0.01 and 15 mg/kg. Apparent residues of propamocarb in control samples from both sites were usually non-quantifiable (<0.01 mg/kg). Any apparent residues in the unfortified control were subtracted from the residues found in the fortified control before the method efficiency was calculated. The mean recovery of PHC from soil was 87 % (standard deviation = 15 %) from 79 trials. The limit of determination was 0.01 mg/kg for this study.
Propamocarb residues were corrected for the GMC in the sample and for the average recovery of the method from all fortified control samples. Mean values of PHC residues detected at different horizons of three randomly selected subplots at the ARC and FSIL field sites are presented below.
At the ARC site the highest residue concentrations, 15 mg/kg, were observed immediately following the final application. At the FSIL site the highest residue concentrations, 12 mg/kg were observed six days after the final application.
At the ARC site no leaching was observed. Residues of PHC were consistently observed in the 0 to 7.5 cm and 7.5 to 15 cm horizons. Only sporadically were residues above the limit of determination observed in the 15 to 30 cm horizon. The data from the ARC site indicates that PHC does not leach under near typical rainfall conditions.

PHC residues at various depth in treated soil plot from the ARC field site:

DAT	Replicate	PHC (mg/kg)							
		0 – 7.5 cm	7.5 – 15 cm	15 – 30 cm	30 – 45 cm	45 – 60 cm	60 – 75 cm	75 – 90 cm	Average residue in total soil column
-15		<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	-
-14	A	4.493	-	-	-				-
	B	5.324	-	-	-				
	C	5.042	0.039	-	-				
	Mean	*4.953*	*0.039*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
-7	A	9.578	0.029	-	-				-
	B	12.424	0.08	-	-				
	C	9.377	0.017	-	-				
	Mean	*10.460*	*0.042*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
0	A	15.411	0.087	-	-				1.170
	B	14.581	0.016	-	-				
	C	11.830	0.038	-	-				
	Mean	*13.941*	*0.047*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
1	A	10.150	0.099	-	-				0.907
	B	10.245	0.074	-	-				
	C	11.967	0.105	-	-				
	Mean	*10.787*	*0.093*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
7	A	9.409	0.077						0.876
	B	11.547	0.019						
	C	10.459	0.032						
	Mean	*10.472*	*0.043*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
14	A	10.126	0.099						0.795
	B	9.057	0.152						
	C	9.119	0.078						
	Mean	*9.434*	*0.110*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
21	A	5.051	0.109						0.432
	B	5.086	0.078	0.015					
	C	5.153	0.046						

DAT	Replicate	PHC (mg/kg)							
		0 – 7.5 cm	7.5 – 15 cm	15 – 30 cm	30 – 45 cm	45 – 60 cm	60 – 75 cm	75 – 90 cm	Average residue in total soil column
	Mean	*5.097*	*0.078*	0.015	<LOQ	<LOQ	<LOQ	<LOQ	
28	A	0.650	0.069						0.083
	B	1.034							
	C	1.219							
	Mean	*0.968*	*0.069*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
48	A	0.546							0.064
	B	0.811	0.026						
	C	0.872	0.032						
	Mean	*0.743*	*0.029*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
58	A	0.590	0.024						0.044
	B	0.425							
	C	0.544							
	Mean	*0.520*	*0.024*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
124	A	0.394							0.043
	B	0.545							
	C	0.603							
	Mean	*0.514*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
181	A	0.297							0.036
	B	0.401							
	C	0.593	0.019						
	Mean	*0.430*	*0.019*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
273	A	0.238							0.023
	B	0.219							
	C	0.361	0.017						
	Mean	*0.273*	*0.017*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
315	A	0.176							0.018
	B	0.231							
	C	0.248							
	Mean	*0.218*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
358	A	0.170							0.013
	B	0.135							
	C	0.173							
	Mean	*0.159*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
449	A	0.125							0.011
	B	0.156							
	C	0.117							
	Mean	*0.133*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
546	A	0.150							0.014
	B	0.244							
	C	0.126							
	Mean	*0.173*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	

Values calculated in the course in writing this summary are given in *italics*

At the FSIL site propamocarb residues above the limit of determination were observed as low as the 75 to 90 cm horizon in isolated cores. However the apparent penetration of the soil by propamocarb was not consistent. For example, at day zero propamocarb residues were observed in the 75 to 90 cm horizon of the third replicate yet in the other two replicates none was detected below 15 cm. Such a pattern is

not typical of leaching, where a more uniform percolation through the horizons is normally observed. In the month immediately following the test substance application (June 1993) the FSIL site was subjected to rainfall in excess of the 100 year maximum for the locality. It is believed that this extraordinarily heavy precipitation saturated portions of the plot. Furthermore the test substance, as formulated, is highly water-soluble. This combination of circumstance may have led to the test substance being more mobile than would be the case under typical weather conditions.

PHC residues at various depth in treated soil plot from the FSIL field site:

DAT	Replicate	Propamocarb, mg/kg							
		0 – 7.5 cm	7.5 – 15 cm	15 – 30 cm	30 – 45 cm	45 – 60 cm	60 – 75 cm	75 – 90 cm	Average residue in total soil column
-15		<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	-
-14	A	2.560	0.24						-
	B	2.430	0.19						
	C	3.450	0.22						
	Mean	*2.813*	0.217	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
-7	A	3.910							-
	B	7.450							
	C	4.210							
	Mean	*5.190*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
0	A	6.730							0.751
	B	9.760	0.01						
	C	8.390		0.12	0.499	0.207	0.113	0.129	
	Mean	*8.293*	*0.010*	*0.120*	*0.499*	*0.207*	*0.113*	*0.129*	
1	A	5.190	0.08	0.03					0.636
	B	7.650	0.03						
	C	8.800	0.14	0.41					
	Mean	*7.213*	*0.083*	*0.220*	<LOQ	<LOQ	<LOQ	<LOQ	
6	A	7.310	0.03	0.01					0.697
	B	5.740	0.03						
	C	11.860	0.09						
	Mean	*8.303*	*0.050*	*0.010*	<LOQ	<LOQ	<LOQ	<LOQ	
14	A	0.910	0.108	0.014	0.391	0.07			0.164
	B	2.287	0.051						
	C	1.471	0.067	0.024					
	Mean	*1.556*	*0.075*	*0.019*	*0.391*	*0.070*	<LOQ	<LOQ	
22	A	0.318	0.046	0.022	0.054				0.048
	B	0.400	0.1	0.095	0.043	0.031	0.016		
	C	0.304	0.014						
	Mean	*0.341*	*0.053*	*0.059*	*0.049*	*0.031*	*0.016*	<LOQ	
28	A	0.289							0.039
	B	0.182		0.051	0.017	0.11	0.086	0.022	
	C	0.178	0.015	0.076					
	Mean	*0.216*	*0.015*	*0.064*	*0.017*	*0.110*	*0.086*	*0.022*	
42	A	0.210							0.029
	B	0.737							
	C	0.101							
	Mean	*0.349*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
64	A	0.084							0.011

DAT	Replicate	Propamocarb, mg/kg							
		0 – 7.5 cm	**7.5 – 15 cm**	**15 – 30 cm**	**30 – 45 cm**	**45 – 60 cm**	**60 – 75 cm**	**75 – 90 cm**	**Average residue in total soil column**
	B	0.164							
	C	0.128							
	Mean	*0.125*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
122	A	0.443							0.021
	B	0.104		0.015					
	C	0.177							
	Mean	*0.241*	<LOQ	0.015	<LOQ	<LOQ	<LOQ	<LOQ	
184	A	0.059							0.006
	B	0.098							
	C	0.074							
	Mean	*0.077*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
294	A	0.095		0.015	0.038	0.024	0.014		0.013
	B	0.152							
	C	0.050							
	Mean	*0.099*	<LOQ	*0.015*	*0.038*	*0.024*	*0.014*	<LOQ	
365	A	ND							0.004
	B	0.096							
	C	0.043							
	Mean	*0.070*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
450	A	0.066							0.003
	B	0.020							
	C	0.022							
	Mean	*0.036*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
548	A	0.026							0.002
	B	ND							
	C	0.054							
	Mean	*0.040*	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	

Values calculated in the course in writing this summary are given in *italics;* ND = none detected. All individual horizons in this replicate were below the limit of determination (0.01 µg/g). For the mean value calculation, a value of 0.00 was used.

B. Kinetics: Inspection of the data provided in the tables below show that the decline of PHC on bare soil exhibits a markedly biphasic pattern. At both sites an early decline during the first 3 to 4 weeks was followed by a much slower decline. Therefore kinetic analysis of the data from both sites was divided into two portions. For the ARC site a primary rate constant (k^1) was calculated using the data from day 0 to day 28, the secondary rate constant (k^2) was calculated for data from day 28 to day 546. Similarly at the FSIL site the primary rate constant (k^1) was calculated using the data from day 0 to day 22, the secondary rate constant (k^2) was calculated for data from day 22 to day 548.
Results of a first order kinetic model for the estimation of field DT_{50} values for the biphasic dissipation of PHC in sandy loam soil from ARC and FSIL field sites are provided in Table 11.1.4.3-122. Calculated DT_{50} values were 9 and 6 days for the primary degradation phase and 187 and 132 days for the secondary degradation phase at the ARC and FSIL sites respectively.

First-order dissipation model parameters and estimated DT_{50} values for biphasic dissipation of PHC in sandy loam soil at ARC and FSIL field sites:

Site	Phase	Time points involved	Results of linear regression			DT_{50}, days
			Slope	y-intercept	Regression coefficient	
ARC	Primary	Day 1 – 28	-0.077	0.306	0.779	9
	Secondary	Day 28 – 546	-0.004	-2.693	0.885	187
FSIL	Primary	Day 1 – 22	-0.126	-0.108	0.938	6
	Secondary	Day 22 – 548	-0.005	-3.398	0.826	132

III. Conclusion

The dissipation of PHC in soil is biphasic with a very rapid early decline phase. Half-lives during the first three to four weeks of the trial were estimated at 9 days and 6 days for sites at ARC and FSIL respectively. No evidence for leaching was observed at the ARC site. However the FSIL site appears to have been compromised by extraordinarily heavy rainfall in the month immediately after application. At this site penetration to lower horizons was observed. No evidence was observed that PHC would leach under near typical rainfall conditions.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Conclusions:

As a result of laboratory tests, some values of the DT_{50} of the active substance in aerobic soils were higher than the specified triggers in the EU for the conduct of terrestrial field dissipation studies.
With no studies performed in the EU, the data requirement had been initially addressed by submission of US field dissipation data under Point 7.1.1.2.2 of the Dossier. The data were from two sites (California and Georgia) following four successive applications (seven day interval) of formulated propamocarb-hydrochloride at each site to bare and cropped soil. The data evaluation revealed that the residues of propamocarb-hydrochloride in bare soils at the two sites were almost exclusively retained in the top 15 cm layer of soil. Following the final application residues of propamocarb-hydrochloride declined to result in non-normalised field dissipation half-lives of 17.6 days for site Georgia and 22.1 days for site California. Values of the $DisT_{50}$ were 13.2 days (site Georgia) and 18.1 days (site California), thus, lower for cropped soil (turf grass), indicating the potential influence of grass layer interception on the dissipation of propamocarb-hydrochloride under conditions of practical use in the field.
Later, the field data were re-visited against actual guidance (FOCUS, 2011 and EFSA, 2014). Following the criteria given in the guidance, the reliability of existing field data was assessed against the requirements. Major points included the time point of 10 mm rainfall after application to result in the availability of sufficient data points for kinetic evaluation (i.e. at least five), the availability of adequate weather data (i.e. daily data on rainfall, irrigation and sunshine hours) for normalisation and, the application to bare soil and the management of the treated soil plots in the following. Following application of the criteria, the existing field data did not qualify for a kinetic evaluation. The reasons included the non-availability of sufficient data points after each of the first three applications in view of the short spraying interval of 7 days. Formally, there were sufficient data points (i.e. five) after the last application. However, the residue level determined directly after last application was influenced by residues from previous applications resulting in no value at time zero for the kinetic evaluation. In addition, degradation was potentially influenced by enhanced microbial degradation after each repeated application. The design of the study therefore did not reflect a worst case situation, i.e. results should not be influenced by enhanced microbial degradation coming from adaptation to the test substance.
Two further terrestrial field soil dissipation studies were performed to support the available data. These studies include field soil dissipation data originated from four trial sites in Canada and from two trial sites in the USA. Overall, both studies confirm the results obtained in study KCA 7.1.2.2.1/01. In three of the four Canadian soils, the field dissipation of PHC was very rapid (calculated DT_{50} = 16.5 to

22.5 days). At one site, the dissipation of PHC was substantially slower (observed DT_{50} ~ 378 days) soil. Presumably, PHC was tightly bound to smectite clay minerals resulting in carry over into the following year. At two US sites in North Carolina and Illinois, the dissipation of PHC in soil was biphasic with a very rapid early decline phase.
Two further terrestrial field soil dissipation studies were performed in the USA and Canada to support the available data. These studies include data originated from four trial sites in Canada and from two trial sites in the USA. Overall, both studies confirm the results obtained in study KCA 7.1.2.2.1/01. In three of the four Canadian soils, the field dissipation of PHC was very rapid (calculated DT_{50} = 16.5 to 22.5 days). At one site, the dissipation of PHC was substantially slower (observed DT_{50} ~ 378 days) soil. Presumably, PHC was tightly bound to smectite clay minerals resulting in carry over into the following year. At two US sites in North Carolina and Illinois, the dissipation of PHC in soil was biphasic with a very rapid early decline phase.
According to the ecoregion crosswalk analysis summarised below in KCA 7.1.2.2.1/04, four root ecoregions representing three North American TFD trial sites are considered representative for European conditions. A kinetic evaluation according to FOCUS (2006, 2014) was performed for these three trial sites in order to determine trigger endpoints. A summary of the kinetic evaluation is provided below in KCA 7.1.2.2.1/05.

Report:	KCA 7.1.2.2.1/04; van der Stouwe, F.; 2020; M-753833-01-1
Title:	Propamocarb: Ecoregion Crosswalk for eight Terrestrial Field Dissipation Study Locations in North America
Report No.:	114899-001
Document No.:	M-753833-01-1
Guideline(s):	not applicable
Guideline deviation(s):	not applicable
GLP/GEP:	**not applicable**

Abstract

The fate and behaviour of the active substance propamocarb hydrochloride (PHC) was investigated in three terrestrial field dissipation (TFD) studies in North America covering in total eight trial sites. The eight trial sites were evaluated using the OECD ENASGIPS tool (Europe – North American Soil Geographic Information for Pesticide Studies) aiming to determine their representativeness throughout Europe based on climate and soil similarity. The ENASGIPS tool uses the ecoregion concept to compare environmental properties such as long-term annual total rainfall, average precipitation, soil texture, soil pH, and soil organic matter to calculate a similarity index.
According to the Ecoregion crosswalk, the analysed eight TFD trial sites are represented by nine [1] North American root ecoregions. A holistic similarity score of at least 80 % was observed for five of the nine identified ecoregions.
In addition to the holistic similarity approach, individual scores of soil and climate were evaluated in a refined assessment. While soil conditions (pH, OC content and texture) reached high scores in all ecoregions, individually and overall, temperature as the main driving parameter for the degradation of pesticides among the climatic parameters (temperature and precipitation) reached low individual scores in one ecoregion (7 % and 10 %). This indicates pronounced differences in temperature conditions between compared ecoregions in North American and Europe. For the remaining four North American ecoregions, similarity of temperature conditions, i.e. an individual similarity score higher than 80 %, was reached for one or more European ecoregion.
In summary, four root ecoregions representing three North American TFD trial sites are considered representative for European conditions.

[1] TFD Trial site Ontario, Canada, is located at the border of root ecoregions *Eastern Great Lakes lowland forests* (NA0407) and *Southern Great Lakes forests* (NA0414). Therefore, both root ecoregions were considered in the crosswalk analyses.

Overview of TFD trial sites and their representativeness for European conditions:

Root Ecoregion	TFD Trial Site	Study	Conclusion on similarity
NA0407 - Eastern Great Lakes lowland forests (CA,USA)	Ontario, Canada [a)]	Belyk, M., 1998	Sufficient similarity; considered representative for European conditions for further evaluation
NA0414 - Southern Great Lakes forests (CA,USA)			
NA0804 - Central forest-grasslands transition (USA)	Wonder Lake, US	Cole, M.G., 1995	
NA0801 - California Central Valley grasslands (USA)	California, US	Willard, T.R., 2002	
NA0802 - Canadian Aspen forests and parklands (CA,USA)	Manitoba, Canada	Belyk, M., 1998	Insufficient similarity due to individual score of temperature
NA0529 - Southeastern conifer forests	Georgia, US	Willard, T.R., 2002	No similarity due to score in holistic approach
NA0517 - Middle Atlantic coastal forests	Pikeville, US	Cole, M.G., 1995	
NA0410 - New England-Acadian forests	New Brunswick, Canada	Belyk, M., 1998	
NA0408 - Gulf of St. Lawrence lowland forests	Prince Edward Island, Canada	Belyk, M., 1998	

[a)] Trial site located at the border of root ecoregions *Eastern Great Lakes lowland forests* (NA0407) and *Southern Great Lakes forests* (NA0414). Therefore, both root ecoregions were considered in the crosswalk analyses.

Introduction

The OECD guidance for conducting pesticide terrestrial field dissipation studies (TFD) provides guidance on how to conduct TFD studies to demonstrate the transformation, transport, and fate of pesticides under representative actual use conditions when a pesticide product is used according to the label (OECD, 2016). TFD studies provide risk assessors with the end-points needed to carry out exposure and risk assessments according to supra-national and national requirements in the member states of the European Union.

In parallel to this OECD guidance document, the ENASGIPS application (**E**urope-**N**orth **A**merica **S**oil **G**eographic **I**nformation for **P**esticide **S**tudies) has been developed (PMRA, 2015). ENASGIPS is a GIS-based tool for identifying similar ecoregions between Europe and North America. The environmental fate and behaviour of a pesticide depends on a range of environmental conditions, such as soil and climate. ENASGIPS uses data on long-term annual total rainfall, average precipitation, soil texture, soil pH, and soil organic matter to calculate a similarity score for comparison of ecoregions located in Europe and North America.

In the present study, eight North American TFD trial sites were assessed to determine their representativeness for regions throughout Europe where propamocarb may be applied. Four trial sites are located in Canada and four in the United States.

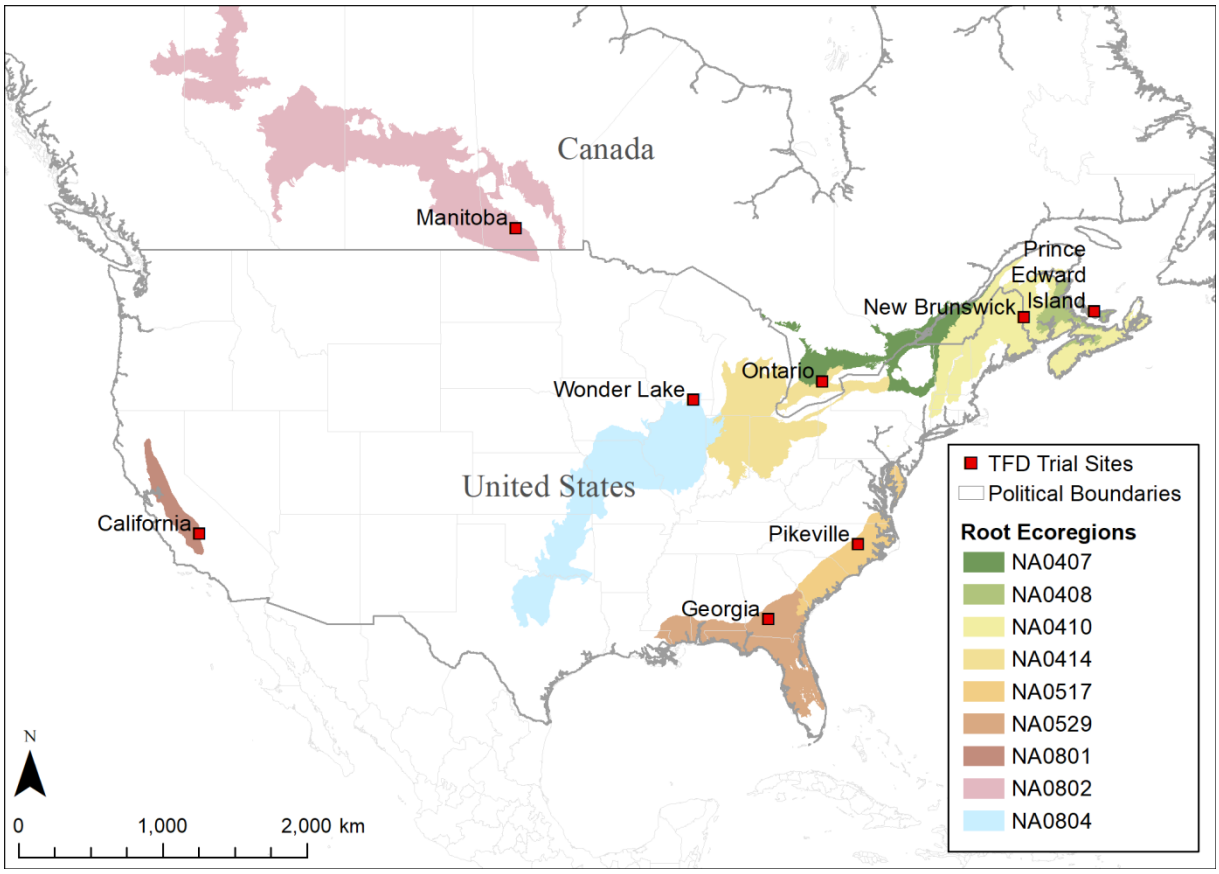
Methods

Trial sites

In the present study, ecoregion similarity of eight North American TFD trial sites was assessed. The locations of the trial sites are depicted in figure below. Four of the assessed sites are located in Canada and four in the United States.

According to the ENASGIPS tool, the eight TFD trial sites are assigned to nine root ecoregions (table and figure presented below). These ecoregions reflect distinct combinations of regional environmental conditions and ecology, e.g. soil and climate characteristics, and cover parts of Eastern Canada, Central, Eastern, Western, and Southeastern America as well as regions along the south-eastern boundary between Canada and America.

Location of assessed propamocarb TFD trial sites in North America with associated root ecoregions (PMRA, 2015)



Ecoregion crosswalk

The ecoregion crosswalk was conducted using the ENASGIPS v3.0 (**E**urope-**N**orth **A**merica **S**oil **G**eographic **I**nformation for **P**esticide **S**tudies) tool (PMRA, 2015). ENASGIPS was developed by the Pest Management Regulatory Agency - Health Canada and US EPA in collaboration with Agriculture and Agri-Food Canada and the European Commission's Joint Research Centre, as part of the Organization for Economic Co-operation and Development (OECD) project "Harmonised International Guidance for Pesticide Terrestrial Field Dissipation Studies and Crosswalk of North American and European Ecoregions." The tool is recommended for conducting ecoregion crosswalks by the OECD Guidance Document for Conducting Pesticide Terrestrial Field Dissipation Studies published in 2016 (OECD, 2016).

For each Canadian and American TFD trial site, the respective root ecoregion was assigned based on the geographical coordinates using the ENASGIPS tool. The 'Holistic Ecoregions Similarity' tool implemented in ENASGIPS allows the user to identify similar ecoregions in Canada, North America, and Europe. A similarity score is calculated between each North American and all European ecoregions based on soil and climate parameters such as mean annual temperature, mean annual precipitation, soil pH, soil organic carbon, and soil texture. Similarity of each of the five parameters is scored separately, and then the five scores are combined with equal weighting into an overall similarity score. For the present assessment, the default similarity threshold value of 80 % was used.

In addition to the holistic similarity approach, individual scores of soil and climate were evaluated in a refined assessment. While soil conditions (pH, OC content and texture) are important to reach good scores individually and overall, temperature is the most important parameter among the climatic parameters as it is known to be a key driving parameter for the degradation of pesticides. Applying the holistic similarity approach does not account for the high impact of temperature on degradation. Thus, holistic similarity results may also include ecoregions in Europe with very low and low temperature

similarity. As a consequence, holistic matches were excluded from the final similarity results if temperature of the root ecoregion was not sufficiently represented by the comparison ecoregions in Europe.

Results

In this study, OECD's ENASGIPS tool was used to determine the representativeness of eight North American TFD trial sites for regions throughout Europe. With the holistic approach, matching ecoregions (80 % similarity) were identified for five out of the nine root ecoregions. Detailed results of the holistic similarity approach for the trial sites Carberry, Branchton, Porteville and Wonder Lake are presented in sections 0 to 0, respectively.

Root Ecoregions of eight North American TFD trial sites and area covered by similar ecoregions in Europe (based on holistic approach, 80% similarity):

Root Ecoregion	TFD Trial Site	Similar ecoregions Europe			
		Area[a] (km²)		Share[b] (%)	
NA0407 - Eastern Great Lakes lowland forests (CA,USA)	Ontario, Canada[c]	699,833.31	1,063,439.68	16.47	25.02
NA0414 - Southern Great Lakes forests (CA,USA)		937,135.69		22.05	
NA0804 - Central forest-grasslands transition (USA)	Wonder Lake, US	983,730.30		23.15	
NA0801 - California Central Valley grasslands (USA)	California, US	647,758.82		15.24	
NA0802 - Canadian Aspen forests and parklands (CA,USA)	Manitoba, Canada	23,740.78		0.56	
NA0529 - Southeastern conifer forests	Georgia, US	no similarity		-	
NA0517 - Middle Atlantic coastal forests	Pikeville, US	no similarity		-	
NA0410 - New England-Acadian forests	New Brunswick, Canada	no similarity		-	
NA0408 - Gulf of St. Lawrence lowland forests	Prince Edward Island, Canada	no similarity		-	

[a] Area quantified with Lambert azimuthal equal-area (LAEA) coordinate map projection in ArcGIS v10.2.

[b] Share relative to area of the Europe Union.

[c] Trial site located at the border of root ecoregions *Eastern Great Lakes lowland forests* (NA0407) and *Southern Great Lakes forests* (NA0414). Therefore, both root ecoregions were considered in the crosswalk analyses.

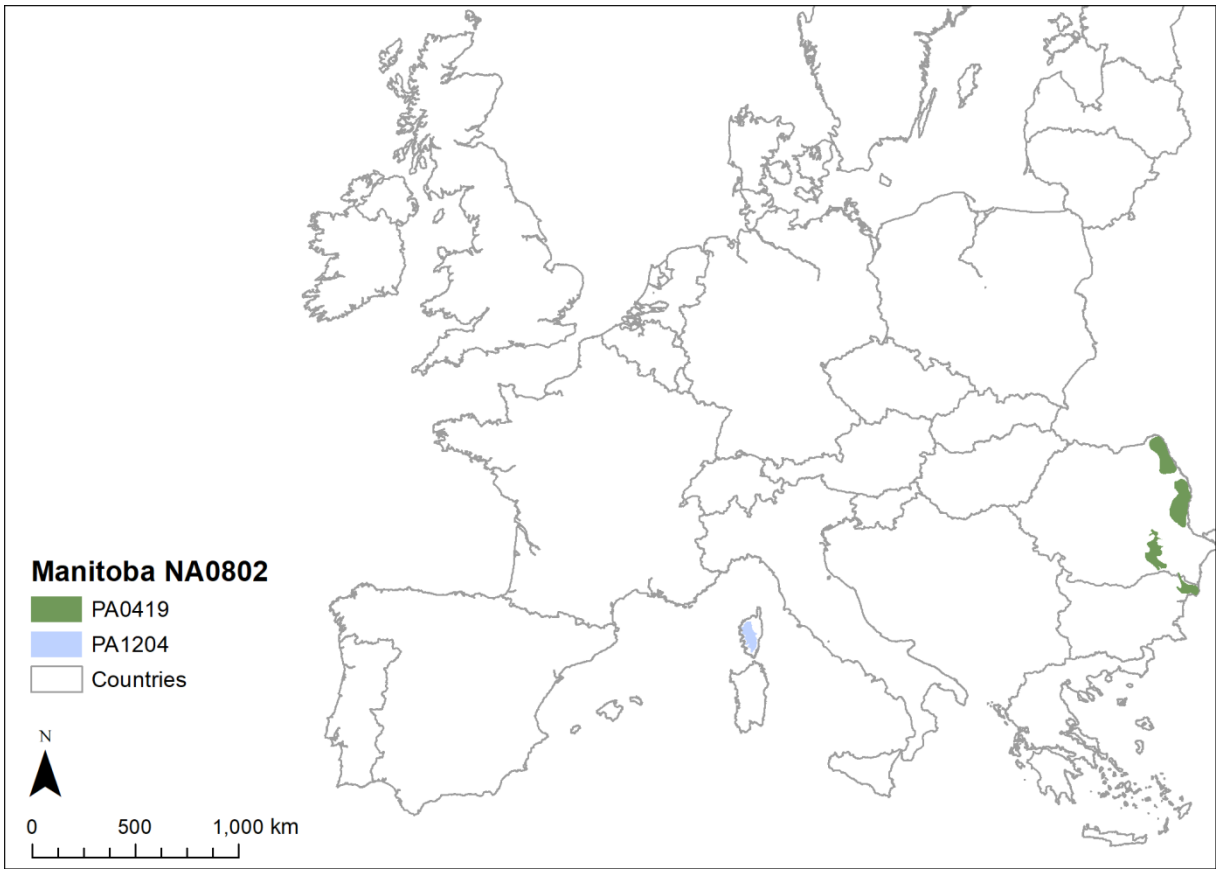
Carberry, Manitoba, Canada

The trial site Carberry, Manitoba, (Belyk, 19928) is located within the root ecoregion *Canadian Aspen forests and parklands* (NA0802).

The ENASGIPS holistic similarity query with a similarity threshold of 80 % identified two European ecoregions similar to the root ecoregion *Canadian Aspen forests and parklands* (figure below).

The identified ecoregions cover small parts in the south of Europe. Similarity scores of the holistic similarity query are summarised in Holistic similarity score of the ecoregions ranges between 80 % and 81 %. Average similarity scores of individual parameters ranges from 9 % (temperature) to 100 % (OC and texture).

European Ecoregions similar to root ecoregion *Canadian Aspen forests and parklands* according to ENASGIPS (holistic similarity model with threshold > 80 %):



Similarity scores calculated by ENASGIPS for the root ecoregion *Canadian Aspen forests and parklands* (NA0802):

Ecoregion	Similarity scores (%)					
	Holistic	Temperature	Precipitation	OC	pH	Texture class
PA0419 - East European forest steppe (EU)	80	10	92	100	96	100
PA1204 - Corsican montane broadleaf and mixed forests (EU)	81	7	100	100	100	100
Average score	**81**	**9**	**96**	**100**	**98**	**100**

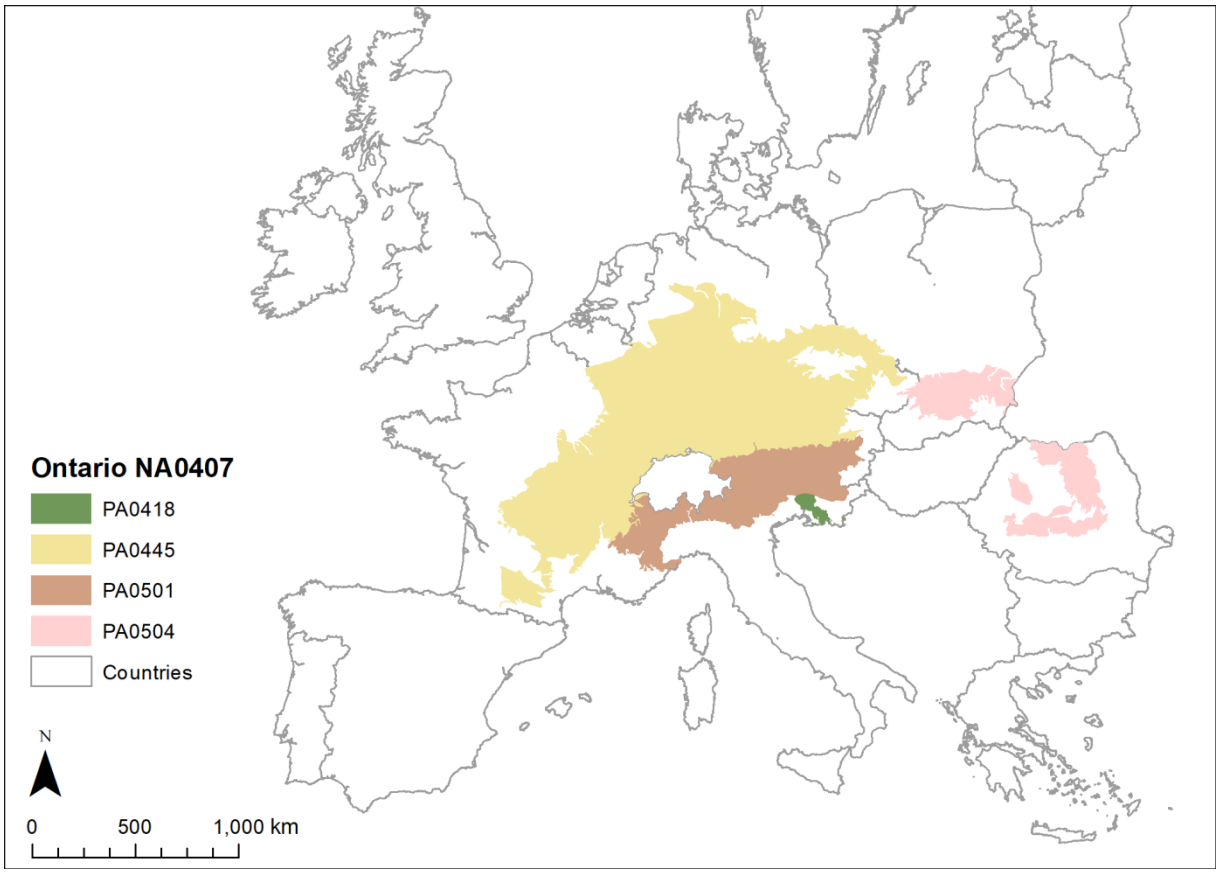
Branchton, Ontario, Canada

The trial site Branchton, Ontario, (Belyk, 1998) is located at the border of the two root ecoregions *Eastern Great Lakes lowland forests* (NA0407) and *Southern Great Lakes forests* (NA0414). Therefore, both root ecoregions were considered in the crosswalk analyses.

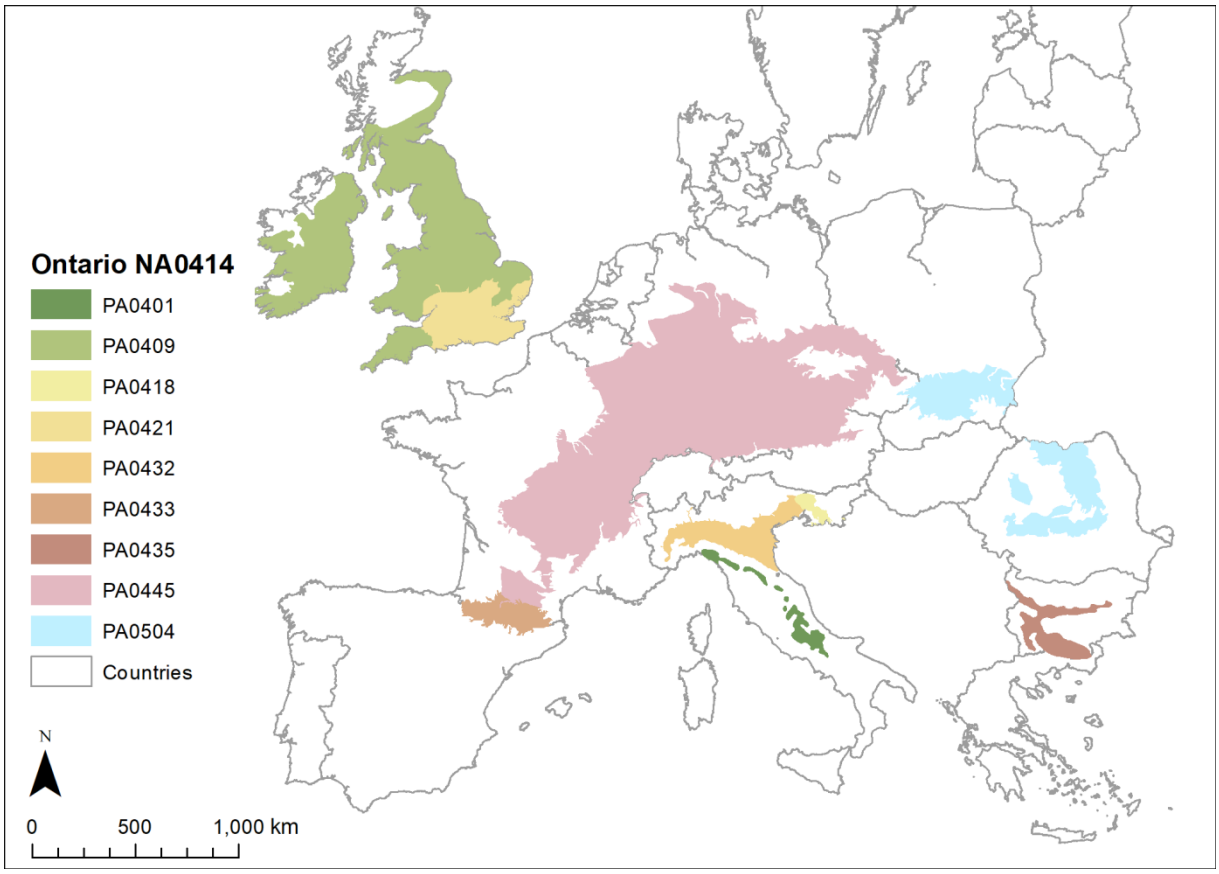
The ENASGIPS holistic similarity query with a similarity threshold of 80 % identified four European ecoregions similar to the root ecoregion *Eastern Great Lakes lowland forests* (figure below) and nine European ecoregions similar to the root ecoregion *Southern Great Lakes forests* (figure below).

The identified ecoregions cover large areas in Europe, i.e. parts of Central and Northwestern Europe as well as regions in Eastern, South, and Southeastern Europe. Similarity scores of the holistic similarity query are summarised in tables below. Holistic similarity score of the ecoregions ranges between 80 % and 92 %. Average similarity scores of individual parameters ranges from 61 % (temperature, NA0407) to 100 % (texture, NA0407).

European Ecoregions similar to root ecoregion *Eastern Great Lakes lowland forests* according to ENASGIPS (holistic similarity model with threshold > 80 %)



European Ecoregions similar to root ecoregion *Southern Great Lakes forests* according to ENASGIPS (holistic similarity model with threshold > 80 %)



Similarity scores calculated by ENASGIPS for the root ecoregion *Eastern Great Lakes lowland forests* (NA0407)

Ecoregion	Similarity scores (%)					
	Holistic	Temperature	Precipitation	OC	pH	Texture class
PA0418 - Dinaric Mountains mixed forests (EU)	87	50	100	100	86	100
PA0445 - Western European broadleaf forests (EU)	81	44	63	100	100	100
PA0501 - Alps conifer and mixed forests (EU)	90	49	100	100	100	100
PA0504 - Carpathian montane forests (EU)	90	100	50	100	100	100
Average score	**87**	**61**	**78**	**100**	**97**	**100**

Similarity scores calculated by ENASGIPS for the root ecoregion *Southern Great Lakes forests* (NA0414)

Ecoregion	Similarity scores (%)					
	Holistic	Temperature	Precipitation	OC	pH	Texture class
PA0401 - Appenine deciduous montane forests (EU)	81	60	61	100	86	100
PA0409 - Celtic broadleaf forests (EU)	83	100	97	17	100	100
PA0418 - Dinaric Mountains mixed forests (EU)	84	100	100	53	67	100
PA0421 - English Lowlands beech forests (EU)	83	100	48	77	100	88
PA0432 - Po Basin mixed forests (EU)	80	41	90	100	70	100
PA0433 - Pyrenees conifer and mixed forests (EU)	84	95	54	88	82	100
PA0435 - Rodope montane mixed forests (EU)	91	100	56	100	100	100
PA0445 - Western European broadleaf forests (EU)	92	100	91	74	97	100
PA0504 - Carpathian montane forests (EU)	80	52	74	76	100	100
Average score	**84**	**83**	**75**	**76**	**89**	**99**

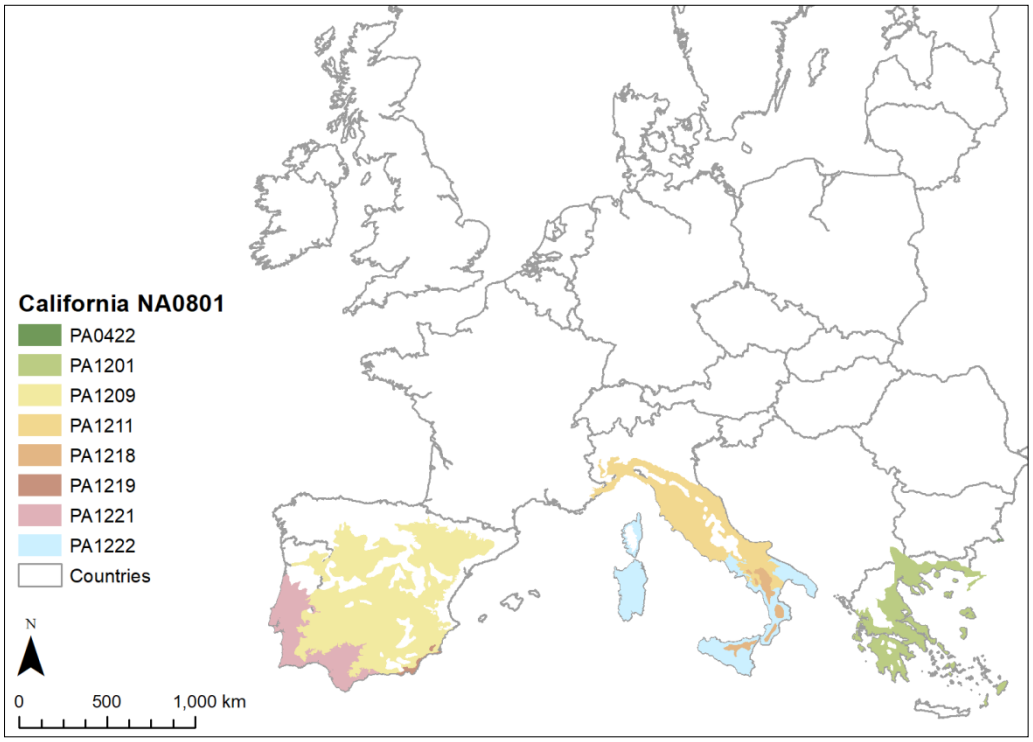
Porterville, California, United States

The trial site Porterville, California, (Willard, 2002) is located within the root ecoregion *California Central Valley grasslands* (NA0801).

The ENASGIPS holistic similarity query with a similarity threshold of 80 % identified eight European ecoregions similar to the root ecoregion *California Central Valley grasslands* (figure below).

The identified ecoregions cover large parts in the south of Europe. Similarity scores of the holistic similarity query are summarised in the table below. Holistic similarity score of the ecoregions ranges between 83 % and 97 %. Average similarity scores of individual parameters range from 66 % (temperature) to 100 % (texture).

European Ecoregions similar to root ecoregion *California Central Valley grasslands* according to ENASGIPS (holistic similarity model with threshold > 80 %)



Similarity scores calculated by ENASGIPS for the root ecoregion *California Central Valley grasslands* (NA0801):

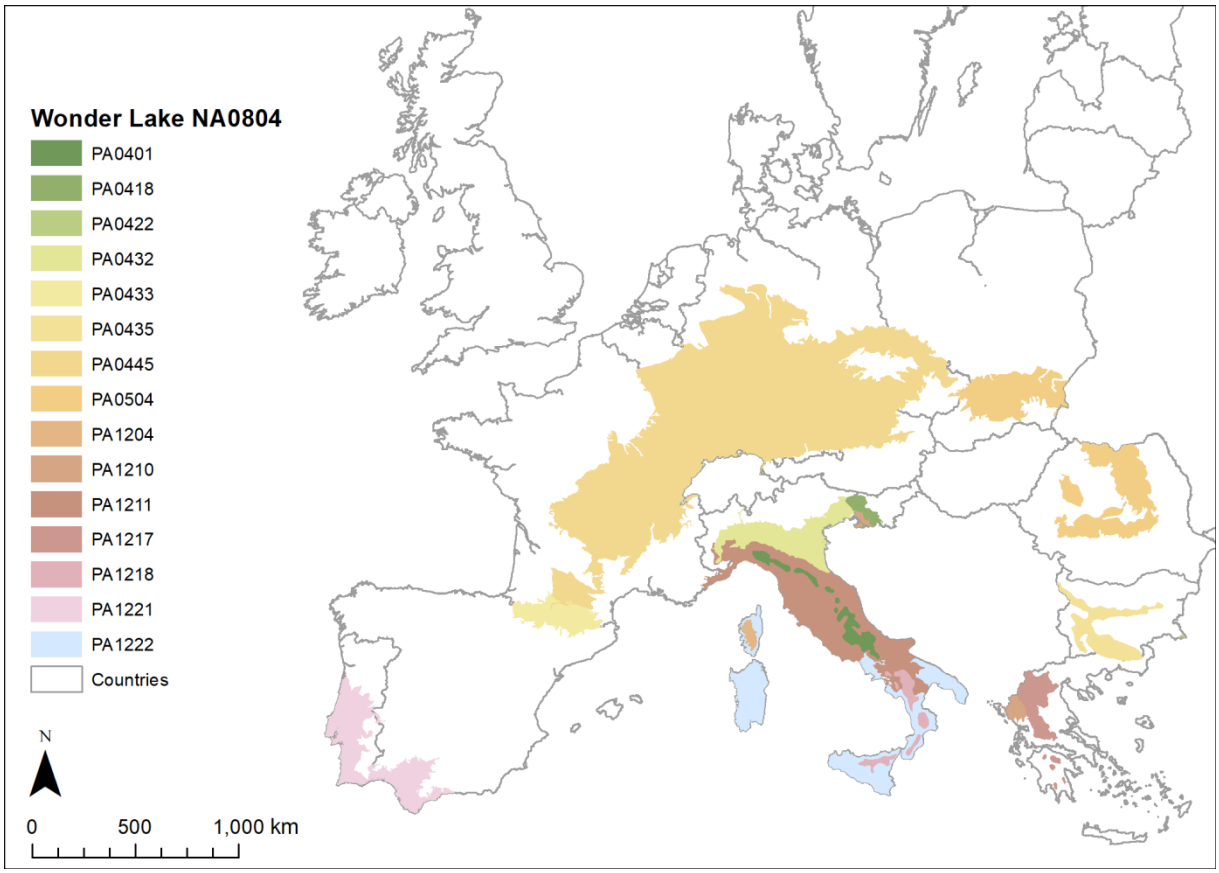
Ecoregion	Similarity scores (%)					
	Holistic	Temperature	Precipitation	OC	pH	Texture class
PA0422 - Euxine-Colchic broadleaf forests (EU)	87	35	100	100	100	100
PA1201 - Aegean and Western Turkey sclerophyllous and mixed forests (EU)	85	60	100	64	100	100
PA1209 - Iberian sclerophyllous and semi-deciduous forests (EU)	84	44	100	85	89	100
PA1211 - Italian sclerophyllous and semi-deciduous forests (EU)	83	39	100	75	100	100
PA1218 - South Appenine mixed montane forests (EU)	90	50	100	100	100	100
PA1219 - Southeastern Iberian shrubs and woodlands (EU)	83	100	71	63	79	100
PA1221 - Southwest Iberian Mediterranean sclerophyllous and mixed forests (EU)	93	100	100	65	100	100
PA1222 - Tyrrhenian-Adriatic Sclerophyllous and mixed forests (EU)	97	100	100	84	100	100
Average score	**88**	**66**	**96**	**80**	**96**	**100**

Wonder Lake, Illinois, United States

The trial site Wonder Lake, Illinois, (Cole, 1995) is located within the root ecoregion *Central forest-*

grasslands transition (NA0804).
The ENASGIPS holistic similarity query with a similarity threshold of 80 % identified fifteen European ecoregions similar to the root ecoregion *Central forest-grasslands transition* (figure below).
The identified ecoregions cover large areas in the centre and south of Europe. Similarity scores of the holistic similarity query are summarised in the table below. Holistic similarity score of the ecoregions ranges between 80 % and 94 %. Average similarity scores of individual parameters ranges from 61% (precipitation) to 99 % (texture).

European Ecoregions similar to root ecoregion *Central forest-grasslands transition* according to ENASGIPS (holistic similarity model with threshold > 80 %)



Similarity scores calculated by ENASGIPS for the root ecoregion *Central forest-grasslands transition* (NA0804)

Ecoregion	Similarity scores (%)					
	Holistic	Temperature	Precipitation	OC	pH	Texture class
PA0401 - Appenine deciduous montane forests (EU)	94	100	69	100	100	100
PA0418 - Dinaric Mountains mixed forests (EU)	81	61	100	53	91	100
PA0422 - Euxine-Colchic broadleaf forests (EU)	84	100	31	91	100	100
PA0432 - Po Basin mixed forests (EU)	87	100	95	45	95	100
PA0433 - Pyrenees conifer and mixed forests (EU)	83	69	57	95	96	100
PA0435 - Rodope montane mixed forests (EU)	87	75	60	100	100	100
PA0445 - Western European broadleaf forests (EU)	82	64	89	58	99	100
PA0504 - Carpathian montane forests (EU)	83	44	89	84	100	100
PA1204 - Corsican montane broadleaf and mixed forests (EU)	84	100	25	100	100	97
PA1210 - Illyrian deciduous forests (EU)	90	100	100	100	49	100
PA1211 - Italian sclerophyllous and semi-deciduous forests (EU)	90	100	51	100	100	100
PA1217 - Pindus Mountains mixed forests (EU)	85	100	69	100	58	100
PA1218 - South Appenine mixed montane forests (EU)	86	100	31	100	100	100
PA1221 - Southwest Iberian Mediterranean sclerophyllous and mixed forests (EU)	80	100	25	100	93	81
PA1222 - Tyrrhenian-Adriatic Sclerophyllous and mixed forests (EU)	84	100	25	97	99	100
Average score	**85**	**88**	**61**	**88**	**92**	**99**

Conclusions

In this report, an ecoregion crosswalk analysis was performed on eight North American TFD trial sites which are represented by nine root ecoregions.

With the holistic similarity approach, matching ecoregions (80 % similarity) were identified for five of a total of nine root ecoregions (NA0407, NA0414, NA0801, NA0802, NA0804). Hence, four TFD trial sites were not considered representative for European conditions based on the holistic similarity approach.

In addition to the holistic similarity approach, individual scores of temperature were evaluated in a refined assessment as temperature is known to be a key driving parameter for the degradation of pesticides. For one root ecoregions (NA0802), individual scores for temperature were low (7 and 10 %), indicating pronounced differences in temperature conditions between root ecoregions and their corresponding ecoregions in Europe. The root ecoregions NA0802 representing one TFD trial site (Manitoba, Canada) is therefore considered not representative for European conditions. For the remaining four root ecoregions (NA0407, NA0414, NA0801, NA0804), individual matches of temperature reached 100 % for one or more European ecoregions.

Based on the refined ecoregion crosswalk analysis, similar soil and climate conditions were identified for four root ecoregions: NA0407, NA0414, NA0801, NA0804, comprising three trial sites of the US

and Canadian TFD studies available for propamocarb hydrochloride. These trials are considered representative for European conditions.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Report:	KCA 7.1.2.2.1/05; Porschewski, R.; 2020; M-756746-01-1
Title:	Estimation of kinetic trigger endpoints for propamocarb from terrestrial field dissipation studies in the United States and Canada
Report No.:	114899-002
Document No.:	M-756746-01-1
Guideline(s):	"Generic Guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". EC Document Reference: None, version 1.1, 2014, amending "Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference Sanco/10058/2005 version 2.0, 2006 EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT50 values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014;12(5):3662.
Guideline deviation(s):	not specified
GLP/GEP:	no

Executive Summary

The fate and behaviour of the active substance propamocarb hydrochloride (PHC) was investigated in three terrestrial field dissipation (TFD) studies in North America covering in total eight trial sites (Cole, 1995, KCA 7.1.2.2.1/03; Belyk, 1998, KCA 7.1.2.2.1/02 and Willard, 2002, KCA 7.1.2.2.1/01). The eight trial sites were evaluated by van der Stouwe (2020, KCA 7.1.2.2.1/05) using the OECD ENASGIPS tool (Europe – North American Soil Geographic Information for Pesticide Studies) aiming to determine their representativeness throughout Europe based on climate and soil similarity.
A kinetic evaluation of the three terrestrial field soil dissipation trials with sufficient similarity was performed for propamocarb. The kinetic endpoints may be used for comparison against regulatory trigger values (trigger/ persistence endpoints).
An overview of the trigger endpoints determined is given in the table below.

Summary of trigger endpoints for PHC:

Study	Soil type (USDA)	Location	pH[a)]	Depth (cm)	Organic Matter [b)]	DT_{50} (d)	DT_{90}	χ^2 error (%)	Kinetic model
Cole, 1995	Sandy loam (bare soil)	Richmond, Illinois, USA	6.3	0 - 15	3.7	8.4	28.0	33.7	SFO
Belyk, 1998	Silt loam (bare soil)	Branchton, Ontario, Canada	6.7	0 - 20	2.9	17.9	59.5	15.3	SFO
Willard, 2002	Sandy loam (bare soil)	Porterville, California, USA	9.0	0 - 30	0.7	23.1	76.8	10.6	SFO

[a)] pH ($CaCl_2$) from upper soil layer with the highest amounts of propamocarb residues; [b)] from upper soil layer

I. Material and Methods

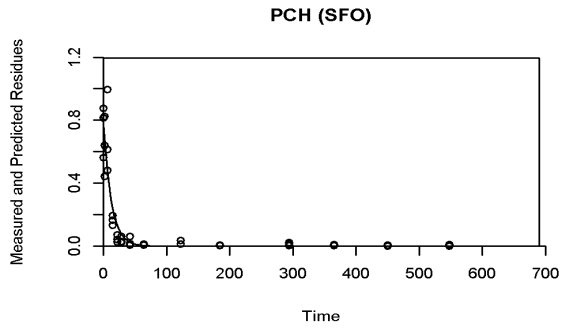
The data from the field trials required pre-processing in order to generate appropriate input datasets for the kinetic evaluation. The standard procedures recommended by FOCUS (2006, 2014) were applied. Single samples were available for all studies.
For derivation of trigger endpoints, the non-normalised dataset was considered and the kinetic evaluation was conducted according to FOCUS guidance (2006, 2014). The best-fit model was accepted for deriving trigger endpoints. The kinetic analyses were conducted using the software package KinGUI v2.1.

II. Results and Discussion

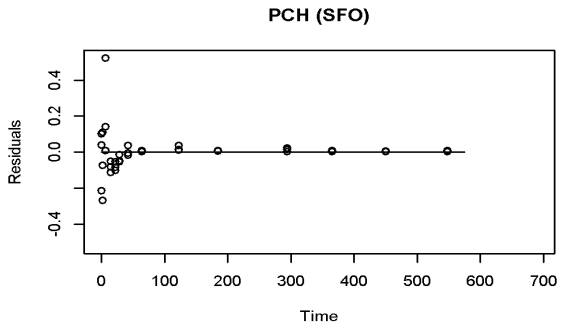
The degradation of propamocarb was well described assuming a simple first-order decay for all trial sites. Some of the fits show a scattering of data resulting in an increased χ^2err but the biphasic FOMC model as well as DFOP and HS did not improve the χ2 err significantly in these cases. All SFO parameters were significantly different from 0, based on a t-test. Consequently the SFO model was selected for the derivation of trigger endpoints for all trial sites. A summary of the parameters of the SFO kinetic models as well as the graphical presentation is presented in the tables below.

Best-fit results for site Richmond, USA:

Kinetic model	Visual assess-ment	M0	Kinetic parameters	χ^2 error (%)	Prob > t (5 % level)	Lower CI (95 %)	Upper CI (95 %)	DT50 (d)	DT90 (d)
SFO	Good	0.8	k: 0.082	33.7	k: <0.001	k: 0.058	k: 0.106	8.4	28.0



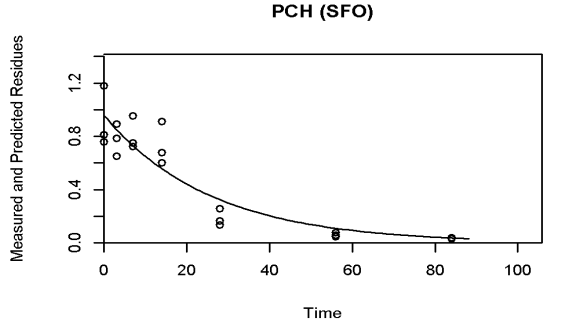
SFO



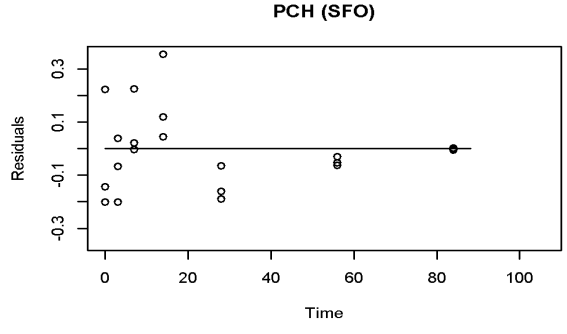
SFO

Best-fit results for site Branchton, Canada:

Kinetic model	Visual assess-ment	M0	Kinetic parameters	χ^2 error (%)	Prob > t (5 % level)	Lower CI (95 %)	Upper CI (95 %)	DT50 (d)	DT90 (d)
SFO	Good	1.0	k: 0.039	15.3	k: <0.001	k: 0.025	k: 0.053	17.9	59.5



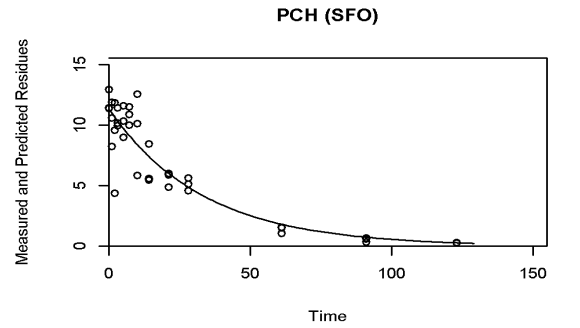
SFO



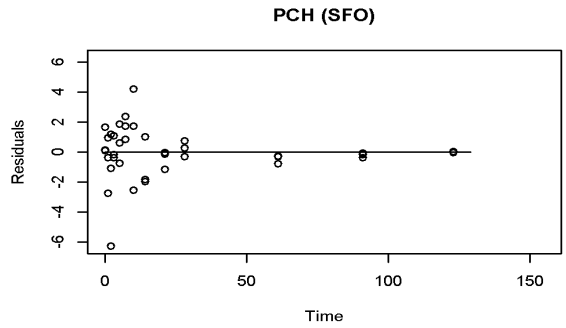
SFO

Best-fit results for site Porterville, USA:

Kinetic model	Visual assess-ment	M_0	Kinetic parameters	χ^2 error (%)	Prob > t (5 % level)	Lower CI (95 %)	Upper CI (95 %)	DT_{50} (d)	DT_{90} (d)
SFO	Good	11.3	k: 0.030	10.6	k: <0.001	k: 0.021	k: 0.039	23.1	76.8



SFO



SFO

III. Conclusion

The evaluation of terrestrial field soil dissipation data according to FOCUS kinetic guidance resulted in non-normalised half-lives ranging from 8.4 to 23.1 days and DT_{90} values ranging from 28.0 to 76.8 days.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

A.2) Soil accumulation studies

In case values of the $DisT_{50}$ in the field were higher than 1 year, two sites out of the set of available dissipation sites were identified to study the accumulation in the field for several successive years to reach the plateau concentration.

According to the working document EU Commission 9188/VI/97 rev. 8 of 12.07.2000, modelling was regarded as adequate for the determination of maximum soil concentrations.

In addition, the following triggers for the accumulation studies were not met: 15 out of 17 values of DT_{50} were far below the 3 months trigger for DT_{50} and the one year for DT_{90}. NER formation was below 70% and mineralisation was > 5% after 100 days.

Modelling based on laboratory values are an acceptable surrogate for data. The data requirement resulting from EU triggers for accumulation can be adequately addressed by laboratory data.

The geomean of aerobic soil degradation of PHC in laboratory studies was 22.3 d.

For calculations, the worst case lab DT50 of 136.7 d and the mixing (tillage) depth of 20 cm were used.

B) Monitoring

No formal monitoring program was requested or required to address this point for propamocarb-hydrochloride (PHC) or its residues in soil and water in the EU. Moreover and specifically for the active substance and its salts, there aren´t available any published data from formal monitoring programs outside BCS that would indicate a specific concern or findings of PHC and its residues in remote environmental areas not being subject to the intended use.

11.1.4.2 Inherent and enhanced ready biodegradation tests

Not available.

11.1.4.3 Water, water-sediment and soil degradation data (including simulation studies)

A) Aerobic mineralisation in surface water (new data requirement)

Report:	KCA 7.2.2.2/01; Iwan, J.; 1983; M-157700-01-1
Title:	Microbial degradation of propamocarb hydrochloride in water
Report No.:	R+S 13/83-PA 66752.73/2; A85467
Document No.:	M-157700-01-1
Guideline(s):	Dutch G.2
Guideline deviation(s):	none
GLP/GEP:	**no**

This study, is regarded as supplemental information and was already summarized in this Report; please, refer to the summary presented under 11.1.2.
The evaluation revealed that propamocarb hydrochloride was 'readily' degraded by microbial processes when sodium acetate was present while degradation was limited (less than 10% after 35 days) in the absence of this additional carbon source.
However and by its design, the test fulfilled key criteria according to the actual OECD Guideline 309, i.e. by diluting a 'mixed microbial population' from surface water (i.e. lake) in a mineral medium, to study the mineralization of the 14C-labeled active substance at 25°C in the dark for a maximum incubation period of 35 days. The tests had been performed in the presence and absence of an additional carbon source (acetate). However, the test concentration used in the study was 20 mg/L while tests to fully follow OECD 309 should be performed at 10 µg/L or lower.

In order to fulfill actual data requirements, a study was, therefore, performed according to OECD Guideline 309.

Report:	KCA 7.2.2.2/02; Heinemann, O.; Kasel, D.; 2015; M-513451-01-1
Title:	[1-14C]propamocarb-hydrochloride: Aerobic mineralization in surface water
Report No.:	EnSa-14-0512
Document No.:	M-513451-01-1
Guideline(s):	OECD Test Guideline No. 309 Commission Regulation (EU) No 283/2013 in accordance with Regulation (EC) No 1107/2009
Guideline deviation(s):	none
GLP/GEP:	**yes**

This study was already summarized in this Report; please, refer to the summary presented under 11.1.2.

The results were in some contradiction to the behavior and observations made in water/sediment tests which indicate good degradability in the presence of sediment. When transferring this into outdoor conditions and considering the use of propamocarb in agricultural practice, water/sediment tests describes better the situation of a ditch adjacent to the agricultural field rather than the 'open water' underlying as principle for the tests according to OECD 309.

B) Aerobic degradation in water/sediment

The route and the rate of degradation of propamocarb-hydrochloride under laboratory conditions and natural water/sediment systems had been investigated in:

- Two contrasting water/sediment systems (sediments and their associated water) obtained in the UK (KCA 7.2.2.3/01; M-157923-01-1), following application of 1-*N*-propyl-^{14}C-labeled propamocarb-hydrochloride and incubation under aerobic conditions at 20°C in the dark (photoperiod of 8 hours light:16 hours dark at 300-350 Lux) for a maximum of 105 days. One test system incorporated a sand sediment with low organic matter –Iron Hatch Stream (IHS) – and the other incorporated a silty clay loam sediment with high organic matter – Mill Stream Pond (MSP).

- Two contrasting water/sediment systems (sediments and their associated water) obtained in the Netherlands (KCA 7.2.2.3/02; M-310804-01-1), following application of 1-N-propyl-14C - labeled propamocarb-hydrochloride and incubation under aerobic conditions at 20°C in the dark (photoperiod of 8 hours:light 16 hours dark at 300-350 Lux) for a maximum of 104 days. The two water/sediment systems were obtained from the Oostvaardersplassen (OVP) and the Schoonrewoerdse Wiel (SW) areas.

Report:	KCA 7.2.2.3/01; Allen, R.; Fordham, L.; 1995; M-157923-01-1
Title:	Propamocarb hydrochloride soluble concentrate 722 g/L (Code: CR18131) - Degradation in sediment/water microcosms
Report No.:	ENVIR/94/36; A85614
Document No.:	M-157923-01-1
Guideline(s):	BBA Guideline, Part IV, 5-1, 1990
Guideline deviation(s):	none
GLP/GEP:	**yes**

Executive Summary

The route and rate of degradation of propamocarb hydrochloride was investigated in two natural water/sediment systems incubated under laboratory conditions. The water/sediment systems were kept incubated under aerobic conditions at 20°C in the dark (photoperiod of 8 h light 16 h dark at 300-350 Lux) for up to 105 days. Two different water/sediment systems were obtained in the UK, one test system incorporating sand sediment with low organic matter –Iron Hatch Stream (IHS) – and the other incorporating silty clay loam sediment with high organic matter – Mill Stream Pond (MSP).
Under aerobic aquatic conditions propamocarb hydrochloride was observed to degrade readily in two water/sediment systems at 20 C. Propamocarb hydrochloride degradation in natural water and associated sediment was principally through the action of micro-organisms resulting in mineralisation of ~70% of the compound to carbon dioxide. Overall recoveries of radioactive material were good for both test systems, as propamocarb hydrochloride was mineralised principally to carbon dioxide and NER. However, by the end of the study NER represented less than 10% of applied radioactivity. No accumulation of intermediate degradation products was observed. In total a maximum of eight minor metabolite peaks were observed during the incubation period, however, the concentration of these components was in all cases < 3.3% of the applied radioactivity. No further efforts were carried out to identify the metabolites. In all cases these proposed metabolites are transient in nature progressing to carbon dioxide. The DT_{50} values of propamocarb hydrochloride in the MSP and IHS water/sediment systems were estimated to be 21.0 days and 16.0 days for the total system, respectively. The DT_{50} values of propamocarb hydrochloride for the water phase were calculated to be 10.0 days (MSP) and 15.0 days (IHS).

I. Material and Methods

A. Materials

1. Test Material: Common name: propamocarb hydrochloride

Chemical name: propyl 3-(dimethylamino)propylcarbamate hydrochloride
Radiolabelled purity: > 95%
Lot # IS1795-10-1
Specific activity 9.9 MBq/mg (269 μCi/mg)
Non-radiolabelled purity: 722 g/L
Lot #CR 18131/01/940203.

2. Test System: Characteristics of the test systems are presented below. Water and sediment were taken from the top layer of the system. The water and sediment fractions of the system were sieved over 0.053 mm. Prior to treatment with the test substance the water/sediment systems were allowed to equilibrate.

Physico-chemical properties of water/sediment systems collected from the Iron Hatch Stream (IHS) system and the Mill Stream Pond (MSP)

Parameter	**Sediment**		**Water**	
	IHS	**MSP**	**IHS**	**MSP**
Particle size distribution:				
Course Sand (0.600 - 2.000 mm) (%)	13.0	1.0	-	-
Medium Sand (0.212 - 0.600 mm) (%)	67.0	1.0	-	-
Fine Sand (0.063 - 0.212 mm) (%)	18.0	18.0	-	-
Course Silt (0.020 - 0.063 mm) (%)	0.0	25.0	-	-
Fine Silt (0.002 - 0.020 mm) (%)	1.0	33.0	-	-
Clay (< 0.002 mm) (%)	1.0	22.0	-	-
Texture:				
ADAS	Sand	Silty Clay Loam	-	-
BBA	Sand	Silt Loam	-	-
USDA	Sand	Silty loam	-	-
pH	8.2	7.7	8.0	7.4
Cation Exchange Capacity (meq/100)	3.4	34.2	-	-
Calcium Carbonate (%)	1.0	20.5	-	-
Organic Matter %	0.6	12.2	-	-
Total Organic Carbon (mg/L)	-	-	7.2	30.6
Total calcium	-	-	33.0	97.0
Total potassium	-	-	1.6	7.0
Total manganese	-	-	12.0	429
Total phosphorus	-	-	128.0	983
Soil microbial Biomass (μg C/g soil):				
- Commencement of study	118.3	1674.41	-	-
- Termination of study	66.6	787.87	-	-

B. Study design

1. Experimental conditions: The study was performed in an open gas-flow incubation system. The systems were ventilated with CO_2-free moistened air, the outgoing air was passed through a trapping system of ethanediol:2-methoxy ethanol (3:2 v/v) and ethanolamine: 2-methoxy ethanol (4:1 v/v) in order to capture evolved volatiles. Twenty-four flasks were filled with wet sediment (2-2.5 cm in each flask) and water to give approximately a 10 % dry weight content of the sediment in the flasks. An additional six flasks for each water/sediment system were sterilised by autoclaving for comparative purposes. Microbial biomass determinations were carried out in a further four flasks for each microcosm.

Both water/sediment systems were treated at an application rate of 595 µg a.s per microcosm, which corresponds to a field application rate of 5.952 kg a.s/ha assuming application onto a body of water 30cm deep and with a nominal volume of 300 mL.

2. Sampling: Sampling of the non-sterile water/sediment test systems were undertaken at intervals of 0 h (immediately after application), 6 h, and then 1, 2, 7, 14, 28, 42, 63, and 105 days. At each sampling point duplicate sub-samples were removed for analysis. Duplicate sterile samples from each microcosm were removed from the incubation system after 0 h and 105 days. Biomass microcosms were removed from the incubation system after 0 h and 105 days for microbial biomass determinations.

3. Analytical procedures: Non-sterile and sterile sediment was acidified with dilute hydrochloride, then extracted with acetonitrile and filtered under vacuum. The filter cakes were further extracted with dilute hydrochloride and acetonitrile. Filtrates were combined and both the volumes of water sample and extract were measured and radioactivity content quantified by LSC. At a later time the sediment filter cake for each sample time was further extracted with acetonitrile: water (4:1 v/v) for 16 hours under soxhlet conditions. Radioactivity remaining in the sediment after extraction was quantified by LSC after combustion. Sterile microcosms were opened under aseptic conditions in a laminar flow cabinet.
Radioactivity in the surface water and sediment extracts was characterised by TLC and HPLC.

C. Determination of degradation kinetics: Degradation rates for propamocarb hydrochloride were determined on the basis of the amounts of the test item extracted from the soils at each sampling interval. Using the data from each water/sediment compartment and the overall system propamocarb hydrochloride degradation was described assuming simple first-order kinetics. The rate of degradation was determined using the kinetic model program (KIM B1.0) developed by Schering AG, Berlin. The rate of degradation and estimates of DT_{50} and DT_{90} values were determined using the non-linear form of the first-order rate equation:

$$C(t) = C_0 \cdot e^{-k \cdot t}$$

Here C(t) is the residue of the active substance at time t (of applied radioactivity), C0 is the initial residue, and k is the degradation rate in d-1. DT_{50} and DT_{90} values for propamocarb hydrochloride were estimated from the degradation rate k using the following equations:

$$DT_{50} = \frac{\ln 2}{k} \qquad DT_{90} = \frac{\ln 10}{k}$$

II. Results and Discussion

A. Data:

Distribution of radioactivity (% of applied) in the Mill Stream Pond and Iron Hatch Stream water/sediment systems following application of propamocarb hydrochloride to the water surface:

Time (days)	Surface water	Sediment			Ethanediol trap (volatiles)	Ethanol-amine trap (CO_2)	Total
		MeCN extract	MeCN/H_2O soxhlet	Unextracted			
MSP – Mill Stream Pond							
0	93.3	6.9	NA	0.2	NA	NA	100.4
	85.4	10.8	NA	1.1	NA	NA	97.3
6 h	91.0	10.0	NA	0.9	NA	NA	101.9
	92.8	10.2	NA	0.8	NA	NA	103.8
1	83.6	16.0	NA	1.6	<0.1	<0.1	101.2
	72.4	22.6	NA	2.2	<0.1	<0.1	97.2
2	70.9	27.4	NA	3.4	<0.1	<0.1	101.7
	73.1	23.4	NA	3.5	<0.1	0.1	100.1
7	47.4	34.1	NA	7.8	0.2	2.8	92.3
	50.5	32.0	NA	7.7	0.1	2.4	92.7
14	34.2	27.5	5.6	6.8	0.5	12.6	87.2
	30.7	33.6	4.8	7.4	1.1	10.5	88.1
28	15.6	16.1	4.5	9.5	3.7	37.8	87.2
	19.4	11.3	4.0	9.1	3.4	35.8	83.0
42	12.9	12.8	3.8	8.8	3.3	46.8	88.4
	16.3	13.9	4.3	7.2	3.0	42.9	87.6
63	2.0	4.5	2.4	10.3	4.2	63.9	87.3
	1.5	3.4	2.1	10.0	4.3	66.2	87.5
105	2.0	3.2	2.2	8.7	3.8	65.3	85.2
	1.3	3.5	2.6	9.4	4.1	67.5	88.4
Sterile control microcosms							
105	27.1	52.4	8.2	4.8	0.03	0.08	92.6
	26.3	47.2	11.1	7.0	<0.01	<0.01	91.6
HIS – Iron Hatch Sediment							
0	103.8	5.2	NA	0.2	NA	NA	109.2
	96.0	9.1	NA	0.8	NA	NA	105.9
6 h	92.4	7.3	NA	0.3	NA	NA	100.0
	89.9	7.6	NA	0.6	NA	NA	98.1
1	84.2	13.3	NA	1.6	<0.1	<0.1	99.1
	88.3	10.5	NA	1.9	<0.1	<0.1	100.7
2	81.0	12.0	NA	1.5	<0.1	0.1	94.6
	87.1	12.5	NA	1.3	<0.1	<0.1	100.9
7	70.9	10.0	NA	4.3	<0.1	1.3	86.6
	82.2	12.2	NA	2.0	<0.1	0.2	96.6
14	69.6	14.8	2.3	1.6	0.5	2.2	91.0
	38.8	4.9	2.6	11.4	2.6	10.4	70.7
28	27.1	4.0	2.4	9.0	4.7	14.3	61.5
	22.5	3.4	2.7	9.1	5.0	37.5	80.2
42	17.4	6.6	2.9	12.4	1.9	34.5	75.7
	28.4	7.9	3.2	6.9	1.7	31.3	79.4
63	4.1	1.7	1.2	8.3	5.0	66.1	86.4
	2.1	1.7	1.1	7.3	7.0	67.7	86.9
105	0.6	0.9	0.9	4.7	6.7	63.6	77.4
	0.8	1.2	1.2	8.4	5.6	73.8	91.0
Sterile control microcosms							
105	47.9	28.1	9.4	2.0	0.0	0.01	87.4
	50.2	19.4	8.4	2.7	<0.01	<0.01	80.7

Characterisation of radioactivity by TLC/HPLC (% of applied) in Mill Stream Pond (MSP) and Iron Hatch Sediment (IHS) extracts and water following application of propamocarb hydrochloride to surface water:

Time (d)	propamocarb hydrochloride				Totals for Water Phase, Sediment (Extract 1), and Sediment (Extract 2)							Total [2)]
	Water Phase	Sediment Extract 1 [1)]	Sediment Extract 2 [1)]	Total	Origin /solvent front	Unknowns	Unresolved background	Uncharacterised	Unextracted	Volatiles	$^{14}CO_2$	
MSP – Mill Stream Pond												
0	87.8	6.7	-	94.5	ND	ND	5.7	ND	0.2	NA	NA	100.4
	81.0	10.3	-	91.3	ND	ND	5.0	ND	1.1	NA	NA	97.3
6 h	86.8	9.9	-	96.7	ND	ND	4.3	ND	0.9	NA	NA	101.9
	88.1	10.1	-	98.2	ND	ND	4.9	ND	0.8	NA	NA	103.8
1	83.4	15.3	-	98.7	ND	ND	1.0	ND	1.6	<0.1	<0.1	101.2
	70.7	21.5	-	92.2	ND	ND	2.8	ND	2.2	<0.1	<0.1	97.2
2	67.4	26.7	-	94.1	ND	ND	4.2	ND	3.4	<0.1	<0.1	101.8
	70.9	22.9	-	93.8	ND	ND	2.8	ND	3.5	<0.1	<0.1	100.1
7	44.9	32.6	-	77.5	ND	ND	4.0	ND	7.8	0.2	2.8	92.3
	48.5	31.4	-	79.2	ND	ND	2.7	ND	7.7	0.1	2.4	92.7
14	33.1	27.3	5.2	65.6	ND	0.1	1.6	ND	6.8	0.5	12.6	87.2
	29.8	32.1	4.8	66.7	ND	ND	2.4	ND	7.4	1.1	10.5	88.1
28	12.7	15.5	3.4	31.6	1.5	1.7	1.4	ND	9.5	3.7	37.8	87.2
	17.1	11.1	3.6	31.8	0.7	0.3	2.1	ND	9.1	3.4	35.8	83.0
42	12.3	12.5	3.5	28.3	0.8	0.1	0.3	ND	8.8	3.3	46.8	88.4
	15.8	12.7	3.6	32.1	1.0	0.6	0.9	ND	7.2	3.0	42.9	87.6
63	0.2	3.7	1.3	5.2	1.0	1.4	0.4	1.2	10.3	4.2	63.9	87.3
	0.1	2.6	2.0	4.7	0.6	0.4	0.1	1.1	10.0	4.3	66.2	87.5
105	NA	2.8	2.0	4.8	0.1	0.2	0.3	2.0	8.7	3.8	65.3	85.2
	NA	3.1	2.5	5.6	0.1	0.2	0.2	1.3	9.4	4.1	67.5	88.4
Sterile control microcosm												
105	24.9	49.9	7.7	82.5	ND	0.7	4.5	ND	4.8	0.03	0.08	92.6
	25.4	47.1	10.6	83.1	ND	ND	1.5	ND	7.0	0.0	0.0	91.6
HIS – Iron Hatch Sediment												
0	102.3	5.1	-	107.4	ND	ND	1.6	ND	0.2	NA	NA	109.2
	94.5	8.9	-	103.4	ND	ND	1.7	ND	0.8	NA	NA	105.9
6 h	88.9	7.2	-	96.1	ND	ND	3.6	ND	0.3	NA	NA	100.0
	87.3	7.4	-	94.7	ND	ND	2.8	ND	0.6	NA	NA	98.1
1	79.5	12.4	-	91.9	ND	ND	5.6	ND	1.6	<0.1	<0.1	99.1
	86.9	10.1	-	97.0	ND	ND	2.8	ND	1.9	<0.1	<0.1	100.7
2	52.5	12.0	-	64.5	16.9	ND	11.5	ND	1.5	<0.1	0.1	94.6
	82.9	10.8	-	93.7	0.7	0.4	4.8	ND	1.3	<0.1	<0.1	100.9
7	67.5	9.9	-	77.4	ND	ND	3.6	ND	4.3	<0.1	1.3	86.5
	80.2	12.1	-	92.3	ND	ND	2.1	ND	2.0	<0.1	0.3	96.7
14	69.3	14.1	1.7	85.1	0.5	0.3	0.8	ND	1.6	0.5	2.2	91.0
	28.1	2.3	0.8	31.2	4.1	5.6	5.2	ND	11.4	2.6	10.4	70.5
28	21.7	2.3	0.6	24.6	3.6	1.8	3.6	ND	9.0	4.7	14.3	61.5
	15.8	1.9	0.8	18.5	3.0	3.3	3.6	ND	9.1	5.0	37.5	80.0
42	10.8	1.5	1.5	13.8	6.7	2.3	4.0	ND	12.4	1.9	34.5	75.6
	18.1	5.9	2.1	26.1	5.2	1.3	6.6	ND	6.9	1.7	31.3	79.1
63	0.3	0.5	0.9	1.7	2.5	0.4	0.2	2.4	8.3	5.0	66.1	86.4
	ND	0.3	0.3	0.6	2.6	0.6	0.1	7.6	7.3	7.0	67.7	86.9
105	NA	NA	0.7	0.7	0.1	0.1	0.1	1.5	4.7	6.7	63.6	77.4
	NA	NA	0.7	0.7	0.2	0.2	0.1	2.0	8.4	5.6	73.8	91.0
Sterile control microcosm												
105	45.6	26.6	8.9	81.1	0.3	ND	4.0	ND	2.0	0.0	0.01	87.4
	48.8	18.0	8.0	74.8	0.4	ND	2.8	ND	2.7	<0.01	<0.01	80.7

Note: [1)] Extract 1 = acetonitrile; Extract 2 = acetonitrile/water soxhlet, [2)] Totals are calculated from the individual values and not from the averaged values reported in the table, ND = Not Detected, NA = Not Applicable

B. Mass balance: Radioactive mass balance and distribution are summarised in the table below. Overall the radioactivity over 105 days was 92.9% and 89.6% for non-sterile MSP and IHS systems, respectively. The mean recoveries for the sterile water/sediment systems were 92.1% and 84.1% of applied radioactivity for the MSP and IHS systems, respectively.

C. Bound and extractable residues: The proportion of applied radioactivity in the surface water declined throughout the incubation period in both systems. At the termination of the study the applied radioactivity had declined to ca. 2% and 1% in the MSP and IHS systems, respectively.

The residues extracted from the sediment were generally greater in the MSP system, reaching a maximum of approximately 30% after 14 days before declining to 5% by the end of the study. The extracted residue from the IHS system followed a similar trend increasing to 17 % by Day 14 in one replicate and declining to approximately 2% by the end of the study.

Throughout the study unextracted residues gradually increased reaching a maximum of 10% and 9% after 63 days and between 28 and 42 days for the MSP and IHS systems, respectively. After the maximum value of NER was achieved the amounts observed either reached a plateau or slightly declined

D. Volatile radioactivity: In both systems the rate of mineralisation to CO_2 was rapid after an initial lag phase of up to seven days. Up to 67% of applied radioactivity was determined from the ethanolamine traps at the end of the study. The lower levels of total recovery of applied radioactivity correspond to the period in which CO_2 production was at its most rapid. It is likely that lower levels of total recovery are because of small losses of CO_2 from the incubation system.

In the sterile microcosms a much larger proportion of radioactivity was present in the surface water than in the corresponding non-sterile samples. Sediment extract residues in the sterile incubation units were greater in the MSP system than the IHS system indicating that adsorption of propamocarb hydrochloride is greater in sediment of a higher organic matter and clay content. No biological activity was evident from the sterility checks and from the absence of CO_2 in ethanolamine traps.

E. Transformation of test substance: Compiled chromatographic results of samples from soil extracts are provided in Table 11.1.4.3-03. The main degradation product of propamocarb hydrochloride was carbon dioxide, accounting for up to 67.5% and 73.8% of applied radioactivity in the MSP and IHS systems, respectively. Propamocarb hydrochloride was also identified in large amounts at the beginning of the incubation period. The amount of propamocarb hydrochloride identified decreased in both systems as the incubation period progressed, decreasing to 5.6% and 0.7% of applied radioactivity by Day 105 for the MSP and IHS systems, respectively. With regard to SANCO/3268/2001 rev.3 the applied radioactivity represented by the parent compound at Day 14 in the sediment was observed to be 36.9% and 15.8% in the MSP and IHS water/sediment systems, respectively. However, by Day 105 propamocarb hydrochloride had decreased in the sediment phase of the MSP and IHS systems to 5.6% and 0.7% of the applied radioactivity, respectively.

In the MSP system at least five unknown components were observed in the system. The maximum quantity of total unknown metabolites and degradation products was observed on Day 28 when 1.7% of applied radioactivity was characterised as four different components, with one component of the sediment residue representing 1.0% of the applied radioactivity.

In the IHS system up to eight unknown metabolites and degradation products were observed. The maximum quantity of total unknowns occurred on Day 14 when 5.6% of applied radioactivity was characterised as at least six different components with one component of the aqueous residue representing 3.3% of the applied radioactivity.

In both systems up to three metabolites were observed periodically throughout the incubation period and were thought to be transient, being degraded further to carbon dioxide and to NER.

F. Degradation kinetics: DT_{50} and DT_{90} values for propamocarb hydrochloride under aerobic conditions in two water/sediment systems are summarised in Table 11.1.4.3-04. Propamocarb hydrochloride was readily degraded in both compartments of both microcosm types. DT_{50} (DT_{90}) values of propamocarb hydrochloride in the water phase were calculated to be 10 (34) days, and 15 (49) days in the MSP and IHS test systems, respectively.

DT_{50} and DT_{90} values for the Mill Stream Pond and Iron Hatch Stream water/sediment systems following application of propamocarb hydrochloride to the water surface:

Water/sediment system	Compartment	DT_{50} (days)	DT_{90} (days)
MSP	Whole microcosm	21	69
	Water column	10	34
	Sediment	26	ND
IHS	Whole microcosm	16	53
	Water column	15	49
	Sediment	23	ND

Note: ND = Not determined

III. Conclusions

Under aerobic aquatic conditions, propamocarb hydrochloride was observed to degrade readily in two water/sediment systems at 20 ºC. Propamocarb hydrochloride degradation in natural water and associated sediment was, principally, through the action of micro-organisms resulting in mineralisation of ~ 70 % of the compound to carbon dioxide. Overall recoveries of radioactive material were good for both test systems, as propamocarb hydrochloride was mineralised, principally ,to carbon dioxide and NER. However, by the end of the study NER represented less than 10 % of applied radioactivity. No accumulation of intermediate degradation products was observed. In total a maximum of eight minor metabolite peaks were observed during the incubation period. However, the concentration of these components was in all cases < 3.3 % of the applied radioactivity. The proposed metabolites are transient in nature and progress to carbon dioxide. No further efforts were carried out to identify the metabolites.

The sediment DT_{50} values of propamocarb hydrochloride were higher compared to the water phase (26 days and 23 days in the MSP and IHS test systems, respectively). The total (water/sediment) system DT50 (DT90) values of propamocarb hydrochloride were estimated to be 21(69) days and 16 (53) days in the MSP and IHS test systems, respectively. The DT50 values of propamocarb hydrochloride (PHC) for the water phase were calculated to be 10 days (MSP) and 15 days (IHS). It should be considered that the DT50 values estimated for the water phase and the total system are also a function of propamocarb hydrochloride dissipation as well as degradation. The higher DT_{50} value for the MSP total system is likely to result from the higher clay and organic matter content of the sediment, binding the test substance to the sediment particles, thus reducing availability to microbial attack.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Report:	KCA 7.2.2.3/02; de Vries, R.; 1997; M-310804-01-1
Title:	Propamocarb hydrochloride: Degradation of propamocarb HCL in aerobic aquatic environment
Report No.:	161369
Document No.:	M-310804-01-1
Guideline(s):	Dutch Guideline for Registration of Pesticides, Section G 2.1: Details on the nature of conversion products and the rate at which they are formed, March 1995; German BBA Guidelines for the Official Examination of Plant Protection Agents, Part IV, Section 5-1 (December, 1990); European Economic Community (EEC), Commission directive 95/36/EC, amending Council Directive 91/414/EEC concerning the placing of plant protection products on the market, EEC Publication no. L172/8, July 1995; Society of Environmental Toxicology and Chemistry (SETAC), Procedures for assessing the environmental fate and ecotoxicity of pesticides, March 1995 (Dr. Mark R. Lynch)
Guideline deviation(s):	not specified
GLP/GEP:	**yes**

Executive Summary

The route and rate of degradation of propamocarb hydrochloride was investigated in two natural water/sediment systems in a laboratory study. The water/sediment systems were kept incubated under aerobic conditions at 20 C in the dark (photoperiod of 8 h light 16 h dark at 300-350 Lux) for up to 104 days. The two different water/sediment systems were obtained from the Oostvaardersplassen (OVP) area and the Schoonrewoerdse Wiel (SW) area in The Netherlands.
Propamocarb hydrochloride was observed to degrade readily in the two water/sediment systems at 20°C. Overall recoveries of radioactive material was good for both test systems, as propamocarb hydrochloride was mineralised principally to carbon dioxide and NER. In total a maximum of three minor metabolite peaks were observed during the incubation period, however, the concentration of these components was in all cases < 4% of the applied radioactivity. No further efforts were carried out to identify the metabolites. Based on literature, a degradation pathway for propamocarb hydrochloride was proposed for aerobic water/sediment system degradation: The active substance, propamocarb hydrochloride, progressed to Propyl-3-(dimethylamino) propylcarbamate, which then could degrade to either N,N-Dimethylpropane-1, 3-diamine or, and in sequence, to propyl-3(methylamino) propylcarbamate and 1-pethyltetrahydro-1,3-diazin-2-one. In all cases the proposed metabolites are transient in nature progressing to carbon dioxide.
The DT_{50} values of propamocarb hydrochloride in the OVP and SW water/sediment systems were estimated to be 15.5 days and 15.9 days for the total system, respectively. The DT_{50} values of propamocarb hydrochloride for the water phase were calculated to be 11.6 days (OVP) and 12.0 days (SW).

I. Material and Methods

A. Materials

1. Test Material: Common name: Propamocarb hydrochloride
Chemical name: propyl 3-(dimethylamino)propylcarbamate hydrochloride;
Radiolabelled purity: >98%
Lot # 96107
Specific activity 1887.0 MBq/mmol (8,35MBq/mg)
Non-radiolabelled purity: 98.5%
Lot #Op.2
Unlabeled substance purity: 722 g/L
Batch # T5665

2.Test System: Characteristics of the test systems are presented in the table below.

Water and sediment were taken from the top layer of the system. The water and sediment fractions of the system were sieved over a 150µm and 2mm sieve, respectively. The incubation flasks were filled 3 days prior to experimentation in order for the systems to obtain equilibrium.

Characterisation parameters for two water/sediment systems used in the investigation of propamocarb hydrochloride degradation:

Parameter	Oostvaardersplassen (OVP)	Schoonrewoerdse Wiel (SW)
Water level (m)[d)]	0.5	2.5
Temperature (°C)[d(]	8.3	4.9
pH[d]	8.2	9.3
Oxygen content (mg/L)	9.4	16.1
Water redox potential (mV)		
10 cm below water surface	+53	+41
10 cm below soil surface	+52	not registered

Sediment redox potential (mV)	+127	+117
Sediment CEC (mEq/100g soil)[b)]		
Beginning	24.9	23.8
End	24.3	27.3
Sediment dry matter (%)[a)]	57	16
Organic carbon content		
Dry sediment TC (%)		
End	1.8	1.9
Wet sediment TC (%)		
End	3.2	11.9
Water DOC (mg/L)		
Beginning	45.7	26.5
End	34.7	32.4
Total Hardness (mg/L $CaCO_3$)		
Beginning	380	175
End	333	577
Phosphorous (total)[b)]		
Sediment (mg/kg)		
Beginning	909	1304
End	945	1490
Water (mg/L)		
Beginning	0.5	0.1
End	0.4	0.6
Nitrogen (total)[b)]		
Sediment (mg/kg)		
Beginning	3787	7378
End	3143	6819
Water (mg/L)		
Beginning	7.0	1.4
End	<0.05	<0.05
Particle size distribution (%)		
<2 µm (clay)	21.3	13.7
2-6 µm (silt)	5.6	8.7
6-20 µm (silt)	17.5	18.7
20-63 µm (silt)	16.2	23.7
63-2000 µm (sand)	39.5	35.2
ATP sediment (µg/kg dry weight)[c)]		
Beginning	2500/5069[e)]	794/798[e)]
End	107.0	25.9

Note: [a)] After decanting the water layer and drying for 16 h at 105 °C; [b)] Determined under GLP at Cranfield University, Silsoe, Bedford [c)] Non-GLP determination at EPAS, University of Gent, Gent; [d)] Determined just before sampling; [e)] Duplicate samples; TC = Total carbon; DOC = Dissolved organic carbon

B. Study design

1. Experimental conditions: The study was performed in an open gas-flow incubation system. The systems were ventilated with CO_2 free moistened air, the outgoing air was passed through a trapping system of 2N NaOH and 2-methoxyethanol for the trapping of CO_2 and organic volatiles, respectively. Each flask was filled with wet sediment (2 - 2.5 cm in each flask) and water to give approximately a 10% dry weight content of the sediment in the flasks. The OVP flasks contained 68 g sediment and 680mL water and the SW flasks contained 32 g sediment and 395 mL water. Both water/sediment systems were treated at an application rate of 10 mg/kg water, which corresponds to a field application rate of 30 kg a.s/ha assuming application to the water surface in the same way as application to field soil, and assuming a homogenous distribution into a 30cm water layer.

2. Sampling: Sampling of the water/sediment test systems was undertaken at intervals of 0 h (immediately after application), 18 hours, and then 2, 7, 14, 28, 42, 56, and 104 days. At each sampling point duplicate sub-samples were removed for analysis.

3. Analytical procedures: Immediately after sampling the water was decanted from the sediment and stored, frozen, until analysis. The maximum storage period until extraction was 28 days.
Radioactivity in the water fraction was determined by flushing the decanted water fraction with NaCl, followed by an addition of 10N NaOH to adjust the pH. The water was then extracted four times with dichloromethane. After each extraction step the dichloromethane fraction was centrifuged. The combined centrifuged dichloromethane fractions were then evaporated and dissolved in methanol. Radioactivity was measured using LSC.
Sediment was extracted with a methanol and NaCl mixture four times. The supernatant was filtered. Filtrates were combined and evaporated. Any aqueous residue was extracted four times with dichloromethane, after the initial pH of the aqueous residue was adjusted. The combined dichloromethane fractions were evaporated and dissolved in methanol. The aliquot was counted with LSC. Samples containing a significant amount of non-extractable radioactivity were subject to three further extraction procedures. In the second extraction procedure sediment samples were ground and then 100 mL of dichloromethane was added and the sediment extracted four times. The third extraction procedure involved three extractions using acetone and the four the extraction procedure involved extraction with soxhlet and methanol. After each extraction procedure the extracts were evaporated to dryness and dissolved in methanol. The aliquots from each extraction were then counted using LSC. Determination of non-extractable residues in the sediment was undertaken by combustion, with the evolving CO_2 trapped and then quantified using LSC.

C. Determination of degradation kinetics: DT_{50}, DT_{90}, and rate parameters of propamocarb hydrochloride in water and the water/sediment system were calculated using the Timme-Frehse method. The best fit determined by the aforementioned technique was given by first order kinetics for each calculation. Therefore, DT_{50} and DT_{90} values were calculated using the formulae below (a is the slope of the best-fit regression):

$$DT_{50} = \frac{-\log 2}{a} \qquad DT_{90} = \frac{\log 10}{a}$$

II. Results and Discussion

A. Data:

Material balance of radioactivity (% recovery) in water/sediment samples collected from OVP and SW systems:

Time (days)	Total $^{14}CO_2$	Water fraction	Sediment fraction				Non-extractables		Total recovery
			EX1	EX2	EX3	EX4	Sediment	Water	
Oostvaardersplassen									
0	-	94.9	0.9	-	-	-	0.8	0.8	97.4
0	-	99.7	1.7	-	-	-	0.5	1.0	102.9
0.75	0.12	80.9	15.6	-	-	-	2.3	0.6	99.5
0.75	0.15	93.0	14.0	-	-	-	2.3	0.6	110.0
2	0.75	70.2	20.3	-	-	-	0.6	0.5	92.3

2	0.08	91.2	15.8	-	-	-	2.6	0.5	110.2
7	2.21	71.3	14.4	0.1	-	7.9	4.4	0.8	100.9
7	1.61	-[1)]	12.9	0.1	1.3	3.8	3.2	-[1)]	-
14	9.25	42.3	30.8	-	-	5.8	3.6	1.2	92.9
14	8.92	66.4	16.2	-	-	3.0	9.3	0.3	104.1
28	15.24	33.8	26.8	-	-	5.3	6.9	0.7	88.8
28	45.95	25.3	10.1	-	-	2.0	13.7	0.8	97.8
42	70.88	7.3	3.9	-	-	0.8	14.1	1.0	97.8
42	73.90	2.5	4.1	-	-	0.9	15.9	0.9	98.2
56	81.78	2.8	0.2	-	-	1.4	11.3	0.2	97.6
56	82.24	5.8	0.8	-	-	1.0	12.0	0.6	102.5
104	94.72	0.3	0.9	-	-	0.3	12.9	0.1	109.3
104	65.97	0.3	3.2	-	-	0.5	13.1	0.1	83.2[2)]
Schoonrewoerdse Wiel									
0	-	89.4	10.3	-	-	-	1.6	0.6	101.9
0	-	84.5	13.4	-	-	-	1.5	0.6	100.0
0.75	0.56	87.6	10.9	-	-	-	3.0	0.7	102.7
0.75	0.75	79.2	16.4	-	-	-	1.9	0.5	98.8
2	0.96	50.0	36.6	0.5	-	2.1	5.9	0.5	96.7
2	1.15	45.4	27.4	0.4	-	2.8	1.7	0.4	79.2[2)]
7	4.61	50.5	32.7	1.5	-	5.4	3.6	0.4	98.7
7	7.39	52.4	30.1	1.2	3.2	6.4	3.2	0.5	104.2
14	12.71	35.4	38.0	-	-	3.0	7.0	0.6	93.1
14	11.81	31.9	22.3	-	-	3.1	7.5	0.5	90.6
28	39.37	13.4	22.3	-	-	2.8	11.1	0.7	90.0
28	36.70	15.8	24.3	-	-	3.0	9.7	0.5	90.1
42	60.31	10.4	11.2	-	-	1.8	11.7	0.4	95.7
42	65.91	4.1	13.8	-	-	2.9	9.5	0.1	96.3
56	79.16	1.4	11.0	-	-	0.6	11.1	0.0	104.2
56	88.03	2.8	1.5	-	-	0.9	13.6	0.5	106.9
104	90.76	0.3	0.9	-	-	0.5	9.9	0.0	102.3
104	89.00	0.5	1.8	-	-	0.6	11.0	0.0	102.9

Note: Volatile organics were in all cases determined to be < 0.01 %; [1)] Sample was lost during the freezing procedure. Total value cannot be calculated; [2)] Mass balance is too low.

Quantification of radioactivity in water and sediment samples collected from OVP and SW systems (mean value of each sampling time and TLC method):

Time (days)	Total radioactivity (%)	propamocarb hydrochloride			Non-extractables (%)	$^{14}CO_2$ (%)	Total metabolites (%)
		Water (%)	Sediment (%)	Total (%)			
Oostvaardersplassen							
0	100.2	96.6	0.0	96.6	1.6	0.0	1.3
0.75	104.8	85.9	14.2	100.1	2.9	0.1	1.6
2	101.3	79.2	17.3	96.5	2.1	0.4	2.2
7[1)]	100.9	69.1	20.7	89.8	5.2	1.9	3.7
14	98.5	53.9	27.1	81.0	7.2	9.1	1.2
28	93.3	23.2	29.5	52.7	11.1	30.6	1.4
42	98.0	4.9	3.6	8.5	16.0	72.4	0.4
56	100.1	4.2	0.0	4.2	12.1	82.0	0.1
104	109.3	0.0	1.6	1.6	13.1	94.7	0.0
Schoonrewoerdse Wiel							
0	101.0	87.0	11.6	98.6	2.2	0.0	0.2
0.75	100.8	82.7	13.5	96.2	3.1	0.7	0.8
2[1)]	96.7	45.1	29.6	74.7	6.5	1.0	0.9
7	101.5	50.1	33.6	83.7	3.9	6.0	2.1
14	91.9	33.5	32.2	65.7	7.8	12.3	1.1
28	90.1	14.3	25.1	39.4	11.0	38.0	1.6
42	96.0	7.0	13.4	20.4	10.9	63.1	0.5
56	105.6	2.8	3.9	6.7	12.6	83.6	0.2
104	102.6	0.0	0.0	0.0	10.5	89.9	0.0

Note: [1)] Value was obtained with only one water/sediment sample

B. Mass balance: Radioactive mass balance and distribution are summarised in Table 11.1.4.3-06. Overall the radioactivity for both test systems was good and varied between 89% and 110%, and 90% and 107% for OVP and SW, respectively.

C. Bound and extractable residues: After application, the majority of the test substance resided in the water phase of the system, this began to steadily decline. A concomitant increase to 36.6% (OVP) and 41.0% (SW) in applied radioactivity was observed in the sediment phase of the two systems, this then decreased to 1.2% in OVP and to 1.4% in SW sediment by Day 104.

The amount of NER that were recovered by combustion of the sediment after extraction increased up to 10-15 % for both systems after 42 days. Thereafter the amount of NER did not significantly increase or decrease in time.

D. Volatile radioactivity: The amounts of radiolabelled carbon dioxide steadily increased over the course of the incubation period up to 95% and 91% for the OVP and SW systems, respectively. In all samples for both systems the amount of organic volatiles formed was < 0.01%.

E. Transformation of test substance: Compiled chromatographic results of samples from soil extracts are provided in the table below. The main radioactive component in each extract was identified as propamocarb hydrochloride in both TLC systems. The amount of propamocarb hydrochloride identified decreased in both systems as the incubation period progressed. With regard to SANCO/3268/2001 rev.3 the applied radioactivity represented by the parent compound at Day 14 in the sediment was observed to be 27.1% and 32.2% in the OVP and SW water/sediment systems, respectively.

However, by Day 104 propamocarb hydrochloride decreased in the sediment phase of the OVP and SW systems to 1.6% and 0.0% of the applied radioactivity, respectively. In both TLC systems three minor peaks were observed in the chromatograms of the extracts, reaching a maximum of 4.16% (after 28 days) and 2.39% (after 7 days) in the OVP and SW systems respectively.

In both systems the sum of the metabolites never exceed 5% of the AR. Rf values of the possible metabolites N, N-dimethyl-1, 3-propanediamine (method I 0.49-0.55; method II 0.15-0.30), Desmethyl-propamocarb hydrochloride (method I 0.60-0.65; method II 0.21-0.36), and N-methyl-1, 3-diazine-2-one (method I 0.74-0.80; method II 0.54-0.64) did not correspond to any Rf values obtained after TLC analysis. Therefore, none of the derived peaks could be attributed to the possible metabolites. Evaluations and calculation were undertaken using data from both TLC systems and duplicated at each time point as outlined in the table above.

F. Degradation kinetics: DT_{50} and DT_{90} values for propamocarb hydrochloride under aerobic conditions in two water/sediment systems are summarised in Table CA-8.2.2.3-08. DT_{50} (DT_{90}) values of propamocarb hydrochloride in the water phase were calculated to be 11.6 (38.4) days, and 12.0 (39.9) days in the OVP and SW test systems, respectively. For the total system DT_{50} (DT_{90}) values were higher compared to the water phase, and were 15.5 (51.5) days, and 15.9 (52.7) days in the OVP and SW test systems, respectively. It should be considered that the DT_{50} values estimated for the water phase and the total system are also a function of propamocarb hydrochloride dissipation as well as degradation.

DT_{50} and DT_{90} values of Propamocarb hydrochloride in water and in the water/sediment system:

	Oostvaardersplassen (OVP)		Schoonrewoerdse Wiel (SW)	
	Water	**Water/sediment**	**Water**	**Water/sediment**
DT_{50} (days)	11.6 ± 2.2	15.5 ± 4.0	12.0 ± 1.7	15.9 ± 3.5
DT_{90} (days)	38.4 ± 7.3	51.5 ± 13.4	39.9 ± 5.6	52.7 ± 11.6
r^2 †	0.9672	0.9055	0.8949	0.9138

Note: † Modified r^2

III. Conclusions

Propamocarb hydrochloride was observed to degrade readily in the two water/sediment systems at 20°C. Overall recoveries of radioactive material were good as propamocarb hydrochloride was mineralised, principally, to carbon dioxide and NER. In total, a maximum of three minor metabolite peaks were observed during the incubation period. However, the concentration of these components was in all cases < 4 % of the applied radioactivity. No further efforts were carried out to identify the metabolites. Based on literature, a degradation pathway for propamocarb hydrochloride was proposed for aerobic water/sediment system degradation: the active substance propamocarb hydrochloride progressed to Propyl-3-(dimethylamino) propylcarbamate which, then, could degrade to either N,N-Dimethylpropane-1, 3-diamine or, and in sequence, to Propyl-3(methylamino) propylcarbamate and 1-Methyltetrahydro-1,3-diazin-2-one. The proposed metabolites are transient in nature and progress to carbon dioxide.
For the two different water/sediment systems obtained from The Netherlands, the DT_{50} values of propamocarb hydrochloride in the OVP and SW water/sediment systems were estimated to be, respectively, 15.5 days and 15.9 days for the total system. The DT_{50} values of propamocarb hydrochloride for the water phase were calculated to be 11.6 days (OVP) and 12.0 days (SW).

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

The evaluations of the two water/sediment systems obtained from UK and two water/sediment systems obtained from The Netherlands revealed that propamocarb-hydrochloride (PHC) was readily degraded in both studies *via* formation of carbon dioxide and non-extractable residues (NER) as predominant transformation products. No major (> 5 % AR) metabolites were observed in the course of the tests. Under the biotic conditions of water/sediment testing, the degradation was paralleled by formation of a number of minor metabolites all below 4% AR in the course of the studies, thus, indicating their transient character. The degradation was, thus, found to occur, in principle, *via* the same pathways as observed in aerobic soil.
The study of Allen and Fordham (KCA 7.2.2.3/01) has a potential major study deviation according to the current test guideline due to recoveries below 90% AR detected after 14 DAT or 7 DAT for Mill Stream Pond and Iron Hatch Steam, respectively. A minor deviation of the study could be the strong decrease of microbial activity until study end. However, as almost complete degradation of the test substance was detected at study end (< 6% AR PHC in total system), the activity was still sufficient for compound degradation presenting a worst-case scenario. Overall, a fast degradation of PHC is shown and the study can be used as supporting information due the deviations mentioned above. The endpoints derived in this study will not be used for the risk assessment.
An evaluation of the water/sediment study performed by De Vries (KCA 7.2.2.3/02) revealed a potential minor deviation of the study which could be seen in the strong decrease of microbial activity in the sediment. The microbial activity of the sediment is measured by a non-specified, non-GLP ATP method. This ATP value decreases within the study from 2500/5069 µg/kg dry weight (duplicate samples) to 107 µg/kg dry weight and from 794/798 µg/kg dry weight (duplicate samples) to 25.9 µg/kg dry weight for Oostvaardersplassen (OVP) and Schoonrewoerdse Wiel (SW), respectively. However, the results of the study show a rapid dissipation of PHC from water to the sediment and finally a complete degradation of the substance. Almost complete mineralisation is detected at the end of the study with 94.7% and 89.9% AR CO_2 for OVP and SW, respectively. This degradation behaviour indicates microbial active test systems and shows great uncertainty in the conversion of ATP into biomass C. Even if these ATP measurements would correctly represent the microbial activity of the sediment, the study would present a worst-case scenario. Thus, the microbial decrease in the sediment is only a minor deviation according to the current test guideline and the study of De Vries (1997) is seen as fully valid.
Under conditions of water/sediment testing, half-lives of degradation of PHC ranged from 15.5 to 15.9 days in total systems and from 11.6 to 12.0 days in water (table below).

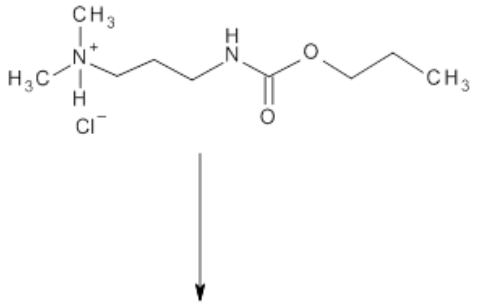
Summary of kinetic data of degradation of propamocarb-hydrochloride under conditions of water/sediment

testing in the laboratory:

Water/sediment system	Kinetic model	Compartment	r^2	DT_{50} (days)	DT_{90} (days)
Oostvaardersplassen	SFO	Water phase	0.967	11.6	38.4
		Total system	0.905	15.5	51.5
Schoonrewoerdse Wiel	SFO	Water phase	0.894	12.0	39.9
		Total system	0.913	15.9	52.7

No transformation products occurred at more than 5 % AR in water/sediment testing, thus, no residue other than the active substance was considered within the environmental risk assessments for surface water.
The proposed pathway of metabolism of propamocarb-hydrochloride in water/sediment systems is summarized graphically in the figure below.

Proposed pathway of metabolism of propamocarb-hydrochloride in water/sediment systems:



Non-Extractable Residues + Carbon dioxide

Data evaluated as supplemental:

In addition, the degradation of propamocarb-hydrochloride in water/sediment systems was investigated under strictly anaerobic conditions (KCA 7.2.2.3/03).

Report:	KCA 7.2.2.3/03; Judge, D. N.; 1998; M-167940-02-1
Title:	Code: AE B039744 - Degradation of [1-14C] propamocarb under laboratory anaerobic aquatic conditions propamocarb free base - Amendment to report number AV97E517
Report No.:	AV97E517; A91240 and Amendment under A91784
Document No.:	M-167940-02-1
Guideline(s):	US EPA Pesticide Assessment Guidelines, Subdivision N, Guideline Section 162-3
Guideline deviation(s):	none
GLP/GEP:	**yes**

Propamocarb-hydrochloride was found to degrade slowly under the conditions of the test to finally form predominantly carbon dioxide at the end of the test. Since this type of test was (and is) not a data requirement in the EU, the data were regarded as supplemental information.

Executive Summary

The route and rate of degradation of Propamocarb hydrochloride was investigated in a natural water/sediment system incubated under laboratory conditions. The water/sediment system was kept incubated under anaerobic conditions at 25°C in the dark for up to 419 days. The water/sediment system was obtained in the USA in Pikeville, North Carolina (PNC) and incorporated clay loam sediment with a high organic matter and clay content.
Under anaerobic aquatic conditions PHC was observed to rapidly partition from the aqueous phase to the sediment phase. Significant dissipation of Propamocarb hydrochloride was observed in the Pikeville water/sediment system through the mineralisation of the parent compound to carbon dioxide. Evidence of methane production from anaerobic methanogenic bacteria was also obtained from additional investigations. Formation of NER (20.1 % after 110 days) was identified; however, by the end of the study NER represented 2.25 % of the applied radioactivity. Overall recoveries of radioactive material were good with the mean material balance for the study being 93.4 % of applied radioactivity. No accumulation of intermediate degradation products was observed. In total a maximum of nine minor metabolite peaks were observed during the incubation period, however, the maximum concentration of one metabolite (unknown metabolite D) only reached 3.9 % and 0.9 % of the applied radioactivity in the water and sediment phase, respectively. Overall no single metabolite exceeded 3.9 % of applied radioactivity. No further efforts were carried out to identify the metabolites. In all cases these proposed metabolites are transient in nature progressing to carbon dioxide and methane.
The DT_{50} values of PHC in the Pikeville water/sediment system were estimated to be 12.1 days, 93.0 days, and 100.0 days for the water phase, sediment phase, and total system, respectively.

I. Material and Methods

A. Materials

1. Test Material: Common name: Propamocarb hydrochloride
Chemical name: propyl 3-(dimethylamino)propylcarbamate hydrochloride;
Radiolabelled purity: >98.5%
Lot # IS1795-21
Specific activity 10.41 MBq/mg (281.35 µCi/mg)
Non-radiolabelled purity: 96.8%
Lot # AZ05620

2. Test System: Characteristics of the test systems are presented in the table below.

Water and sediment were taken from the top layer of the system. The water and sediment fractions of the system were sieved over a 2 and 0.5 mm. Prior to treatment with the test substance, the water/sediment systems were allowed to equilibrate for approximately 24 hours.

Characterisation parameters for the water/sediment system used in the investigation of PHC degradation:

Parameter	Pikeville
Water	
pH	6.8
Conductivity [mS/cm]	0.26
Hardness [mg/L $CaCO_3$]	20.0
Total suspended solids [mg/L]	15.0
Sediment	
Textural class (USDA)	Clay loam
Particle size distribution (%) <2 µm (clay) 2-50 µm (silt) 50-2000 µm (sand)	 28.8 45.3 25.9
Organic carbon [%]	4.02
Organic matter [%] [a)]	6.92
Cation exchange capacity [meq/100 g soil]	11.70
Maximum water holding capacity (%) 1/3 bar 15 bar	 43.42 11.85

[a)] Organic carbon = organic matter/1.72

B. Study design

1. Experimental conditions: The study was performed in a nitrogen gas-flow incubation system in order to maintain anaerobic conditions. Outgoing air was passed through a trapping system of polyurethane foam followed by an ethylene glycol trap and then an ethanolamine trap in order to capture evolved volatiles. Redox potential (Eh), pH, and dissolved oxygen determinations were carried out to monitor the development and maintenance of anaerobic conditions. The water/sediment system was treated at an application rate of 1.73 mg a.s per flask, which corresponds to a field application rate of 27.46 kg a.s/ha after correction of the ratio of molecular weights of Propamocarb hydrochloride as a free base and hydrochloride salts (188.3 g/mole and 224.7 g/mole, respectively).

2. Sampling: Sampling of the treated water/sediment test flasks was undertaken at intervals of 0 h (immediately after application), 13, 28, 54, 82, 110, 167, 258, and 370 days. At each sampling point duplicate sub-samples were removed for analysis.

3. Analytical procedures: Water and sediment were separated prior to the partition and extraction of Propamocarb hydrochloride from the aqueous phase and the sediment phase, respectively. Aliquots of separated water were adjusted to approximately pH 9 and then partitioned in three consecutive times with dichloromethane (150 mL). The dichloromethane fractions were combined and radioactivity was determined using LSC. The sediment was extracted with acetonitrile:0.13 M Hydrochloric acid (9:1 v/v), and the extracts were combined and measured using LSC. Further extraction of the sediment was undertaken by Soxhlet extraction with acetonitrile /water (4:1 v/v). These extracts were also combined and measured by LSC for radioactivity.

After Soxhlet extraction sediment was subjected to further fractionation designed to identify and separate the unextractable bound residue into components associated with humic and fulvic acid fractions. The sediment was combusted in order to quantify unextracted radioactivity, which was measured using LSC.

Radioactivity in the surface water and sediment extracts was characterised by normal phase and reverse phase TLC on extracts that contained > 5 % of the applied radioactivity. HPLC was utilised to confirm the identity of PHC and its degradation products in representative extracts.

C. Determination of degradation kinetics: Degradation rates for PHC were determined on the basis of the amounts of the test item extracted from the soils at each sampling interval. Using the data from each water/sediment compartment and the overall system, PHC degradation was described assuming simple first-order kinetics.

The rate of degradation was determined using the kinetic model program (KIM 1.0). Degradation rate constants were calculated from the following equation (in the form y = mx + b): $\ln C \square kt \square \ln C_0$

DT_{50} and DT_{90} values for PHC were estimated from the degradation rate k using the following equations:

$$DT_{90} = \frac{ln10}{k}$$

II. Results and Discussion

A. Data:

Material balance and distribution of radioactivity (% recovery) in water/sediment samples collected from Pikeville system:

(d)	Fl No.	Volatile Phase				Water Phase				Sediment Phase						Total
		Organic Volatiles		$^{14}CO_2$		Water before partition [a]	DCM Partition [b]			Solvent Extractable			Alk.-extractable	Un-extractable	Total	
		PUF	EG	EA	Total		Partition	Rem. H_2O	Total	Am	Sox	Total				
0	1	0.0	0.0	0.0	0.0	99.6	NA	NA	NA	1.8	0.1	1.9	NA	0.1	2.0	101.6
	2	0.0	0.0	0.0	0.0	97.0	NA	NA	NA	1.8	0.1	1.9	NA	0.1	2.0	99.0
0	31	0.0	NA	0.0	0.0	102.7	98.1	2.8	100.9	0.8	0.0	0.9	NA	0.1	0.9	103.7
	32	0.0	NA	0.0	0.0	102.9	98.0	2.8	100.8	0.5	0.1	0.6	NA	0.1	0.7	103.7
13	3	0.0	0.0	1.4	1.4	54.2	52.1	1.2	53.3	43.0	1.8	44.9	NA	2.8	47.7	103.3
	4	0.0	0.0	1.7	1.7	48.8	46.5	0.8	47.3	47.6	2.1	49.7	NA	2.6	52.2	102.7
28	5	0.0	0.0	5.1	5.1	21.6	21.4	0.5	21.9	60.3	2.4	62.7	NA	9.2	71.9	98.6
	6	0.0	0.0	4.4	4.4	18.6	18.0	0.5	18.5	60.9	2.5	63.4	NA	10.9	74.3	97.3
54	7	0.0	0.0	8.9	8.9	10.4	9.7	0.2	10.0	57.3	6.0	63.3	NA	15.3	78.6	97.9
	8	0.0	0.0	8.4	8.4	10.8	10.1	0.2	10.3	57.4	6.3	63.8	NA	16.4	80.1	99.3
82	9	0.0	0.0	14.3	14.3	6.7	5.9	0.8	6.7	45.2	7.6	52.8	NA	17.1	69.9	90.9
	10	0.0	0.0	16.7	16.7	6.6	5.9	0.8	6.8	43.4	7.7	51.1	NA	17.0	68.1	91.3
110	11	0.0	0.0	21.0	21.0	4.6	3.8	0.8	4.5	36.4	5.6	42.0	NA	20.1	62.1	87.7
	12	0.0	0.0	27.8	27.8	4.6	3.9	0.8	4.7	36.5	5.9	42.4	NA	16.6	58.9	91.3
167	13	0.0	0.0	46.3	46.3	2.5	1.5	0.7	2.3	22.7	5.6	28.3	NA	11.5	39.8	88.6
	15	0.0	0.0	41.1	41.1	2.8	1.6	0.9	2.5	21.9	5.1	26.9	NA	10.4	37.4	81.2
258	16	0.0	0.0	58.3	58.3	1.4	0.6	0.7	1.2	10.3	4.0	14.3	NA	6.4	20.7	80.4
	17	0.0	0.0	57.3	57.4	1.4	0.6	0.8	1.3	10.2	4.0	14.2	NA	6.7	20.9	79.7
370	18	0.0	0.0	69.0	69.1	0.8	0.2	NA	0.2	5.4	2.7	8.0	3.7	2.2	14.0	86.1
	19	0.0	0.0	66.1	66.1	1.0	0.3	NA	0.3	5.3	2.7	8.0	3.6	2.3	13.9	83.2

a Water decanted from flask; b Dichloromethane partition of water phase and the remaining water portion after partition;
PUF/EG/EA = Polyurethane Foam Traps/Ethyleneglycol traps/Ethanolamine traps – for the trapping of organic volatiles and carbon dioxide;
NA = Not Analysed; Am/Sox = Ambient temperature extraction using organic solvents/Soxhlet extraction

Quantification of radioactivity in water and sediment samples collected from Pikeville system (mean value of each sampling time and TLC method):

DAT	Origin	PCH	Unknown Metabolite									Remainder
			A	B	C	D	E	F	G	H	I	
Normal Phase TLC												
Aqueous Phase												
0	ND	92.7	ND	1.1	0.4	ND	0.5	0.5	1.1	1.8	ND	0.3
13	0.1	38.5	0.3	ND	ND	3.9	ND	3.3	2.3	0.5	ND	0.3
28	0.3	17.2	0.1	0.1	0.1	ND	ND	ND	1.7	ND	ND	0.2
54	<0.05	7.9	ND	ND	0.3	ND	ND	ND	1.6	ND	ND	0.2
82	<0.05	4.9	<0.05	0.2	<0.05	ND	ND	ND	0.7	ND	ND	0.1
110	<0.05	3.0	<0.05	0.1	<0.05	ND	ND	ND	0.7	ND	ND	<0.05
167	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
258	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
370	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sediment Phase (ambient)												
0	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
13	0.4	39.5	ND	ND	ND	0.9	ND	ND	ND	ND	ND	2.3
28	ND	59.6	ND	ND	ND	ND	ND	ND	ND	ND	ND	1.0
54	ND	55.8	ND	0.2	0.5	ND	ND	ND	ND	ND	ND	1.0
82	0.1	43.3	<0.05	0.1	0.3	ND	ND	ND	0.1	ND	ND	0.4
110	ND	35.6	ND	0.1	0.3	ND	ND	ND	0.1	ND	ND	0.2
167	ND	21.5	ND	ND	0.3	ND	ND	ND	0.1	ND	ND	0.4
258	0.2	9.3	ND	0.1	0.4	ND	ND	ND	0.1	0.1	0.1	0.2
370	0.3	3.8	ND	0.3	0.6	ND	ND	ND	ND	0.2	ND	0.1
Sediment Phase (Soxhlet)												
0	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
13	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
28	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
54	0.1	5.9	<0.05	<0.05	<0.05	ND	ND	ND	ND	ND	ND	0.1
82	0.1	7.2	0.1	<0.05	0.1	ND	ND	ND	<0.05	ND	ND	0.1
110	<0.05	5.6	<0.05	<0.05	<0.05	ND	ND	ND	<0.05	ND	ND	<0.05
167	0.1	5.1	ND	0.1	ND	ND	ND	ND	ND	ND	ND	0.1
258	<0.05	3.8	<0.05	<0.05	0.1	ND	ND	ND	0.0	ND	ND	<0.05
370	0.1	2.3	ND	ND	0.1	ND	ND	ND	ND	0.1	ND	0.1

NA = Not Analysed; ND = Not Detected (<0.001 %); NR = Not Reported; DAT = Days After Treatment; PCH = propamocarb hydrochloride

B. Mass balance: Overall the radioactive material balance over the first 110 days was ≥ 90.0% for the Pikeville system. However, after 110 days the material balance began to decrease to a minimum of 79.7% in a single flask on Day 258. It might be expected that losses of radioactivity were the result of

methane production escaping from the trapping system of the flow-through system. Methane is known to be difficult to trap in a flow-through system and further investigation was undertaken to confirm methane production. The presence of methane was confirmed in the headspace of a sealed flask. The inability to trap [^{14}C] methane being mineralised during the study would account for the observed decrease in mass balance. The mean recovery for the Pikeville water/sediment system was 93.4% of the applied radioactivity.

The proportion of the applied radioactivity in the surface water declined throughout the incubation period in the Pikeville system. The initial aqueous phase samples (Day 0) contained an average of 100.6% of the applied radioactivity. By Day 13 the aqueous phase contained approximately 52% of the applied radioactivity, and at the termination of the study the applied radioactivity had declined to slightly less than 1 % of the applied radioactivity.

C. Bound and extractable residues: The residues extracted from the sediment at ambient temperatures using organic solvents increased at each sampling point to a maximum of 60.6 % at Day 28; decreasing until the end of the study. The initial ambient sediment extracts contained approximately 2% of the applied radioactivity. By the end of the incubation period the radioactivity recovered had declined to 5.35%. Levels of radioactivity in the Soxhlet extracts increased slowly reaching of the applied radioactivity by Day 82. Levels of radioactivity then declined to 2.7% of the applied radioactivity by Day 370. Throughout the study unextracted residues gradually increased reaching a maximum of 20.1% in one sample by Day 110, levels of NER then decreased to 2.25% of applied radioactivity by the end of the incubation period.

Results of sediment analysed for the proportion of humic and fulvic acids are provided in Table11.1.4.3-13 . After extraction the supernatant of humic and fulvic acid fraction contained 2.1% and 1.2 % of the AR, respectively. The humin fraction contained 2. % of the AR.

Results of the humic and fulvic acid extraction from sediment in the solvent extracted sediment from the Pikeville water/sediment system:

Fraction	Total radioactivity in fractions (%)	Total of applied radioactivity (%)
Hydrochloride Hydrolysate	4.6	0.3
Fulvic acid	20.7	1.2
Humic acid	36.2	2.1
Humin	38.4	2.3
Overall Recovery	100.0	5.9

D. Volatile radioactivity: In the Pikeville water/sediment system the radioactivity detected in volatile traps increased during the study, totalling 67.6% of applied radioactivity by the end of the study (Day 370). More than 99.9% of the detected volatile radioactivity was found in the ethanolamine traps, designed to capture carbon dioxide. The identity of the radioactivity in the ethanolamine traps was confirmed as being $^{14}CO_2$, using the barium chloride precipitation method.

E. Transformation of test substance:

The main degradation product of Propamocarb hydrochloride was carbon dioxide, and accounted for 99.9% of the radioactivity recovered from the trapping system. Propamocarb hydrochloride was also identified in large amounts at the beginning of the incubation period in the aqueous phase. However, Propamocarb hydrochloride rapidly partitioned from the water phase to sediment with nearly 50% of the applied radioactivity detected in the sediment by Day 13. Chromatographic analysis was not performed on the aqueous samples past day 110 because the radioactivity recovered had decreased to < 5% of the applied. Propamocarb hydrochloride was the predominant compound analysed in the sediment extracts after application of the test compound, and reached a maximum for the ambient and Soxhlet

sediment extracts of 59.6% (Day 28) and 7.2% (Day 82), respectively. The amount of Propamocarb hydrochloride identified decreased in both sediment extracts as the incubation period progressed, decreasing to 3.8% and 2.3% of applied radioactivity by Day 370 for the ambient and Soxhlet extracts, respectively.

In the Pikeville system at least nine unknown components (A-I) were observed in the system. The maximum quantity of a single metabolite was observed on Day 13 in both the aqueous phase and sediment; 3.9% and 0.9% of applied radioactivity was allocated to unknown metabolite D using normal phase TLC. Overall, no single metabolite in the aqueous phase or sediment exceeded 2.0% or 0.5% of the applied radioactivity, respectively. None of the observed metabolites were identified. In the Pikeville system the metabolites were observed periodically throughout the incubation period and were thought to be transient, being degraded further to carbon dioxide and to NER.

F. Degradation kinetics: Propamocarb hydrochloride rapidly dissipated from the aqueous phase under anaerobic conditions with less than 10% of the originally applied propamocarb hydrochloride left in the water by Day 54.

During the 49 day pre-incubation equilibrium period and the 370 day test period the Eh, pH, and dissolved oxygen monitoring indicated that anaerobic conditions were maintained throughout the investigation.

Mean Eh measurements did not exceed 200 mV (the pre-defined limit of anaerobic conditions) and pH decreased (7.23 on Day 12 to 6.16 on Day 343) which is typical of a microbial metabolism shift to acidogenesis under low to no oxygen conditions.

DT_{50} and DT_{90} values of propamocarb hydrochloride in water and in the water/sediment system:

Water/sediment system	Compartment	DT_{50} (days)	DT_{90} (days)
Pikeville	Water phase	12.1	40.1
	Sediment	93.0	309.1
	Total system	100.0	332.3

III. Conclusions

The DT_{50} and DT_{90} values for Propamocarb hydrochloride in the aqueous phase under anaerobic conditions in the Pikeville water/sediment system was calculated (k = 0.05747) to be 12.1 days and 40.1 days, respectively. For the sediment DT_{50} and DT_{90} values were higher compared to the water phase, and were estimated (k = 0.00745) to be 93.0 days and 309.1 days, respectively. Half-life estimation for sediment was determined after a hinge point representing the maximum amount of applied radioactivity reached on Day 54. For the total system DT_{50} (DT_{90}) values were calculated (k = 0.00693) to be 100.0 (332.3) days. Propamocarb hydrochloride is unlikely to accumulate in water/sediment systems under similar conditions.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

New kinetic evaluation of existing data:

The data from existing water/sediment tests (KCA 7.2.2.3/01 and KCA 7.2.2.3/02) were kinetically re-evaluated, according to actual FOCUS guidance (2011), as detailed in document KCA 7.2.2.3/04.

Report:	KCA 7.2.2.3/04; Oberdoerster, C.; Hoerold, C.; Boiselle, N.; 2015a; M-541774-01-1
Title:	Kinetic evaluation of the aerobic aquatic metabolism of propamocarb-HCl in two water sediment laboratory studies
Report No.:	EnSa-14-1370
Document No.:	M-541774-01-1
Guideline(s):	"Generic Guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". EC Document Reference: None, version 1.1, 2015 amending "Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference Sanco/10058/2005 version 2.0, 2006
Guideline deviation(s):	not applicable
GLP/GEP:	**no**

Executive Summary

The kinetics of degradation and dissipation was evaluated for propamocarb-hydrochloride for four data sets resulting from two studies performed each with two differing water/sediment systems after application of the ^{14}C-labeled active substance and incubation at 20°C (KCA 7.2.2.3/01 and KCA 7.2.2.3/02). The kinetic evaluation followed FOCUS guidance (2011).

Degradation in total systems:
Degradation rates in total sediment/water systems were derived from best fits to measured data for use as modelling endpoints in aquatic exposure assessments. The use of the SFO kinetic model resulted in acceptable fits to measured data for all data sets. Analysis was performed at Level I for total systems with results summarised in the table below. No acceptable fits were derived at Level II.
The kinetic evaluation resulted in a geometric mean $DegT_{50}$ of 20.5 days for PHC in total systems as modelling endpoint.

Total system $DegT_{50}$ values for propamocarb hydrochloride according to FOCUS Level I

Water/Sediment system	Total system $DegT_{50}$ (days)
Mill Stream Pond (Study 1)	*20.7* [b)]
Iron Hatch Stream (Study 1)	*16.1* [b)]
OVP (Study 2)a)	20.7
SW (Study 2)a)	20.3
Geometric mean (n=2)	**20.5**

Study 1: KCA 7.2.2.3/01; Study 2: KCA 7.2.2.3/02; [a)] OVP = Oostvaardersplassen; SW = Schoonrewoerdse Wiel; [b)] Values were not considered for geometric mean calculation during dossier update as study is considered as supporting information

Dissipation from water phase:

Dissipation rates from water were derived considering the same set of water/sediment studies. The use of the SFO kinetic model resulted in acceptable fits to measured data for all data sets. Analysis was performed at Level I with results summarised in the table below.
The kinetic evaluation resulted in a geometric mean $DisT_{50}$ of 12.6 days for propamocarb-hydrochloride dissipation from the water as modelling endpoint.

Values of the $DisT_{50}$ from water for PHC according to FOCUS Level I:

Water/Sediment system	Total system $DegT_{50}$ (days)
Mill Stream Pond (Study 1)	*10.2* [b)]
Iron Hatch Stream (Study 1)	*14.8* [b)]
OVP (Study 2)[a)]	15.1
SW (Study 2)[a)]	10.5
Geometric mean (n = 2)	**12.6**

Study 1: KCA 7.2.2.3/01; Study 2: KCA 7.2.2.3/02; [a)] OVP = Oostvaardersplassen; SW = Schoonrewoerdse Wiel; [b)] Values were not considered for geometric mean calculation during dossier update as study is considered as supporting information

Dissipation from sediment phase:

Dissipation rates from sediment were derived considering the same set of water/sediment studies. The use of the SFO kinetic model resulted in acceptable fits to measured data for all data sets. Analysis was performed at Level I wich results are summarised in the table below.
The kinetic evaluation resulted in a geometric mean $DisT_{50}$ of 22.2 days for propamocarb-hydrochloride (PHC) dissipation from the sediment as modelling endpoint.

Values of the $DisT_{50}$ from sediment for PHC according to FOCUS Level I

Water/Sediment system	Total system $DegT_{50}$ (days)
Mill Stream Pond (Study 1)	*20.6* [b)]
Iron Hatch Stream (Study 1)	*22.1* [b)]
OVP (Study 2)[a)]	17.6
SW (Study 2)[a)]	28.0
Geometric mean (n = 2)	**22.2**

Study 1: KCA 7.2.2.3/01; Study 2: KCA 7.2.2.3/02; [a)] OVP = Oostvaardersplassen; SW = Schoonrewoerdse Wiel; [b)] Values were not considered for geometric mean calculation during dossier update as study is considered as supporting information

I. Material and Methods

The kinetic evaluation was based on data of two water/sediment studies (KCA 7.2.2.3/01 and KCA 7.2.2.3/02) conducted with 1-*N*-propyl-^{14}C-labeled propamocarb-hydrochloride in four different water/sediment systems (silty loam sediment Mill Stream Pond, sand sediment Iron Hatch, sediments Oostvaardersplassen, OVP, and Schoonrewoerdse Wiel, SW) and their associated water at 20°C in the dark for a maximum of 105 days.

Data pre-processing
Generally, replicates were taken into account separately. The data were checked for consistency and clear outliers. Data for non-extractable residues (NER) and CO_2 were not fitted within the evaluation (open system).

For the residues in the water the following procedure was applied:
- For data processing of day zero samples, radioactivity assigned to metabolites, non-extractable residues (NER) and CO_2 was added to the parent compound and thus metabolite concentrations were set to 0 %. Parent compound was attributed to the water phase only thus resulting in a value of zero for the sediment phase, since the test substance was applied to the water phase.
- Residue values below the limit of detection (LOD = 0.1% of AR) were set to 0.5 times the LOD or NA for the first non-detect at the end of the curve. The curve could be cut at this time point in case of no later detects.

Kinetic models
The inferring of kinetic degradation parameters followed the proposed metabolic pathway as given in Figure11.1.4.3-01.
Following the recommended procedure for determining modelling endpoints [FOCUS, 2006, 2011], all datasets were evaluated using SFO kinetics with free optimisation of parameters, along with FOMC, DFOP and HS kinetics where appropriate.
Each compound was represented by one compartment as the total of measured occurrences in water and sediment with no values associated with a sink compartment. Between compartments transformation reactions were assumed to proceed only one-way. The initial amount of the parent compound was free fitted and the initial amount for metabolites was fixed to a value of zero. All data were weighted equally thus corresponding to an absolute error model.
At least four kinetic models consisting of single first-order (SFO), first-order multiple-compartment (FOMC, Gustafson-Holden), double first-order in parallel (DFOP), and the hockey-stick (HS) model were available, in principle, according to the set of models proposed by FOCUS.
While best-fits should be taken to derive trigger or persistence endpoints SFO should be used to derive modeling input parameters if an acceptable fit can be obtained.
Before a use of bi-phasic kinetic models FOMC, DFOP and HS the following major cases were taken into account:
1. A check whether a degradation or dissipation to 10% of the initial amount M_0 was reached within experimental period, then the estimation of the DT_{50} could be simplified according to the relation $DT_{50} = DT_{90}/(\ln(10)/\ln(2))$. By this method the equivalent SFO-curve meets the bi-phasic curve at the time $DT_{90\ bi\text{-}phasic}$ and consequently the residue values at earlier times are over-predicted.
2. In case a value of 10% for M_0 was not reached within the runtime of the study, however, FOMC should not be used to derive modelling endpoints.
3. In case a value of 10% for M_0 was not reached within the runtime of the study, the DT_{50} could be derived for DFOP and HS models from the slower part of the bi-phasic curve using the relation $DT_{50} = \ln(2)/k_2$.

The kinetic evaluations were performed according to the respective decision flowcharts for the determination modelling endpoints for parent (Level P-1) and metabolites and to result in dissipation kinetics in water and sediment. Evaluations according to Level II were performed, however, did not result in statistically acceptable fits. Anyway, for lower-tier calculations or the comparison with persistence triggers a Level I evaluation of the dissipation is mostly regarded as appropriate.

Statistical evaluation
The identification of the most appropriate kinetic model for the description of experimental data according to FOCUS is mainly based on the three criteria of visual assessment of fits of calculated transformation curves to experimental data, the value of error of Chi-square (χ^2) test and a single-sided significance t-test.
The choice of the appropriate kinetic model was primarily based on visual assessment of the fit and the Chi^2- (χ^2-) error.
Within the current evaluation, single first-order (SFO) kinetics had been tested first, since SFO is being used as the simplest kinetic model almost exclusively in environmental exposure models. In case the SFO fit should not be visually acceptable or in case of a significant exceedance of value for χ^2-error of 15%, bi-phasic models were tested. Finally the model was chosen which was visually acceptable and provided a significantly better fit in terms of the χ^2-error.
The approach avoided the use of over-parameterised models simply and only being chosen on the basis of a marginally better fit. Finally it should be noted that a value of χ^2-error below 15% should only be considered as guidance and not as an absolute cut-off criterion. This is true, in particular, for the modelling of metabolite data with errors for χ^2 being higher, but with fits still representing a reasonable description of their formation and degradation behaviour.

The kinetic evaluations and the statistical calculations were conducted with KinGUI (v2.0) using iteratively re-weighted least-squares (IRLS) optimisation.

II. Results and Discussion

The kinetic evaluation of water-sediment data was performed according to FOCUS Level I to result in degradation kinetics in total systems and in dissipation kinetics in water and sediment. Evaluations according to Level II were performed, however, did not result in statistically acceptable fits.

SFO, FOMC and DFOP kinetics were initially applied to all data sets. However, FOMC and DFOP showed no improvement over SFO kinetics for all data sets.

In case the DFOP kinetic model should have resulted in an improvement, a conservative approach was taken by back-calculation from the slow phase of DFOP kinetic model to derive the corresponding $DegT_{50}$ or $DisT_{50}$.

Degradation in total systems:

For the active substance propamocarb-hydrochloride, values of the $DegT_{50}$ from SFO kinetics of the total systems were summarized detailed in the table below.

Values of the $DegT_{50}$ in total system for propamocarb-hydrochloride according to FOCUS Level I (SFO):

Sediment system	Label position	DT_{50} (days)	Chi^2 (%)	t-test (p)	VA[b)]	Kinetic model
Mill Stream Pond (Study 1)	*1-^{14}C*	*20.7 c)*	*5.9*	*<0.1*	++	*SFO*
Iron Hatch Stream (Study 1)	*1-^{14}C*	*16.1 c)*	*9.6*	*<0.1*	++	*SFO*
OVP (Study 2)[a)]	1-^{14}C	20.7	13.8	<0.1	O	SFO
SW (Study 2)[a)]	1-^{14}C	20.3	8.2	<0.1	+	SFO
Geometric mean		**20.5**				

Study 1: KCA 7.2.2.3/01; Study 2: KCA 7.2.2.3/02
a) OVP = Oostvaardersplassen; SW = Schoonrewoerdse Wiel
b) VA: Visual assessment: + = good, o = acceptable, - = inacceptable
c) Values were not considered for geometric mean calculation during dossier update as study is considered as supporting information

Dissipation from water phase:

For the active substance propamocarb-hydrochloride, values of the $DegT_{50}$ from SFO kinetics the total systems were summarized more detailed in the table below.

Values of the $DisT_{50}$ from water for PHC according to FOCUS Level I (SFO)

Sediment system	Label position	DT_{50} (days)	Chi^2 (%)	t-test (p)	VA[b)]	Kinetic model
Mill Stream Pond (Study 1)	*1-^{14}C*	*10.2 c)*	*7.2*	*<0.1*	+	*SFO*
Iron Hatch Stream (Study 1)	*1-^{14}C*	*14.8 c)*	*10.0*	*<0.1*	++	*SFO*
OVP (Study 2)[a)]	1-^{14}C	15.1	7.3	<0.1	+	SFO
SW (Study 2)[a)]	1-^{14}C	10.5	17.1	<0.1	++	SFO
Geometric mean (n = 2)		**12.6**				

Study 1: KCA 7.2.2.3/01; Study 2: KCA 7.2.2.3/02
a) OVP = Oostvaardersplassen; SW = Schoonrewoerdse Wiel
b) VA: Visual assessment: + = good, o = acceptable, - = inacceptable
c) Values were not considered for geometric mean calculation during dossier update as study is considered as supporting information

Dissipation from sediment:

For the active substance propamocarb-hydrochloride, values of the $DegT_{50}$ from SFO kinetics of the total systems were summarized more detailed in the table below.
Although the fits for the test systems Iron hatch stream and OVP show a large scatter of data with chi^2 above 15 % the visual fits were good showing no systematic deviation and the t-test is statistically significant. Thus, the endpoint for the OVP system is considered to be appropriate for the risk assessment.

Values of the $DisT_{50}$ from sediment for propamocarb-hydrochloride according to FOCUS Level I (SFO):

Sediment system	**Label position**	**DT_{50} (days)**	**Chi^2 (%)**	**t-test (p)**	**VA[b)]**	**Kinetic model**
Mill Stream Pond (Study 1)	*1-^{14}C*	*20.6 [c)]*	*15.2*	*<0.1*	+	*SFO*
Iron Hatch Stream (Study 1)	*1-^{14}C*	*22.1 [c)]*	*18.6*	*<0.1*	+	*SFO*
OVP (Study 2)[a)]	1-^{14}C	17.6	26.6	<0.1	+	SFO
SW (Study 2)[a)]	1-^{14}C	28.0	5.9	<0.1	++	SFO
Geometric mean		**22.2**				

Study 1: KCA 7.2.2.3/01; Study 2: KCA 7.2.2.3/02
a) OVP = Oostvaardersplassen; SW = Schoonrewoerdse Wiel
b) VA: Visual assessment: + = good, o = acceptable, - = inacceptable
c) Values were not considered for geometric mean calculation during dossier update as study is considered as supporting information

Below, the visual fits and statistics for sediment modelling endpoints of the Iron Hatch Stream and OVP are presented. The results demonstrate that FOMC has a slightly higher chi-square. Thus, SFO fit is more appropriate than FOMC and acceptable.

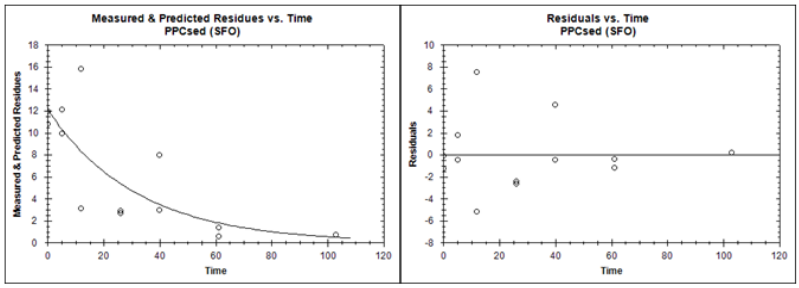
Iron Hatch Stream (Study 1) – Sediment – Modelling:

SFO

5.2.2.2 Dissipation in sediment

Table 25: Iron Hatch Stream, dissipation in sediment: Modelling endpoints and statistical parameters of propamocarb-HCl

Model	DT_{50} [d]	DT_{90} [d]	M_0 [%]	k_1 / α	k_2 / β	tb / g	p k_1 / α	p k_2 / β	Visual fit	χ^2
SFO	**22.1**	73.5	12.10	0.031	---	---	<0.01	---	+	**18.55**
► SFO fit visually good and statistically still acceptable (although Chi² error above 15%)										
► **Conclusion:** use DT50 from SFO										



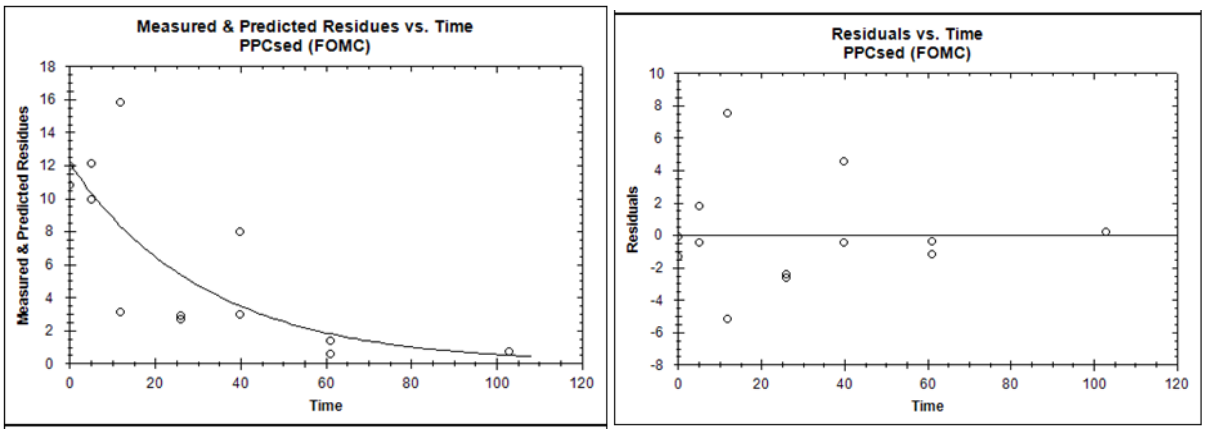
FOMC

```
# ---------------------------------
# Chi2 error estimation
# ---------------------------------
                              PPCsed         All
             Chi2Err% :        20.04       20.04
       Kinetic model :          FOMC

# ---------------------------------
# Parameter estimation
# ---------------------------------

 Degrees of Freedom   : 11
 Parameter                  Estimate     Lower 95% CI     Upper 95% CI       St.Dev       Prob > t
 M(0)  PPCsed         :       12.095            8.509           15.68        1.830
 alpha PPCsed         :     1800.028          527.167         3072.89      649.430
 beta  PPCsed         :    57424.974        57385.090        57464.86       20.349

# ---------------------------------
# DT50 and DT90 values
# ---------------------------------
                              PPCsed
                DT50 :        22.12
                DT90 :         73.5
       Kinetic model :          FOMC
```



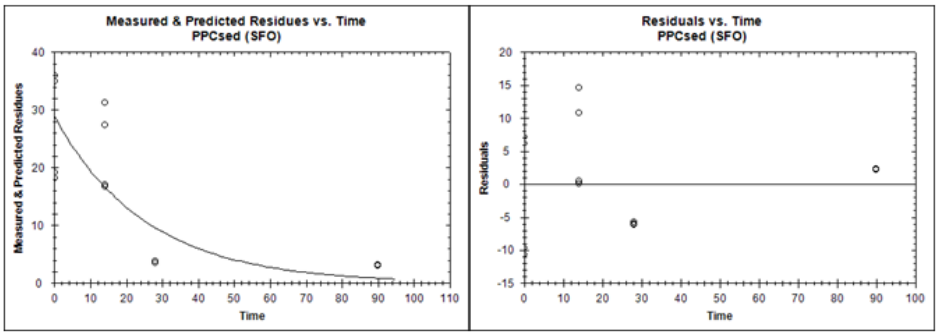
OVP – Sediment – Modelling:

SFO

5.2.3.2 Dissipation in sediment

Table 28: Oostvaardersplassen, dissipation in sediment: Modelling endpoints and statistical parameters of propamocarb-HCl

Model	DT_{50} [d]	DT_{90} [d]	M_0 [%]	k_1 / α	k_2 / β	tb / g	p k_1 / α	p k_2 / β	Visual fit	χ^2
SFO	**17.6**	58.3	28.89	0.039	---	---	<0.01	---	+	**26.56**
► SFO was considered statistically still acceptable (although Chi² error above 15%) and visually good										
► **Conclusion:** use DT50 from SFO										



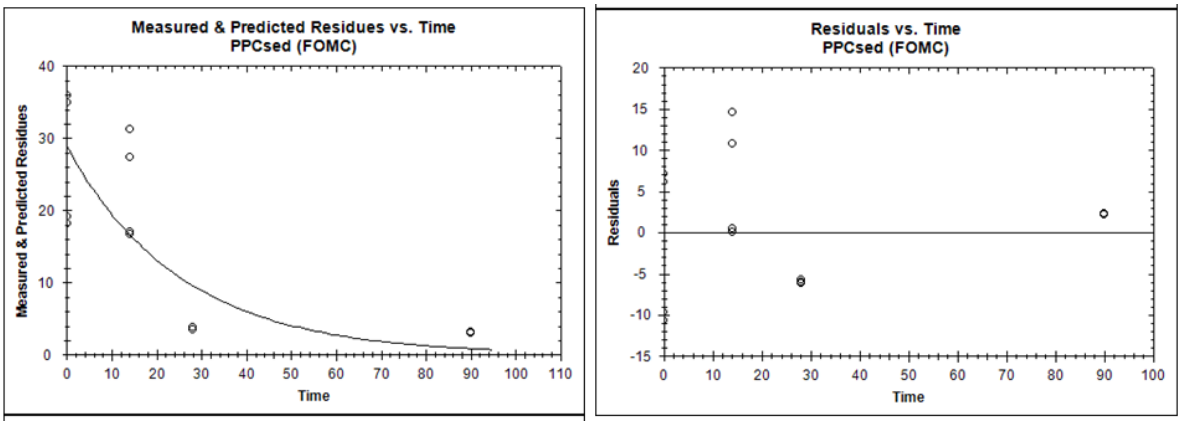
FOMC

```
# ---------------------------------
# Chi2 error estimation
# ---------------------------------
                              PPCsed         All
            Chi2Err% :         33.17       33.17
        Kinetic model :          FOMC

# ---------------------------------
# Parameter estimation
# ---------------------------------

 Degrees of Freedom   : 11
 Parameter                   Estimate     Lower 95% CI     Upper 95% CI       St.Dev       Prob > t
 M(0)   PPCsed         :     2.889e+01        2.086e+01            36.92    4.095e+00
 alpha  PPCsed         :     1.436e+04        4.605e+03         24118.08    4.978e+03
 beta   PPCsed         :     3.638e+05        3.634e+05        364212.43    1.965e+02

# ---------------------------------
# DT50 and DT90 values
# ---------------------------------
                              PPCsed
                DT50 :         17.56
                DT90 :         58.34
        Kinetic model :          FOMC
```



III. Conclusion

Kinetic evaluation of degradation in total systems as modelling endpoint:

For the active substance propamocarb-hydrochloride acceptable to excellent fits to measured data were derived by use of the SFO kinetic model for all data sets to result in a geometric mean value for the $DegT_{50}$ of 20.5 days.

Kinetic evaluation of dissipation from water phase as modelling endpoint:

For the active substance propamocarb-hydrochloride, good to excellent fits to measured data were derived by use of the SFO kinetic model for all data sets to result in a geometric mean value for the $DisT_{50}$ of 12.6 days.
Level II evaluations were performed for all systems but revealed poor results regarding statistical parameter (t-test) and the Fsed test and were therefore excluded.

Kinetic evaluation of dissipation from the sediment as modelling endpoint:

For the active substance propamocarb-hydrochloride, good to excellent fits to measured data were derived by use of the SFO kinetic model for all data sets to result in a geometric mean value for the $DisT_{50}$ of 22.2days.
Level II evaluations were performed for all systems but revealed poor results regarding statistical parameter (t-test) and the Fsed test and were, therefore, excluded.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Irradiated water/sediment study

This is regarded as a new optional data requirement in the EU. The degradation of propamocarb-hydrochloride was well understood under standard conditions of water/sediment testing.

Within the existing water/sediment data submitted, the design of study KCA 7.2.2.3/02 included the influence of mixed light conditions on degradation by irradiation of samples for 8 hours at 300 to 350 Lux followed by a 16 hours dark interval.
However, results on route and rate of degradation were found to be insignificantly different from data of study KCA 7.2.2.3/01 where samples were incubated in the dark only. This finding supported the overall limited potential of propamocarb-hydrochloride to undergo direct or indirect photolytic degradation in aquatic media (KCA 7.2.1.2/01 to KCA 7.2.1.2/03 and KCA 7.2.1.3/01).
Consequently, the conduct of an irradiated water/sediment study would not result in a significantly better understanding of the behaviour of propamocarb-hydrochloride and its residues in the aquatic environment.
A new irradiated water/sediment study was, therefore, not performed or regarded as necessary.

Degradation in the saturated zone

The separate investigations on the degradation in the saturated zone are not regarded as necessary, since the risk assessment for the groundwater demonstrated no significant risk for a contamination of sub-

soils or the saturated zone by the active substance and its metabolites when being applied according to good agricultural practice.

C) Degradation in Soil

C.1) Laboratory studies

To address the route/rate of degradation of propamocarb hydrochloride, a number of studies were provided, as listed below:

- **Aerobic degradation in soil:**

KCA 7.1.1.1/01; Bruehl, R.; Celerio, J.; 1978; M-157704-01-1
KCA 7.1.1.1/02; Bruehl, R.; 1979; M-157706-01-1
KCA 7.1.1.1/03; Bruehl, R.; Celorio, J.; 1980; M-157708-01-1
KCA 7.1.1.1/04; Bruehl, R.; Celorio, J.; 1980; M-157709-01-1
KCA 7.1.1.1/05; Bruehl, R.; Celorio, R.; 1986; M-157783-01-2
KCA 7.1.1.1/06; Fent, G.; Hein, W.; 2001; M-203298-01-1
KCA 7.1.1.1/07; Schnoeder, F.; 2003; M-310828-02-1
KCA 7.1.1.1/08; Iwan, J.; 1979; M-157719-01-1 (regarded as Supplemental information)
KCA 7.1.1.1/09; Iwan, J.; 1980; M-157721-01-1 (regarded as Supplemental information)

- **Anaerobic degradation in soil** :

KCA 7.1.1.2/01; Bruehl, R.; 1979; M-157717-01-1
KCA 7.1.1.2/02; Schnoeder, F.; 2002; M-310969-01-1

These studies are regarded as scientifically valid by ZRMS. Summary reports of these studies are here presented.

C.1.1) Aerobic degradation in soil (laboratory studies)

- One German soil (25°C, moisture at 75% maximum water holding capacity (MWHC)) after application of ^{14}C-labeled propamocarb-hydrochloride (KCA 7.1.1.1/01);
- One US soil (25°C, moisture at 75% MWHC) after application of 1-*N*-propyl-^{14}C-labeled active substance (KCA 7.1.1.1/02);
- Two German soils (15°C, moisture at 75% MWHC) after application of 1-N-propyl-14C-labeled active substance (KCA 7.1.1.1/03);
- One German soil (25°C, moisture at 75% MWHC) following repeated application of of 14C-labeled propamocarb-hydrochloride (KCA 7.1.1.1/04);
- One German soil (25°C, moisture at 40% MWHC) following repeated application of 1-*N*-propyl-^{14}C-labeled active substance (KCA 7.1.1.1/05);
- Four soils under standard conditions (20°C, moisture at 40% MWHC) after application of 1-*N*-propyl-^{14}C-labeled active substance (KCA 7.1.1.1/06)
- Four soils under standard conditions (20°C, moisture at 45% MWHC) after application of 2-*N*-propyl-^{14}C-labeled active substance (KCA 7.1.1.1/07).

Supplemental information **(**studies that do not contribute to the set of data available for determination of the rate of degradation in aerobic soil of the active substance):

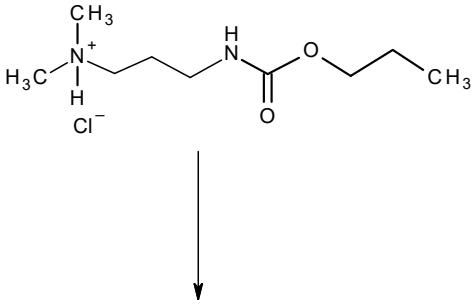
- Investigations in a cultural media with microbial cultures derived from one German soil after application of 1-*N*-propyl-^{14}C-labeled propamocarb hydrochloride and incubation at 25°C (KCA 7.1.1.1/08). Although this study is still regarded as scientifically valid, the reason for its evaluation as supplemental was the fact that the investigations were performed in cultural media with microbial populations derived from soil instead of the use of fully 'native' soil. Design and results were, thus, not comparable to those of a standard aerobic soil study;
- Investigations in one German soil (22° C, moisture at 70% MWHC) following application of 1-*N*-propyl-^{14}C-labeled propamocarb hydrochloride to sterilized and non-sterilized soil samples (KCA 7.1.1.1/09). As for actual guideline studies, the key elements in design and conduct were also reported in study KCA7.1.1.1/09 to still result in scientific validity. However, no samples were taken for analysis at day zero. This fact was accompanied by a low total recovery below 90% AR for first sampling interval (day 1 after application). The design and results were, thus, not comparable to minimum standards in aerobic soil degradation testing.

The investigations under laboratory conditions revealed that:

- Propamocarb-hydrochloride was rapidly degraded in most soils. Degradation was rapid in view of the high range of test concentrations starting from 4.8 mg/kg to 250 mg/kg, equivalent to field application rates of 3.6 kg a.s/ha (KCA 7.1.1.1/06) to 187.5 kg a.s/ha (KCA 7.1.1.1/07). Degradation was slower in US soil Minnesota, explained by a high clay and organic matter content of the soil, thus, enhancing adsorption. Results of adsorption tests support this view with strong adsorption, causing limitation in bioavailability for microbial transformation. Anyway, significant mineralisation to carbon dioxide was also observed in Minnesota soil under the conditions of the soil degradation test;
- Carbon dioxide was the predominant degradation product formed in all soils to range from 22.8% AR (soil Minnesota, day 120, KCA 7.1.1.1/06) to 94.99% (soil Hatzenbuehl 2.3, day 67, KCA 7.1.1.1/03) in maximum;
- Mineralisation was accompanied by the formation of non-extractable residues (NER), to range from 12.4% (California loamy sand soil, day 180, KCA 7.1.1.1/02) to 55.9% of AR in maximum (Minnesota soil, day 14, KCA 7.1.1.1/06). The further transformation of NER was documented by a decline of NER from maximum observed till the end of incubation. For example, decline of NER from maximum was to 11.3% AR for California loamy sand soil by day 360 (KCA 7.1.1.1/02) and to 43.0% for Minnesota soil by day 120 (KCA 7.1.1.1/06);
- The degradation of propamocarb-hydrochloride was accompanied by the formation of several unidentified metabolites. Their transient character was documented by the absence of consistent patterns of formation and decline caused by the occurrence at trace level (i.e. below 3% AR) and, thus, significantly below 5% AR for the predominant number of soils investigated. Consequently, with no major transformation product observed, no compound had been addressed in environmental risk assessment. In addition, polar radioactivity (peak retention time in HPLC of about 2.5 min) was observed at 7.3% AR in maximum (soil B6, sandy loam 'Woolverstone', 10 mg/kg, day 58, study KCA7.1.1.1/07). The components could not be identified by further chromatographic investigations, as demonstrated in the existing amended study report. The polar components were also observed in test soil B6 (Woolverstone) of study KCA 7.1.1.1/07 at the higher test concentration of 250 mg/kg at 5.3% (Day 30), 5.5% (Day 58) and 6.8% (Day 90) to decline to 3.8% by Day 120.

The existing metabolic pathway from the results of the degradation tests in aerobic soils under laboratory conditions is summarized in figure presented below.

Existing route of degradation of propamocarb-hydrochloride in aerobic soils, under laboratorial conditions:



Non-Extractable Residues + Carbon dioxide

Report:	KCA 7.1.1.1/01; Bruehl, R.; Celerio, J.; 1978; M-157704-01-1
Title:	Degradation of SN 66 752 in a loamy sand soil
Report No.:	PA 66752.71/6; A85470
Document No.:	M-157704-01-1
Guideline(s):	None
Guideline deviation(s):	None
GLP/GEP:	**No**

Comment: key elements in design and conduct of the study reported as for actual guideline studies. Study regarded as scientifically valid. The study summary is presented below.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Report:	KCA 7.1.1.1/02; Bruehl, R.; 1979; M-157706-01-1
Title:	Degradation of propamocarb hydrochloride in a californian loamy sand soil
Report No.:	R+S 29/79-PA 66752.71/6; A85471
Document No.:	M-157706-01-1
Guideline(s):	None
Guideline deviation(s):	None
GLP/GEP:	**No**

Comment: key elements in design and conduct of the study reported as for actual guideline studies. Study regarded as scientifically valid. The study summary is presented below.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Report:	KCA 7.1.1.1/03; Bruehl, R.; Celorio, J.; 1980; M-157708-01-1
Title:	Degradation of propamocarb hydrochloride in German standard soils 2.2 and 2.3 at 15 degree
Report No.:	R+S 58/80- PA 66752.71/6; A85472
Document No.:	M-157708-01-1
Guideline(s):	None
Guideline deviation(s):	None
GLP/GEP:	**No**

Comment: key elements in design and conduct reported as for actual guideline studies. Study regarded as scientifically valid. The study summary is presented below.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Report:	KCA 7.1.1.1/04; Bruehl, R.; Celorio, J.; 1980; M-157709-01-1
Title:	Degradation of propamocarb hydrochloride in a loamy sand
Report No.:	R+S 58/80- PA 66752.71/6; A85473
Document No.:	M-157709-01-1
Guideline(s):	None
Guideline deviation(s):	None
GLP/GEP:	**No**

Comment: key elements in design and conduct reported as for actual guideline studies. Study regarded as scientifically valid. The study summary is presented below.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Report:	KCA 7.1.1.1/05; Bruehl, R.; Celorio, R.; 1986; M-157783-01-2
Title:	Degradation of propamocarb hydrochloride in a loamy sand after repeated (twofold) application
Report No.:	UPSR 1/86-PA 66752.71; A85521
Document No.:	M-157783-01-2
Guideline(s):	Guideline No: 162-1
Guideline deviation(s):	None
GLP/GEP:	**No**

Comment: key elements in design and conduct reported as for actual guideline studies. Study regarded as scientifically valid. Results from repeated application were excluded from calculation of degradation rate. The study summary is presented below.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

For the five studies referred above

Executive Summary

In all five studies between eight and eleven 50 g samples (dry weight) of the test soils were thoroughly mixed with radiolabelled propamocarb hydrochloride to give a concentration of 200 mg/kg for maximal 360 days, corresponding to a field application rate of 150 kg a.s/ha, based on 5 cm depth and bulk density of 1.5 g/cm^3. For Study UPSR 1/86-PA 66 752.71 (Document: M-157783-01-2; previously submitted under A85521) an additional 10mg of propamocarb hydrochloride was added to the remaining samples 31 days after the initial treatment, raising the concentration of the applied parent compound to 400 mg/kg.

In all studies propamocarb hydrochloride was metabolised quickly under aerobic conditions at both temperatures of 15°C and 25°C. Lag phases were observed in the mechanics of propamocarb hydrochloride metabolism in two studies, which ranged from 5 to 21 days. The principal products of metabolism were CO_2 and non-extractable soil 'bound' residues. Several unidentified metabolites were detected although none were present in more than 3% of the applied active substance for all studies.

I. Material and Methods

A. Materials

1. Test Material:

Test Material

Propamocarb hydrochloride	A85470	A85471	A85472	A85473	A85521
specific act. (Bq/mg)	0.59 µCu/10µL [1)]	8.55×10^3	1.24×10^4	2.20×10^4	4.3×10^3
radio purity (%)	> 99	> 99	> 97	96	> 99
(mg/kg soil)	200	200	200	200	400

Note [1)] specific radioactivity of the test item not applicable, the concentration of the application solution is given

2. Soil:

Characteristics of the test soils

Parameter	Study number					
	PA 66 752.71/6	R+S 29/79-PA 66 752.71/6	R+S 58/80-PA 66 752.71/6		R+S 71/80-PA 66 752.71/6	UPSR 1/86-PA 66 752.71
Course Sand (0.200 – 2.000 mm) (%)	54.1	33.8	54.1	35.6	42.4	54.1
Fine Sand (0.020 – 0.200 mm) (%)	32.6	54.6	32.6	40.1	43.0	32.6
Silt (0.002 – 0.020 mm) (%)	8.3	7.5	8.3	15.4	7.4	8.3
Clay (< 0.002 mm) (%)	5.0	4.1	5.0	8.9	7.2	5.0
pH	6.6	5.2	6.6	5.7	6.6	6.6
Organic carbon (%)	2.36	1.12	2.36	0.92	2.25	2.36
CEC (mEq/100 g soil)	11.2	5	11.2	6.0	-	11.2
MWHC (g/100 g soil)	36	30	36	31	45.5	36
Texture (USDA)	Loamy sand [1)]	Loamy sand	Loamy sand [1)]	Sandy loam	Loamy sand	Loamy sand [1)]

Note: [1)] Same soil sample used for experimentation; MWHC = Maximum Water Holding Capacity; CEC = Cation Exchange Capacity

B. Study design

1. Experimental conditions: All the samples were transferred to biometer flasks and the water content adjusted to 75% of the maximum water holding capacity. Samples were stored in a climatic chamber in the dark at 25 °C, with the exception of Study R+S 58/80-PA 66 752.71/6 (Document: M-157708-01-1; previously submitted under A85472) in which samples were stored at 15°C. For all studies a 0.1 N KOH solution (10 mL) was used as a means of trapping evolved $^{14}CO_2$ from the system. The trapping solutions were changed three times a week.

2. Sampling: Samples were taken for extraction and chromatographic analysis at Days 0, 7, 14, 30, 60, 90, 180, and 360 for Study PA 66 752.71/6 (Document: M-157704-01-1; previously submitted under A85470) and Study R+S 29/79-PA 66 752.71/6 (Document: M-157706-01-1; previously submitted under A85471). For studies R+S 58/80-PA 66 752.71/6 (Document: M-157708-01-1; previously submitted under A85472) and R+S 71/80-PA 66 752.71/6 (Document: M-157709-01-1; previously submitted under A85473), samples were taken for analysis at Days 0, 1, 4, 7, 13, 20 or 21, 32, and 46. Additional "Neuhofen" samples were extracted after 61, 75, and 103 days, while the remaining "Hatzenbuehl" samples were all extracted and analyzed after day 67 for Study R+S 58/80-PA 66 752.71/6 6 (Document: M-157708-01-1; previously submitted under A85472). For Study UPSR 1/86-

PA 66 752.71 (Document: M-157783-01-2 (previously submitted under A85521) samples were taken for analysis at Days 0, 3, 7, 10, 14, 20, 25, 31, 34, 38, 45, 59, and 87.

3. Analytical procedures: All analytical investigations were performed by TLC, autoradiography and LSC as combustion of radioactive compounds.

II. Results and Discussion

A. Data:

Degradation of propamocarb hydrochloride in soil 2.2 (Neuhofen) under aerobic conditions (M-157704-01-1, PA 66 752.71/6; expressed as % AR)

Compound	DAT							
	0	7	14	30	60	90	180	360
Propamocarb hydrochloride	93.2	83.3	53.0	6.2	2.7	2.2	-	-
Origin	0.2	-	0.2	-	0.2	0.5	-	-
I	-	1.3	0.2	0.2	0.3	0.1	-	-
II	-	-	-	0.3	0.2	0.2	-	-
III	-	-	-	0.4	-	0.3	-	-
Carbon Dioxide	-	3.6	25.1	71.4	80.4	83.6	82.6	88.6
Organic solvent extraction	65.4	56.6	31.1	4.2	2.3	2.0	-	-
Other extractions [1]	27.9	28.1	22.2	2.5	1.1	1.2 [2]	0.1 [3]	0.1 [3]
Total extractable residues	93.3	84.7	53.3	6.7	3.4	2.2	0.1	0.1
Non-extractable residues	4.9	3.1	5.6	9.1	6.6	7.8	-	-
Combustion	1.5	1.9	8.6	11.1	6.4	4.8	13.1	11.9
Total Recovery	99.7	93.3	92.6	98.3	96.8	99.4	95.8	100.6

DAT: days after treatment; I, II and III: unknown metabolites; [1] Unless otherwise indicated, Soxhlet extraction;
[2] NaCl extraction; [3] Water wash; Values given in *italics* were recalculated based on values of the report.

Degradation of propamocarb hydrochloride in soil Californian loamy sand under aerobic conditions (M-157706-01-1, R+S 29/79-PA 66 752.71/6; expressed as %AR)

Compound	DAT							
	0	7	14	30	60	90	180	360
Propamocarb hydrochloride	66.4	79.8	63.1	45.9	11.4	2.8	-	-
Origin	-	0.1	-	-	0.7	0.3	-	-
I	-	0.5	0.1	0.1	0.2	0.8	-	-
II	-	0.2	-	-	-	-	-	-
III	-	-	-	-	0.1	0.9	-	-
Carbon Dioxide	-	0.3	1.7	18.6	66.9	82.2	87.1	88.5
Organic solvent extraction	57.2	51.4	52.7	37.1	10.3	3.6	-	-
Other extractions [1]	9.2	29.1	10.6	9.0	2.2	1.2 [2]	0.2 [3]	0.1 [3]
Total extractable residues	*66.4*	*80.5*	*63.3*	*46.1*	*12.5*	*4.8*	*0.2*	*0.1*
Non-extractable Residues	20.6	7.6	23.2	23.1	9.7	5.1	-	-
Combustion	1.4	0.9	3.2	6.0	7.4	6.7	12.4	11.3
Total Recovery	88.4	89.3	91.4	93.8	96.4	98.7	99.7	99.8

DAT: days after treatment; I, II and III: unknown metabolites;
Values given in *italics* were recalculated based on values of the report.
[1] Unless otherwise indicated, Soxhlet extraction;
[2] NaCl extraction
[3] Water wash

Degradation of propamocarb hydrochloride in soil 2.2 under aerobic conditions at 15 °C (M-157708-01-1, R+S 58/80-PA 66 752.71/6; expressed as % AR):

Compound	DAT										
	0	1	4	7	13	21	32	46	61	75	103
propamocarb hydrochloride	91.72	97.85	89.67	86.32	77.96	58.56	5.35	4.41	5.12	-	-
Origin	0.01	0.08	-	0.01	-	-	0.30	0.32	0.28		
Unknown I	0.45	0.02	-	-	0.86	0.30	0.11	0.10	0.06	-	-
Unknown II	2.77	0.23	0.04	0.55	-	0.13	1.48	0.37	0.49	-	-
Unknown III	0.14	0.06	0.05	0.02	-	-	0.77	-	-	-	-
Other Unknowns	0.19	0.63	0.65	1.34	0.27	0.27	1.57	2.21	0.99	-	-
Carbon Dioxide	-	0.13	1.25	2.33	6.99	23.04	57.00	54.74	63.08	63.23	58.17
Organic solvent extraction	79.67	78.59	74.31	71.92	64.76	43.21	6.13	4.87	4.51	3.10	2.97
NaCl extraction	15.60	20.21	16.11	16.35	14.34	16.05	3.45	2.53	2.44	2.32	2.66
Total extractable residues	*95.27*	*98.80*	*90.42*	*88.27*	*79.10*	*59.26*	*9.58*	*7.40*	*6.95*	*5.42*	5.63
Non-extractable Residues	0.9	1.21	1.65	1.81	2.44	4.81	12.08	8.03	8.7	6.17	11.88
Combustion	0.43	0.50	0.76	1.41	1.53	2.81	20.81	12.32	13.69	15.84	14.90
Total Recovery	96.60	100.64	94.08	93.82	90.06	89.92	99.47	82.49	92.42	90.66	90.58

DAT: days after treatment
Values given in *italics* were recalculated based on values of the report.

Degradation of propamocarb hydrochloride in soil 2.3 under aerobic conditions at 15° C (M-157708-01-1, R+S 58/80-PA 66 752.71/6; expressed as % AR):

Compound	DAT								
	0	1	4	7	13	20	32	46	67*
propamocarb hydrochloride	83.33	90.06	84.70	85.98	78.30	74.62	20.33	4.41	5.05
Origin	0.10	-	-	0.01	-	-	2.28	0.79	0.17
Unknown I	1.40	0.15	0.08	1.49	0.96	0.24	0.56	0.10	-
Unknown II	0.01	-	0.11	-	-	-	1.26	-	-
Other Unknowns	3.69	1.82	1.89	0.52	0.16	0.34	0.97	2.64	0.60
Carbon Dioxide	-	0.08	0.48	1.67	5.15	140.6	62.04	92.37	94.99
Organic solvent extraction	50.68	52.60	50.03	49.85	46.97	40.99	11.23	4.58	3.52
NaCl extraction	37.85	39.53	36.79	38.16	32.44	34.21	14.16	3.35	2.34
Total extractable residues	*88.53*	*92.13*	*86.82*	*88.01*	*79.41*	*75.20*	*25.39*	*7.93*	*5.86*
Non-extractable Residues	5.75	4.11	3.78	4.13	4.71	4.46	11.40	6.35	6.83
Combustion	0.89	0.69	0.97	1.37	1.81	1.91	15.30	12.54	13.53
Total Recovery	95.17	97.01	92.05	95.18	91.08	95.63	114.13	119.19	121.21

DAT: days after treatment
* Average results from 3 samples.
Values given in *italics* were recalculated based on values of the report.

Degradation of propamocarb hydrochloride in soil loamy sand under aerobic conditions (M-157709-01-1, R+S 71/80-PA 66 752.71/6; expressed as % AR):

Compound	DAT							
	0	1	4	7	13	20	32	46
propamocarb hydrochloride	84.38	81.99	76.33	67.12	20.46	1.03	4.01	0.15
Origin	0.16	0.14	0.09	0.15	0.49	0.75	0.29	0.28
I	-	0.05	-	0.09	0.20	0.16	0.02	0.13
II	-	0.03	-	0.11	0.37	0.03	0.04	0.15
III	0.41	0.50	0.97	1.40	0.84	0.06	0.02	0.13
IV	0.61	0.41	0.45	0.78	0.35	0.40	0.28	-
V	0.91	1.10	0.89	0.79	0.68	0.36	0.30	0.01
VI	0.80	0.86	0.47	0.46	0.30	0.05	0.15	-
Other Unknowns	0.53	0.92	1.21	1.46	1.70	1.60	1.01	1.57
Carbon Dioxide	-	0.64	4.11	11.48	46.44	70.66	70.35	79.99
Organic solvent extraction	62.70	63.61	57.95	51.23	16.86	2.70	3.79	1.57
NaCl extraction	25.16	22.38	22.46	21.15	8.49	1.73	2.33	0.91
Total extractable residues	*87.86*	*85.99*	*80.41*	*72.38*	*25.35*	*4.43*	*6.12*	*2.48*
Non-extractable Residues	11.56	10.66	14.51	18.88	23.40	21.48	16.74	14.55
Total Recovery	99.42	97.29	99.03	102.74	95.19	96.57	93.21	97.02

DAT: days after treatment
I to VI: unknown metabolites
Values given in *italics* were recalculated based on values of the report.

Degradation of propamocarb hydrochloride in soil loamy sand under aerobic conditions after twofold application (M-157783-01-2, UPSR 1/86-PA 66 752.71 expressed as % AR):

Compound	Appl.	DAT												
		0	3	7	10	14	20	25	31	34	38	45	59	87
propamocarb hydrochloride	1	90.9	90.7	76.1	70.2	44.6	22.4	11.7	6.4					
	2									46.7	39.6	19.4	2.6	1.7
Carbon Dioxide	1	-	0.7	3.6	8.8	22.9	39.2	48.5	54.7					
	2									29.5	35.2	44.7	61.8	66.0
Organic solvent extraction	1	59.0	62.3	55.6	49.7	30.4	15.2	7.7	4.4					
	2									35.1	29.4	14.2	2.3	1.0
NaCl extraction	1	31.9	29.6	21.6	22.1	15.7	8.2	4.5	3.3					
	2									12.7	11.2	6.2	1.7	1.0
Total extractable residues	1	90.9	91.9	77.2	71.8	46.1	23.4	12.2	7.7					
	2									47.8	40.6	20.4	4.0	2.0
Non-extractable Residues	1	4.4	1.0	1.8	3.0	4.9	6.0	5.8	6.2					
	2									4.2	4.6	5.7	7.5	5.0
Total Recovery	1	95.3	97.2	89.9	90.9	83.5	77.1	74.1	76.0					
	2					14				89.3	88.2	79.4	77.9	76.2

DAT: days after treatment
Values given in *italics* were recalculated based on values of the report.

In the study PA 66 752.71/6, approximately 80 % of the propamocarb hydrochloride (PHC) had been mineralised after two months. Carbon dioxide reached a maximum of 88.6 % of the applied radioactivity (AR). Bound residues reached a maximum of 13.1% at Day 180. Three metabolites were detected in very low concentrations (< 2% of AR).

In study R+S 29/79-PA 66 752.71/6, more than 80% of the PHC had been mineralised to $^{14}CO_2$ after 90 days. Carbon dioxide reached a maximum of 88.5% of the applied radioactivity. Bound residues reached a maximum of 12.4% at Day 180 and then decreased to 11.3% by Day 360. Three metabolites were detected in very low concentrations (<1% of AR).

In study R+S 58/80-PA 66 752.71/6, PHC was rapidly degraded after an initial lag phase of approximately 3 weeks in German standard soil 2.2 (Neuhofen, loamy sand) and 2.3 (Hatzenbuehl, sandy loam). After 61 and 67 days greater than 63% and 94% of the PHC in the German standard soil 2.2 (Neuhofen, loamy sand) and 2.3 (Hatzenbuehl, sandy loam) respectively had been mineralized to $^{14}CO_2$. Bound residues in both soils reached a maximum of between 15.30 to 20.81% at Day 32 and then decreased to 13.53 to 14.90% by the last sampling day. Three metabolites were detected in very low concentrations (< 3% of applied) and other unkowns in minor concentrations (3.69% of AR).

In study R+S 71/80-PA 66 752.71/6, PHC was rapidly degraded under aerobic conditions. After 46 days greater than 75% of the PHC had been mineralized to $^{14}CO_2$. Bound residues reached a maximum of 23.4% at Day 13 and decreased thereafter to 14.55% by Day 46. Three metabolites were detected in very low concentrations (< 2% of AR).

In study UPSR 1/86-PA 66 752.71, PHC was applied twice, under aerobic conditions. After both applications the test substance was rapidly degraded, however, after the first application an initial lag phase of approximately 5 days occurred. After the second application of radiolabelled PHC, no lag phase was observed. Thus once the mineralisation process was activated by the initial soil treatment no degradation lag phase was seen after an additional treatment. This effect is typical of soil microorganism mediated degradation. No degradation products other than $^{14}CO_2$ were detected in appreciable amounts (< 2% of AR) and bound residues reach a maximum of 7.5 % at Day 59 but had declined to 5.0% of applied by Day 87.

III. Conclusion

In all five studies, propamocarb hydrochloride was readily mineralised. Soil metabolites are of transient nature and occurred only in minor concentrations (all well below 5% of applied).

RMS´s opinion:

Reliability of the five studies: score 1 of the scoring system of Klimisch *et al*.(1997).

Report:	KCA 7.1.1.1/06; Fent, G.; Hein, W.; 2001; M-203298-01-1
Title:	Degradation and metabolism of propamocarb-HCL (AE B066752) in four different soils
Report No.:	AGR 20; C012748
Document No.:	M-203298-01-1
Guideline(s):	SETAC-Europe, Procedures for Assessing the Environmental Fate and Ecotoxicity of Pesticides, Part 1, Section 1.1 (1995).
Guideline deviation(s):	None
GLP/GEP:	**Yes**

Comment: key elements in design and conduct reported as for actual guideline studies. Study regarded as scientifically valid.

Executive Summary

The route of degradation of propamocarb hydrochloride was investigated in a laboratory study at 20° C ± 2 °C using four different soils under aerobic conditions at 40 % of their maximum water holding capacity in the dark for maximal 120 days.

Propamocarb hydrochloride was applied at a rate of 0.48 mg/100 g dry soil (corresponding to a field application rate of 3.6 kg a.s/ha) and degraded readily under aerobic experimental conditions in the Sarotti, Abington, and Borstel test soils, and less readily in Minnesota soil. Carbon dioxide was the principal degradation product formed in all soils except the Minnesota test soil, reaching a maximum range of between 58.2 % and 66.2 %. In the Minnesota soil the maximum $^{14}CO_2$ determined reached 22.8 % of applied radioactivity. NER bound to soil also accounted for a significant portion of the applied radioactivity. In the Sarotti, Abington, and Borstel soils NER reached a maximum of 21.4 %, 20.0 %, and 23.8 % of applied radioactivity. However, for the Minnesota soil large amounts of applied radioactivity became associated with organic fractions bound to the soil, as NER accounted for between 42.7 % and 55.9 % of the applied radioactivity for the study duration. Under experimental conditions the Minnesota soil was atypical, when compared to the other test soils. The high clay and organic matter content of the soil enhances adsorption of the test substance and the limited bioavailability of the test material is likely to reduce overall mineralisation in the form of $^{14}CO_2$ amounts. Up to eight unidentified polar metabolites were observed during the study, however, the sum of the unknown metabolites never exceeded 8.1% of the applied radioactivity and no single component exceeded 3.3% AR at any sampling interval in any soil.

I. Material and Methods

A. Materials

1. Test Material: Common name: propamocarb hydrochloride
Chemical name: propyl 3-(dimethylamino) propylcarbamate hydrochloride
Radiolabelled purity: >99.0 %, lot # IS1795-21, specific activity 8.76 MBq/mg
Non-radiolabelled purity: 76.6 %, lot #934578.

2. Soil:

Characteristics of the test soils:

Soil number	**I**	**II**	**III**	**IV**
Name	Minnesota	Sarotti	Abington	Borstel
Origin	USA	Germany	England	Germany
Sampling date	Oct. 17, 1999	Oct. 07, 1999	Oct. 07, 1999	Oct. 04, 1999
Sampling depth	0-6 inches (0 – 15 cm)	0-20 cm	5-20 cm	0-20 cm
Soil texture[1),2)]	Clay loam	Loamy silt	Loamy sand	Silty sand
Sand (%)[2)] (63 µm - 2 mm)	25.3	12.1	61.6	77.5
Silt (%)[2)] (2 µm – 63 µm)	42.5	70.2	22.5	18.5
Clay (%)[2)] (< 2 µm)	32.2	17.7	16.4	4.0
pH ($CaCl_2$) [3)]	5.803	7.383	7.43	5.813
Organic substance [2)]				
org. Substance (%)	5.42	2.24	3.20	1.79
org. Carbon (%)	3.15	1.30	1.86	1.04
Cation exchange capacity [2)] (meq/100 g)	24	13	18	8
Nitrogen content [2)] (mg/100 g)	290	110	160	80
Lime content [2)] (in % $CaCO_3$)	< 0.1	0.9	10.4	<0.1
Maximum water holding capacity (g H_2O/100 g dry soil)	56.92	40.57	49.43	30.53
Internal SLFA soil number	90	91	92	93

Note: 1) According to DIN 19682
2) Determined by Lufa Speyer, Obere Langgasse 40, 67436 Speyer (report dated Feb. 17, 2000)
3) Determined by the Test Facility

B. Study design

1. Experimental conditions: The test system was connected with soda lime traps and oil-wetted glass wool for the adsorption of volatile organics and $^{14}CO_2$. Soil samples were treated with propamocarb hydrochloride at an application rate of 0.48 mg/100 g dry soil, corresponding to a rate equivalent to 3.6 kg a.s/ha (based on a soil depth of 5 cm and bulk density of 1.5 g/cm^3). The temperature was held at 20°C ± 2°C, in dark conditions, and the moisture content of the soils was set to 40% of the maximum water holding capacity (MWHC) giving soil moisture content of 22.8 g water/100g dry soil for Minnesota, 16.2 g water/100g dry weight for Sarotti, 19.8 g water/100 g dry weight for Abington, 12.2 g water/100g dry weight for Borstel. Gas exchange was kept aerobic. Microbial biomass was tested in the soils simultaneously to the application and at the end of the incubation period according to the Anderson and Domsch method.[2]

2. Sampling: Sampling of the soil test systems were undertaken at intervals of 0 h (immediately after application), 1, 2, 3, 7, 14, 28, 42, 59, 90, and 120 days. At each sampling point duplicate sub-samples were removed for analysis (i.e. extraction and chromatography). At each sampling date the units were flushed with air in order to transfer all organic volatiles into the trapping system.

3. Analytical procedures: Each soil sample was exhaustively extracted 3 times with 100 mL acetonitrile/water (4:1 v/v; pH < 4 with formic acid). However, if non-extractable radioactivity was greater than 10% of the applied then further extraction was undertaken using acetonitrile/water (4:1 v/v). Radioactivity of extracts was determined by Liquid Scintillation Counting (LSC). Soil samples that were not directly analysed were stored at ≤ -18 °C.

[2] Anderson, J. P. E. and Domsch, K. H. (1978): A physiological method for the quantitative measurement of microbial biomass in soils. Soil. Biol. Biochem., 10, 215-221.

The soda lime trap was dissolved in 70mL of 6 M HCl to release the $^{14}CO_2$, which was then transferred to LSC vials by a stream of CO_2 free air. The vials were then directly measured by LSC. Volatiles were extracted from the quartz wool with 40 mL acetone. Two 10 mL aliquots of the extract were subsequently measured by LSC.

Investigation of non-extractable residues (NER) was conducted on extracted soil samples. After day 59 soil residues were dried directly after extraction, however, previously soil residues were frozen at ≤ -18 C and the soils were dried after thawing. The soil residue was then homogenised in a mill and 2 - 4 soil aliquots were combusted, which was followed by radioactivity measurements by LSC.

The identification and determination of radiochemical purity of ^{14}C-propamocarb hydrochloride was done using High Performance Liquid Chromatography (HPLC). However, HPLC proved to be unsuitable for the determination of the identity and quantity of the propamocarb hydrochloride in the soil extracts. Therefore, Thin Layer Chromatography (TLC) was utilised instead to determine the distribution of the radioactivity in the soil extracts.

II. Results and Discussion

A. Data:

Biomass in test soils at the beginning and the end of experimental incubation. expressed as mg C/kg

Soil	Microbial carbon before incubation		Microbial carbon Day 120	
	Repetition a	Repetition b	Repetition a	Repetition b
Minnesota	375.23	371.54	270.64	314.88
Sarotti	642.91	632.90	531.84	494.07
Abington	540.56	545.90	387.78	404.47
Borstel	219.83	219.45	146.95	158.61

Distribution and material balance of radioactivity in the test soils during the 120-day incubation period

Sampling time (d)	Percent of total applied radioactivity						
	$^{14}CO_2$	Quartz wool	Extracted radioactivity			NER	Material Balance
			1st extract	2nd extract	Total		
Minnesota							
0a	-	-	29.1	25.8	54.9	50.2	105.1
0b	-	-	28.0	20.9	48.9	50.0	98.9
1	0.1	0.0	27.5	23.6	51.1	49.6	100.8
2	0.2	0.0	26.4	24.5	50.9	50.6	101.7
3	0.2	0.0	27.5	23.2	50.7	49.2	100.1
7	0.5	0.0	26.1	26.1	52.2	50.7	103.4
14	1.3	0.0	27.0	23.4	50.4	55.9	107.6
28	3.5	<0.1	24.3	27.1	51.4	43.8	98.7
42	9.4	<0.1	23.3	20.0	43.3	52.1	104.8
59	14.0	<0.1	18.5	20.3	38.8	42.7	95.5
90	11.72	<0.1	15.4	18.0	33.4	46.2	91.33
120	22.8	<0.1	16.1	13.8	29.9	43.0	95.7

Sampling time (d)	Percent of total applied radioactivity						
	$^{14}CO_2$	Quartz wool	Extracted radioactivity			NER	Material Balance
			1st extract	2nd extract	Total		
Sarotti							
0a	-	-	66.5	24.0	90.5	5.6	96.1
0b	-	-	67.0	31.8	98.8	2.5	101.3
1	0.2	0.0	61.7	27.7	89.4	6.7	96.3
2	0.6	0.0	59.9	23.5	83.4	6.0	90.0
3	1.3	0.1	63.3	18.8	82.1	5.8	89.3
7	5.2	<0.1	57.2	22.2	79.4	10.0	94.6
14	15.8	<0.1	35.0	16.7	51.7	14.4	81.9
28	41.1	<0.1	8.0	5.5	13.5	21.4	76.0
42	61.6	<0.1	3.5	3.5	7.0	20.2	88.8
59	62.2	<0.1	2.9	2.8	5.7	18.6	86.5
90	52.52	<0.1	2.7	2.5	5.2	18.2	75.93
120	66.2	<0.1	2.4	2.1	4.5	16.8	87.5
Abington							
0a	-	-	75.0	20.3	95.3	2.3	97.6
0b	-	-	77.4	21.2	98.6	1.5	100.0
1	0.1	0.0	67.9	21.7	89.6	2.4	92.1
2	0.7	0.0	68.7	27.5	96.2	7.7	104.6
3	1.2	0.0	72.1	19.2	91.3	8.8	100.1
7	5.9	<0.1	60.9	17.3	78.2	7.1	91.2
14	21.0	<0.1	36.3	12.1	48.4	15.1	84.5
28	46.6	0.0	5.7	4.3	10.0	20.0	76.6
42	57.8	<0.1	3.1	3.1	6.2	18.7	82.7
59	60.5	0.0	2.5	2.9	5.4	19.0	84.9
90	36.92	0.0	2.4	2.4	4.8	19.3	61.03
120	64.7	0.0	2.0	2.0	4.0	16.7	85.4
Borstel							
0a	-	-	95.3	-	95.3	6.3	101.6
0b	-	-	93.9	-	93.9	5.9	99.8
1	0.3	0.0	87.8	9.5	97.3	0.5	98.1
2	0.4	0.0	89.2	9.9	99.1	1.2	100.7
3	1.0	0.0	89.9	9.8	99.7	1.0	101.7
7	2.2	<0.1	88.1	10.6	98.7	1.9	102.8
14	5.4	0.1	78.7	11.7	90.4	3.4	99.2
28	10.7	<0.1	55.1	13.2	68.3	20.0	99.0
42	39.3	<0.1	12.5	8.0	20.5	23.8	83.6
59	44.1	<0.1	18.3	10.0	28.3	15.1	87.5
90	42.52	<0.1	6.5	5.5	12.0	17.8	72.33
120	58.2	0.0	7.2	4.8	12.0	16.3	86.5

Note: - = Not determined

1) Applied radioactivity was 54.1196 kBq,
2) Balance gap owing to a malfunction of the $^{14}CO_2$ trapping system
3) Value not used for averaged recovery calculation for each test soil owing to the balance gap

Summary of the characterisation of radioactivity extracted from the test soils

Sampling date (d)	(% of total applied radioactivity)					
	propamocarb hydrochloride			Sum of unknown metabolites		
	1st extract	2nd extract	Total	1st extract	2nd extract	Total
Minnesota						
0a	27.8	24.4	52.2	1.3	1.4	2.7
0b	26.7	19.9	46.6	1.3	1.0	2.3
1	26.3	22.3	48.6	1.2	1.4	2.6
2	25.5	23.2	48.7	1.0	1.4	2.4
3	26.2	21.9	48.1	1.3	1.3	2.6
7	24.9	24.8	49.7	1.2	1.3	2.5
14	25.6	22.0	47.6	1.4	1.4	2.8
28	22.9	25.6	48.5	1.5	1.5	3.0
42	21.8	18.9	40.7	1.5	1.1	2.6
59	16.9	19.0	35.9	1.6	1.3	2.9
90	13.8	16.6	30.4	1.6	1.4	3.0
120	14.4	12.7	27.1	1.7	1.1	2.8
Sarotti						
0a	63.6	22.8	86.4	2.9	1.2	4.1
0b	64.3	30.2	94.5	2.8	1.6	4.4
1	58.2	26.2	84.4	3.5	1.5	5.0
2	55.9	22.3	78.2	4.0	1.2	5.2
3	58.4	17.9	76.3	4.9	0.9	5.8
7	50.3	21.3	71.6	6.9	1.2	8.1
14	28.9	14.7	46.6	6.1	2.0	8.1
28	3.8	4.9	8.7	4.2	0.6	4.8
42	0.8	1.7	2.5	0.7	1.8	2.5
59	0.3	1.3	1.6	2.7	1.5	4.2
90	0.0	0.9	0.9	2.7	1.6	4.3
120	0.2	0.9	1.1	2.1	1.2	3.3
Abington						
0a	72.3	19.3	91.6	2.8	1.0	3.8
0b	74.2	20.3	94.5	3.2	0.9	4.1
1	64.5	20.8	85.3	3.5	0.9	4.4
2	64.5	26.0	90.5	4.2	1.5	5.7
3	66.9	21.7	88.6	5.2	1.0	6.2
7	54.6	16.2	70.8	6.3	1.0	7.3
14	31.2	11.0	42.2	5.2	1.1	6.3
28	2.5	3.9	6.4	3.1	0.4	3.5
42	0.8	2.3	3.1	2.4	0.8	3.2
59	0.3	1.9	2.2	2.2	0.7	2.9
90	0.3	1.5	1.8	2.1	0.9	3.0
120	0.2	1.4	1.6	1.8	0.6	2.4
Borstel						
0a	91.5	-	91.5	3.9	-	3.9
0b	89.8	-	89.8	3.9	-	3.9
1	84.0	8.7	92.7	3.9	0.8	4.7
2	85.2	9.1	94.3	4.0	0.8	4.8
3	86.3	9.0	95.3	3.6	0.8	4.4
7	84.3	9.7	94.0	3.8	0.8	4.6
14	72.8	10.7	83.5	5.9	0.9	6.8
28	51.9	12.0	63.9	3.2	1.3	4.5
42	9.8	6.5	16.3	2.7	1.5	4.2
59	14.6	8.8	23.4	3.7	1.2	4.9
90	3.9	4.4	8.3	2.6	1.2	3.8
120	5.0	3.6	8.6	2.2	1.2	3.4

Distribution of the unknown metabolites observed in the Sarotti soil investigated at 20°C: up to eight unidentified polar metabolites were observed, however, the sum of the unknown metabolites never exceeded 8.1% of the applied radioactivity and each single component never exceeded 5% (see tables below, directly copied from original study report).

Table 08: **Characterization of radioactivity extracted with the 1st extraction in the Sarotti soil**

Sampling Date	A.I.[1)]	Unknown Metabolites relative R_f –value / % of total applied radioactivity[2)]			
0a	63.6	2.55/0.7	0.56/1.1	0.03/1.1	
0b	64.3	2.59/1.0	0.57/0.9	0.03/0.8	
1	58.2	2.99/1.1	0.60/1.4	0.38/0.6	0.05/0.4
2	55.9	2.60/1.0	0.56/1.7	0.36/0.8	0.07/0.5
3	58.4	2.62/0.9	0.58/2.4	0.40/1.1	0.09/0.5
7	50.3	2.93/1.0	0.59/3.3	0.42/2.1	0.09/0.6
14	28.9	4.13/0.6	0.71/1.5	0.29/4.0	
28	3.8	3.76/0.2	0.69/1.0	0.42/1.4	0.15/1.5
42	0.8	0.53/0.2	0.10/2.5		
59	0.3	0.20/0.2	0.00/2.4		
90	0.0	0.00/2.7			
120	0.2	0.32/0.1	0.00/2.0		

[1)] Propamocarb-hydrochloride % of total applied radioactivity
[2)] Applied radioactivity was 54.1196 kBq equivalent to 0.49 mg/100 g ^{14}C -propamocarb-hydrochloride

Table 09: **Characterization of radioactivity extracted with the 2nd extraction (Soxhlet) in the Sarotti soil**

Sampling Date	A.I.[1)]	Unknown Metabolites relative R_f –value / % of total applied radioactivity							
0a	22.8	1.73/0.1	0.74/0.2	0.37/0.7	0.03/0.1				
0b	30.2	1.74/0.3	0.36/1.1	0.11/0.1	0.04/0.1				
1	26.2	2.07/0.1	0.42/1.0	0.23/0.1	0.16/0.3	0.01/0.1			
2	22.3	0.82/0.1	0.42/0.8	0.23/0.2	0.15/0.1	0.02/0.1			
3	17.9	0.34/0.7	0.17/0.1	0.01/0.1					
7	21.3	0.36/0.8	0.17/0.3	0.01/0.2					
14	14.7	1.64/0.1	1.62/0.1	1.57/<0.1	0.39/0.8	0.22/0.4	0.15/0.2	0.07/0.2	0.00/0.3
28	4.9	0.42/0.3	0.23/0.1	0.16/0.1	0.08/<0.1	0.00/0.1			
42	1.7	0.48/0.4	0.19/0.7	0.08/0.7					
59	1.3	0.45/0.4	0.11/0.4	0.03/0.7					
90	0.9	0.43/0.4	0.10/0.5	0.01/0.7					
120	0.9	0.12/0.4	0.03/0.8						

[1)] Propamocarb-hydrochloride % of total applied radioactivity
[2)] Applied radioactivity was 54.1196 kBq equivalent to 0.49 mg/100 g ^{14}C -propamocarb-hydrochloride

Table 10: **Summarized results characterization of the extracted radioactivity in the Sarotti soil**

Sampling Date	Propamocarb-hydrochloride			Sum of unknown Metabolites		
	1st Extract	2nd Extract	Total	1st Extract	2nd Extract	Total
	% of total radioactivity applied[1)]					
0a	63.6	22.8	86.4	2.9	1.2	4.1
0b	64.3	30.2	94.5	2.8	1.6	4.4
1	58.2	26.2	84.4	3.5	1.5	5.0
2	55.9	22.3	78.2	4.0	1.2	5.2
3	58.4	17.9	76.3	4.9	0.9	5.8
7	50.3	21.3	71.6	6.9	1.2	8.1
14	28.9	14.7	43.6	6.1	2.0	8.1
28	3.8	4.9	8.7	4.2	0.6	4.8
42	0.8	1.7	2.5	0.7	1.8	2.5
59	0.3	1.3	1.6	2.7	1.5	4.2
90	0.0	0.9	0.9	2.7	1.6	4.3
120	0.2	0.9	1.1	2.1	1.2	3.3

[1)] Applied radioactivity was 54.1196 kBq equivalent to 0.49 mg/100 g ^{14}C-propamocarb-hydrochloride

B. Mass balance: Microbial biomass decreased under the test conditions, possibly owing to the lack of nutrient supply. However, the results of the test show that propamocarb hydrochloride showed increased metabolism in the Borstel soil having a lower content of microbial biomass than the Minnesota soil, which had higher microbial biomass content.

Mean mass balance of applied radioactivity in duplicate samples extracted from the test soils ranged from 101.1 % (Minnesota soil), 89.8 % (Sarotti soil), 90.9 % (Abington soil), and 96.4 % (Borstel soil).

C. Bound and extractable residues: The amount of radioactivity extractable from the soil decreased in all test soils. For the Minnesota, Sarotti, Abington, and Borstel the percent recovery decrease from Day 0 to Day 120 ranged from 54.9% to 29.9%, 98.8% to 4.5%, 98.6% to 4.0%, and 95.3% to 12.0%, respectively. The formation of NER increased in all test soils apart from the Minnesota soil where NER remained between 42.7% and 55.9% of the applied radioactivity for the study duration. For the Sarotti soil NER increased from 2.5% at Day 0 to 21.4% on Day 28. For the Abington soil NER increased from 1.5% at Day 0 to 20.0% on Day 28. Finally, for the Borstel soil the NER increased from 0.5% at Day 1 to 23.8% at Day 42. Minnesota soil residues from the sampling dates 7, 59, and 120 days after application were subjected to an additional organic matter fractionation. More than 50% of the NER was located in the fulvic acid fraction. After 7 days 37.5% of the radioactivity applied was determined in the fulvic acid fraction and 120 days after treatment this amount decreased to 25.8%. The results of the organic matter fractionation are given in Table 11.1.4.3-26. Minnesota test soil differs from the other soils in that its average day-0 NER value was 50.1% of the applied radioactivity, whereas average day-0 NER values for the other soils ranged from 1.9 - 6 % of the applied radioactivity. It seems that in Minnesota soil approximately half of the applied propamocarb hydrochloride was rapidly incorporated into the soil as bound residue, possibly owing to the high clay content of this test soil. It is suggested that propamocarb hydrochloride exists as a base in its protonated form in these soils. Therefore it will be attracted by the negative charges on the surfaces of organic matter and clay minerals. It is likely that adsorption is positively correlated with clay content. If this is so, then it is not surprising that degradation is least in Minnesota soil (highest clay content and organic matter content), since sorption tends to decrease the degradation rate of substances by reducing their availability to microbial attack. Microbial degradation is most important in the degradation of propamocarb hydrochloride.

Summarised results of the organic matter fractionation with the Minnesota soil expressed as the mean of two determinations

Fraction	7 days after application		59 days after application		120 days after application	
	(%) [1)]	(% TAR)	(%) [1)]	(% TAR)	(%) [1)]	(% TAR)
Fulvic acid	74.0	37.52	63.3	27.01	59.9	25.76
Humic acid	12.7	6.42	11.7	4.99	13.9	5.96
Humin	11.3	5.74	16.9	7.22	19.3	8.28
Total	98.0	49.69	91.9	39.22	93.0	40.00

Note [1)] % of the total radioactivity in the soil subjected to the organic matter fraction.
TAR = Total Applied Radioactivity. Applied radioactivity was 54.1196 kBq

D. Volatile radioactivity: In all test soils formation of $^{14}CO_2$ increased steadily during the experimental period, reaching 22.8% for the Minnesota, 66.2% for the Sarotti soil, 64.7% for the Abington soil, and 58.2% for the Borstel soil after 120 days.

Over the experimental period recovery losses were observed to increase. It was considered that losses resulted principally from the $^{14}CO_2$ trapping system, especially during periods of high mineralisation. For example, on Day 90 a balance gap was observed in all four soils, which was considered to result from the direct malfunction of the $^{14}CO_2$ trapping system.

Organic volatiles trapped by the quartz wool were below 0.1% throughout the study, except with the observation of organic volatiles accounting for 0.1% of radioactivity in the Sarotti and Borstel test soils

E. Transformation of test substance: Chromatographic results of metabolites from soil extracts are provided in Table CA-8.1.1.1-12. For all test soils the major portion of applied radioactivity was assigned to be unchanged propamocarb hydrochloride. However, over the period of experimentation the portion of propamocarb hydrochloride determined from the soil extracts continuously decreased. For the Sarotti, Abington, and Borstel soils on Day 0 a portion of 90.5%, 93.1%, and 90.7% of the applied radioactivity was assigned as unchanged propamocarb hydrochloride, respectively. By the end of the incubation period, 1.1%, 1.6%, and 8.6% of the applied radioactivity, respectively, still were unchanged propamocarb hydrochloride. However, for the Minnesota soil on Day 0 a portion of 49.4% of the applied radioactivity was determined to be unchanged propamocarb hydrochloride. Over the incubation period this value decreased down to 27.1% of the applied radioactivity. Over the incubation period up to eight unknown polar metabolites were observed in the soil extracts. The sum of unidentified radioactivity components never exceeded values of over 8.1% of the applied radioactivity and no single component exceeded 3.3% AR at any sampling interval in any soil.

III. Conclusion

For all metabolites observed in the study, no recognisable pattern of formation could be determined, indicating that the metabolites are transient in nature. Up to eight unidentified polar metabolites were observed during the study, however, the sum of the unknown metabolites never exceeded 8.1% of the applied radioactivity and no single component exceeded 3.3% AR at any sampling interval in any soil

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Report:	KCA 7.1.1.1/07; Schnoeder, F.; 2003; M-310828-02-1
Title:	Amendment to final report - (14C)-propamocarb hydrochloride - Aerobic route and rate of soil degradation
Report No.:	1760-1669-007
Document No.:	M-310828-02-1
Guideline(s):	OECD 1998, ENV/MC/CHEM (98) 17; EC Directive 95/36/EC. Active Substances, Section 7.1.1.2 (July 1995); SETAC Procedures for assessing the Environmental Fate and Ecotoxicity of Pesticides. Section 1.1 (March 1995), EPA, Subdivision N. Section 162-1 (October 1982); requirement for safety evaluation of agricultural chemicals published in 59NohSan No. 4200, Japanese Ministry of Agriculture Forestry and Fisheries (28 January 1985).
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

Comment: key elements in design and conduct reported as for actual guideline studies. Study regarded as scientifically valid.

Executive Summary

The route of degradation of propamocarb hydrochloride was investigated in a suite of laboratory studies.

Propamocarb hydrochloride, applied at a rate of 250 mg/kg, corresponding to a field rate of 187.5 kg a.s/ha, degrades readily under aerobic experimental conditions in the laboratory. Carbon dioxide and NER were the principal degradation products formed, reaching a maximum of 48.38 % and 47.45 % of the applied radioactivity. One of the metabolites formed was a polar component, which was observed at a maximum value of 7.3 % of the applied radioactivity with a retention time of ~2.5 minutes. For

identification of metabolite Unknown 1 (Unk 1) a wide range of chromatographic and mass spectrometer conditions were attempted but specific ions could not be assigned to Unk 1 with any certainty. In conclusion, the attempts to identify failed and a reasonable separation of the Unk l peak with different analytical methods (liquid chromatography and mass spectrometry techniques) was not achieved although it has been shown that the isolated Unk 1 may produce several radioactive peaks., but could not be identified after further investigation (for further characterisation and identification, see study KCA 7.1.1.1/10). A further six unidentified transient degradation products were also formed over the duration of the experiment. These degradation components were only detected occasionally and individually did not exceed 2.03 % of the applied radioactivity. Beside metabolite Unk 1 no other metabolite observed accounted for greater than 5 % of the applied radioactivity.

I. Material and Methods

A. Materials

1. Test Material: Common name: propamocarb-hydrochloride
Chemical name: Propyl 3-(dimethylamino) propylcarbamate hydrochloride
Radiolabelled purity: 98.2 %
Lot # 3389-191
Specific activity 8.645 MBq/mg (52.2 mCi/mmol)
Non-radiolabelled purity: 69.1 % w/w (formulation 750.5 g/L)
Lot #31491.

2. Soil:

Characteristics of the test soils:

Characteristic	Value			
	Soil B6	**Soil B7**	**Soil B8**	**Soil B9**
Textural class (UK)	Sandy loam	Clay loam	Clay loam	Sandy loam
Sampling location	Woolverstone, UK	Quarter, UK	Empingham, UK	Baylham, UK
Sand (%)	52	23	32	74
Silt (%)	37	57	34	14
Clay (%)	11	20	34	12
Organic carbon (%)	2.5	4.5	2.7	1.3
Organic matter (%)	4.3	7.8	4.7	2.2
CEC (mEq/100g)	14.6	17.8	22.2	11.1
pH in H_2O	7.1	6.7	8.0	5.5
WHC at pF 0.0 (%)	62.8	110.9	73.4	42.3
WHC at pF 2.5 (%)	21.2	34.7	29.6	16.6
Biomass (µg C/g) Day 0	451.35	620.57	394.94	198.78
Biomass (µg C/g) Day 120 [1)]	380.77 [1)]	640.22	371.54	123.84
Biomass (µg C/g) Day 365	230.97 [1)]	-	-	-

Note: CEC = Cation Exchange Capacity
WHC = Water Holding Capacity
[1)] Values measured in report 1669-009

B. Study design

1. Experimental conditions:

Summary of soil incubation units established for laboratory investigation:

Incubation group	Soil type	Application rate	Temperature conditions	MWHC conditions (%)
A	Sandy loam (B6)	250 mg/kg	20 ± 2 °C	45
B	Clay loam (B7)	250 mg/kg	20 ± 2 °C	45
C	Clay loam (B8)	250 mg/kg	20 ± 2 °C	45
D	Sandy loam (B9)	250 mg/kg	20 ± 2 °C	45
E	Sandy loam (B6)	250 mg/kg	10 ± 2 °C	45
F	Sandy loam (B6)	10 mg/kg	20 ± 2 °C	45

All test soils for each investigation were kept incubated in the dark. Test systems A-F consisted of incubation units equipped with a solid phase trap system for catching organic volatiles and liberated [^{14}C]-carbon dioxide. The first and second layers of the trapping system consisted of paraffin coated glass wool and soda lime, respectively. Soil samples (50 g dry weight equivalent) were weighed into individual open containers and were maintained under experimental incubation conditions for 4 days prior to application of propamocarb hydrochloride. Soil samples were treated at an application rate of 250 mg/kg (test system A-E), with an additional dose group of 10 mg/kg (test system F) applied to the sandy loam test soil. The test substance was applied dropwise to the surface of 22 soil samples. Based on 5 cm soil depth and bulk density of 1.5 g/cm^3, 250 and 10 mg/kg corresponds to a field application rate of 187.5 and 7.5 kg a.s/ha.

2. Sampling: Sampling of the soil test systems were undertaken at intervals of 0 h (immediately after application), 1, 3, 7, 14, 30, 58, 90, 120, 125, 181, 269, and 365 days (group A) and 0, 1, 3, 7, 14, 30, 58, 90, and 120 days (groups B to F). At each sampling point duplicate sub-samples were removed for analysis of group A samples, except at 90 and 125 days when a single spare sample was extracted and single units were samples sampled for groups B to F. At each sampling date the units were flushed with air in order to transfer all organic volatiles into the trapping system.

3. Analytical procedures: Each soil incubated was transferred to a centrifuge beaker and extracted four times with 150 mL acetonitrile/deionised water/hydrochloride (70:30:1 v/v/v). Radioactivity of the extracts was determined by liquid scintillation counting (LSC). If more than 3 % of applied radioactivity was determined after the fourth extraction procedure the soil was further extracted with 150 mL methanol/saturated NaCl (100:25 v/v). After any extraction procedure the soil was extracted with 150 mL of acetone and allowed to air dry. After extraction and drying both the soil and filters were combusted and radioactivity was counted by LSC.

The paraffin coated glass wool was extracted with ~40 mL of hexane. Any [^{14}C]-carbon dioxide was liberated using hydrochloride and adsorbed in 10 mL of 2-aminoethanol/methanol (4:2 v/v). All radioactivity measurements were quantified by LSC.

Non-extractable (bound) residue (NER) fractionation was undertaken on one sample collected at Day 60. A 20 g aliquot of soil was extracted three times with 60 mL 0.1 N NaOH for 30 minutes and the supernatant decanted after centrifugation. Humic acids in the decanted supernatant were precipitated with hydrochloride and separated from fulvic acids by centrifugation. Aliquots were counted by LSC. Analysis of samples taken from the incubation units was undertaken using High Performance Liquid Chromatography (HPLC).

II. Results and Discussion

A. Data: From an initial value of 451.35 µg C/g, the microbial biomass of the sandy loam soil (B6) decreased to 84.9 % and 47.2 % of the initial biomass determination at Day 120 and 365, respectively. The reduction in biomass especially over the 365-day period is indicative of long-term, closed system experimental testing and the results of propamocarb hydrochloride degradation require careful interpretation after day 120. For the other test soils a decline in the biomass of the test soil was observed except for soil B7 which showed a slight increase in microbial biomass.

Distribution of radioactivity in test soils from incubation groups A-F and overall mass balance, expressed as percent radioactivity (values represent the mean of duplicate analyses):

Timepoint (d)	CO_2	Organic volatiles	Soil extract	Soil residue	Mass balance
Group A1 – soil B6, 250 mg/kg, 20 °C					
0	<LOD	<LOD	94.02	3.69	97.71
1	0.15	<LOD	93.84	4.11	98.11
3	0.65	<LOD	89.27 [1)]	4.27	94.19
7	1.68	<LOD	88.83	5.71	96.22
14	4.01	<LOD	79.87	13.29	97.17
30	14.79	<LOD	49.64	29.88	94.30
58	36.64	<LOD	11.04	44.52	92.19
90 [2)]	40.84	<LOD	10.59	42.70	94.13
120 [2)]	45.28	<LOD	7.87	39.84	93.00
181	47.35	<LOD	6.61	34.95	88.91
269	47.36	<LOD	5.32	34.02	86.70
365	42.67	<LOD	5.83	31.09	79.59

Timepoint (d)	CO_2	Organic volatiles	Soil extract	Soil residue	Mass balance
Group B – soil B7, 250 mg/kg, 20 °C					
0	<LOD	<LOD	94.31	4.12	98.43
1	0.33	<LOD	91.76 [1)]	4.57	96.67
3	0.91	<LOD	87.31	4.82	93.05
7	2.65	<LOD	84.71 [1)]	7.11	94.48
14	5.17	<LOD	79.88	12.27	97.32
30	15.92	<LOD	48.72	28.45	93.08
58	27.40	<LOD	14.33	46.67	88.40
90	41.03	<LOD	7.18	49.00	97.22
120	48.38	<LOD	7.89	43.80	100.08
Group C – soil B8, 250 mg/kg, 20 °C					
0	<LOD	<LOD	93.26	4.37	97.63
1	0.12	<LOD	92.27	4.62	97.01
3	0.56	<LOD	95.20 [1)]	5.28	101.02
7	1.09	<LOD	88.84 [1)]	6.56	96.49
14	3.48	<LOD	76.97	15.97	96.43
30	17.18	<LOD	25.56	47.97	90.70
58	36.76	<LOD	9.07	47.21	93.04
90	41.72	<LOD	6.72	46.68	95.11
120	47.68	<LOD	6.34	43.10	97.11
Group D – soil B9, 250 mg/kg, 20 °C					
0	<LOD	<LOD	95.65 [1)]	4.20	99.85
1	0.10	<LOD	92.63 [1)]	4.35	97.08
3	0.26	<LOD	89.64	4.26	94.16
7	0.65	<LOD	90.69 [1)]	2.70	94.04
14	1.03	<LOD	91.63	4.95	97.61
30	4.25	<LOD	85.03	8.36	97.63
58	10.32	<LOD	70.92	13.55	94.79
90	18.16	<LOD	57.31	21.49	96.96
120	30.72	<LOD	29.50	29.35	89.57

Timepoint (d)	CO_2	Organic volatiles	Soil extract	Soil residue	Mass balance
Group E – soil B6, 250 mg/kg, 10 °C					
0	<LOD	<LOD	95.13 [1)]	3.77	98.90
1	0.16	<LOD	94.20	3.68	98.04
3	0.28	<LOD	94.00	4.13	98.41
7	0.48	<LOD	91.98	3.84	96.30
14	1.65	<LOD	89.61	6.28	97.54
30	3.86	<LOD	80.25 [1)]	10.43	94.57
58	10.86	<LOD	59.71	31.12	101.68
90	24.01	<LOD	26.78	45.33	96.12
120	31.50	<LOD	14.70	47.45	93.65
Group F – soil B6, 10 mg/kg, 20 °C					
0	<LOD	<LOD	93.23	3.65	96.88
1	0.47	<LOD	95.04	4.70	100.21
3	1.64	<LOD	89.97	8.82	100.43
7	3.35	<LOD	81.88	13.84	99.07
14	9.84	<LOD	59.52	29.11	98.47
30	25.27	<LOD	25.97	42.95	94.19
58	31.87	<LOD	14.22	46.38	92.47
90	36.31	<LOD	11.66	45.00	92.98
120	33.04	<LOD	10.32	42.45	85.81

Note: LOD = Limit of Detection

1) Value for soil extract represented concentrated extract plus third extraction step plus acetone extract due to too low recovery in the original extract.

2) Duplicate sample B data rejected for calculation of the mean value owing to poor mass balance, spare sample

analysed at Day 125 and combined with duplicate sample A in order to determine the mean value.

Chromatographic results obtained from soil extracts from incubation groups A-F (as percent of applied radioactivity)

Time point (d)	P RT=10 min	Unk 1 RT=2.5 min	Unk 2 RT=3 min	Unk 3 RT=6 min	Unk 4 RT=9 min	Unk 5 RT=12 min	Unk 6 RT=14 min	Unk 7 RT=29 min	UR
Group A1 – soil B6, 250 mg/kg, 20 °C									
0	92.02	0.22	<LOD	<LOD	0.12	<LOD	0.14	<LOD	0.92
1	91.44	0.44	<LOD	<LOD	0.11	0.09	0.08	<LOD	0.85
3	85.70	0.61	<LOD	0.05	0.09	0.59	<LOD	<LOD	0.90
7	85.61	1.17	<LOD	<LOD	<LOD	<LOD	0.21	<LOD	1.40
14	76.00	1.10	<LOD	0.05	0.03	0.82	0.04	<LOD	1.35
30	40.70	5.26	<LOD	0.36	0.16	0.81	0.22	0.46	0.93
58	2.42	5.47	<LOD	0.45	<LOD	<LOD	<LOD	0.88	0.07
90	0.83	6.77	<LOD	0.53	<LOQ	0.18	<LOD	<LOD	0.22
120 [1)]	0.61	3.82	2.03	0.36	<LOQ	<LOD	<LOD	<LOD	0.12
181	<LOQ	4.57	<LOD	<LOD	<LOD	<LOQ	0.30	<LOD	0.04
269	0.31	3.18	0.18	0.16	<LOD	<LOD	<LOD	<LOD	0.07
365	<LOD	4.29	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.07
Group B – soil B7, 250 mg/kg, 20 °C									
0	92.30	<LOD	<LOD	<LOD	<LOD	<LOQ	<LOQ	<LOD	0.08
1	88.92	0.64	<LOD	<LOD	<LOD	<LOQ	<LOD	<LOD	0.77
3	84.04	1.19	<LOD	<LOD	<LOD	<LOQ	<LOD	<LOD	0.71
7	81.26	1.47	<LOD	<LOD	<LOD	<LOQ	<LOD	<LOD	0.52
14	75.36	2.06	<LOD	<LOD	<LOD	<LOQ	<LOD	<LOD	0.77
30	42.46	2.51	<LOQ	<LOD	<LOD	<LOQ	<LOD	<LOD	0.22
58	6.34	6.10	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
90	<LOQ	4.08	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.06
120	<LOD	4.39	2.23	<LOD	<LOD	<LOD	<LOD	<LOD	0.07
Group C – soil B8, 250 mg/kg, 20 °C									
0	91.39	<LOD	<LOD	<LOD	<LOD	<LOQ	<LOD	<LOD	0.13
1	88.94	<LOQ	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.99
3	90.31	0.47	<LOD	<LOD	<LOD	<LOD	0.78	<LOD	0.95
7	87.01	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.25
14	74.23	<LOQ	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.08
30	17.62	4.69	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.47
58	<LOD	6.17	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.13
90	<LOD	3.62	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.02

Time point (d)	P RT=10 min	Unk 1 RT=2.5 min	Unk 2 RT=3 min	Unk 3 RT=6 min	Unk 4 RT=9 min	Unk 5 RT=12 min	Unk 6 RT=14 min	Unk 7 RT=29 min	UR
120	0.41	3.51	1.01	<LOD	<LOD	<LOD	<LOD	<LOD	0.09
Group D – soil B9, 250 mg/kg, 20 °C									
0	93.29	<LOD	<LOD	<LOD	<LOD	<LOQ	<LOQ	<LOD	0.37
1	90.44	<LOQ	<LOD	<LOD	<LOD	<LOD	<LOQ	<LOD	0.55
3	87.32	<LOQ	<LOD	<LOD	<LOD	<LOD	0.54	<LOD	0.45
7	85.57	1.19	<LOD	<LOD	<LOD	1.94	<LOD	<LOD	0.42
14	88.70	<LOQ	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.60
30	80.61	1.88	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.40
58	65.89	2.44	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.25
90	51.89	2.92	0.84	<LOD	<LOD	<LOD	<LOD	<LOD	0.14
120	22.06	4.02	0.75	<LOD	<LOD	<LOD	<LOD	<LOD	0.29
Group E – soil B6, 250 mg/kg, 10 °C									
0	93.72	<LOD	<LOD	<LOD	<LOD	<LOD	<LOQ	<LOD	0.28
1	91.96	<LOQ	<LOD	<LOD	<LOD	<LOD	0.57	<LOD	0.43
3	91.15	<LOQ	<LOD	<LOD	<LOD	<LOD	<LOQ	<LOD	1.09
7	89.05	1.42	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.42
14	86.74	<LOQ	<LOD	<LOD	<LOD	<LOD	0.88	<LOD	0.21
30	75.82	2.77	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.48
58	52.43	3.06	0.91	<LOD	<LOD	<LOD	<LOQ	<LOD	0.18
90	16.77	5.69	<LOD	<LOQ	<LOD	<LOD	1.09	<LOD	0.05
120	0.89	7.13	2.90	0.67	<LOQ	<LOD	0.28	<LOD	0.24
Group F – soil B6, 10 mg/kg, 20 °C									
0	92.29	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.29
1	90.21	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	1.70
3	87.47	<LOQ	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.11
7	77.19	<LOQ	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.03
14	52.63	<LOQ	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.11
30	14.89	<LOQ	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.00
58	<LOQ	7.28	<LOQ	<LOD	<LOD	<LOD	<LOD	<LOD	0.00
90	<LOD	4.34	<LOQ	<LOD	<LOD	<LOQ	<LOD	<LOD	0.16
120	2.31	5.22	1.17	<LOD	<LOD	<LOD	<LOD	<LOD	0.09

Note: Values represent the mean of duplicate analyses

[1)] Data rejected from calculation of mean for 120 day sample, instead the values from the spare sample collected at Day 125 were used.

LOD = Limit of Detection

LOQ = Limit of Quantification

P = propamocarb hydrochloride

UR = sum of radioactivity exceeding the background in the HPLC chromatograms but not integrated

Overview of the applied HPLC separation techniques used to identify Unk1 metabolite (amendment 1760-1669-007)

HPLC method number	Column with different stationary phases	RT of Unk1 (min)	RT of propamocarb (min)	Separation of Unk1
1[1)]	Aqua 5µ C18 125A	4.3	25.0	Failed
2[1)]	Inertsil Sil 100A 5µ	No peak signal	No peak signal	N/A [2)]
3[1)]	Multospher 120 RP18 HP	3.1	19.9	Failed
4[1)]	Multospher 120 RP18 AQ	3.0	17.2	Failed

Note: [1)] Numerical order ascending
[2)] N/A = Not Applicable

B. Mass balance: Mean mass balance of applied radioactivity in duplicate samples extracted from Group A ranged from 79.59 % to 98.11 %. Beyond day 120 for Group A the mass balances decreased slightly with time. It is likely, this occurred owing to carbon dioxide escape during the long sampling intervals. For incubation Groups B-F the individual mass balances ranged from 88.40% to 100.08%, 90.70% to 101.02%, 89.57% to 99.85%, 93.65% to 101.68%, and 85.81% to 100.43% of applied radioactivity. The amount of radioactivity also decreased in incubation groups B-F from 94.31 % to 7.89 %, from 93.26 % to 6.34%, from 95.65% to 29.50%, from 95.1% to 14.70%, and from 93.23% to 10.32% of applied radioactivity after 120 days, respectively.

C. Bound and extractable residues: The formation of NER peaked at 44.52% on Day 58, and then decreased to 39.84% after 120 days, decreasing further to 31.09% after 365 days in incubation group A. Similarly the increase in formation of NER was evident in incubation groups B-F, reaching a maximum of 43.80%, 43.10%, 29.35%, 47.45%, and 42.45% after 120 days.

NER in the soil was further investigated by fractionation into fulvic acid, humic acid, and humin. These investigations were performed using the soil sample collected after day 60, 90, 90, and 120 for soil B6, B7, B8, and B9, respectively. The sampling days represent the date with the maximum amount of NER.. The majority of radioactivity was detected in the humin fraction and accounted for between 56.85 % and 73.48 % of the radioactivity present in the test soils after extraction. The remaining radioactivity was found in amounts ranging between 6.93 % and 11.72% for the fulvic acid fraction and between 17.42 % and 29.11% for the humic acid fraction in the incubation groups A-D.

Results of the investigations of the NER in test soils (Groups A-D). Expressed as percent non-extractable from soil

Sample	Fulvic acid (%)	Humic acid (%)	Humin (%)	Procedural recovery (%)
Group A (soil B6)	7.84	27.66	63.71	99.21
Group B (soil B7)	6.93	29.11	56.85	92.90
Group C (soil B8)	11.72	17.42	67.49	96.63
Group D (soil B9)	8.25	27.45	73.48	109.19

D. Volatile radioactivity: Organic volatiles were below the LOD throughout the study. The amount of radioactivity extractable from the soil in Group A decreased from 94.02 to 7.87% after 120 days and still further to 5.83% after 365 days of incubation under experimental conditions.

The formation of $^{14}CO_2$ in incubation group A increased to 45.28% of applied radioactivity after 120 days. For incubation groups B-F the CO_2 fraction reached up to 48.38%, 47.68%, 30.72%, 31.50%, and 33.04% after 120 days. The distribution of extracTable A1nd non-extractable radioactivity in incubation group D and also the lower amount of CO_2 indicated a slower conversion of the test item in this soil.

E. Transformation of test substance: For all soils, propamocarb hydrochloride represented the majority of radioactivity in the soil extract. The percentage amount of propamocarb hydrochloride decreased from an initial value of 92.0% to 0.6% after 120 days and continued to decrease to below the LOD after 365 days in incubation group A. The amount of propamocarb hydrochloride decreased from 92.3% to <LOD. From 91.4% to 0.4%, 93.3% to 22.1%, from 93.7% to 0.9%, and from 92.3% to 2.3% of applied radioactivity after 120 days for incubation groups B-F, respectively.

Unknown metabolites with retention times of ~2.5, 3, 6, 12, 14, and 29 minutes were observed in some samples. The major unknown metabolite was a polar component (Unk1) with a retention time of ~2.5 minutes. The maximum percentage amount of Unk 1 was 6.8% (Day 90), which decreased to 4.3 % by Day 365 in incubation group A. Unk 1 maximum values for incubation groups B, C, and F after 90 days were 6.1%, 6.2%, and 7.3% of applied radioactivity, respectively. The unknown metabolite decreased in groups B, C, and F to 4.4%, 3.5%, and 5.2% after 120 days, respectively. In incubation groups D and E the maximum values were observed after 120 days with 4.0% and 7.1% of applied radioactivity. This indicated that conversion of the test item and the formation of the main metabolite were slower in the soil B9 and also at the lower incubation temperature. Further work to identify the Unk 1 metabolite was carried out but it was not possible to assign ions with any certainty to the peaks owing to the lack of chromatographic retention in the reverse phase system. However, it was determined that the isolated Unk 1 degradation product may produce several peaks indicating a mixture of substances. For further characterisation and identification see study KCA 7.1.1.1/10.

III. Conclusion

Carbon dioxide and NER were the principal degradation products formed, reaching a maximum of 48.38% and 47.45% of the applied radioactivity. One of the metabolites formed was a polar component, which was observed at a maximum value of 7.3% of the applied radioactivity. The component had a retention time of ~ 2.5 minutes, but could not be identified after further investigation. A further six unidentified transient degradation products were also formed over the duration of the experiment. These degradation components were only detected occasionally and individually did not exceed 2.03% of the applied radioactivity. . Beside metabolite Unk1 no other metabolite observed accounted for greater than 5% of the applied radioactivity. For further characterisation and identification of Unk 1 see study KCA 7.1.1.1/10.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Report:	KCA 7.1.1.1/08; Iwan, J.; 1979; M-157719-01-1
Title:	Metabolism of propamocarb hydrochloride by soil microorganisms - Report of progress no. 1
Report No.:	R+S 38/79- PA 66752.73/2; A85480
Document No.:	M-157719-01-1
Guideline(s):	None
Guideline deviation(s):	None
GLP/GEP:	**No**

Comment: study regarded as scientifically valid. However, investigations were performed in cultural media with microbial populations derived from soil rather than fully ‘native’, microbial active soil. Design and results, thus, were not comparable to standard aerobic soil study.

RMS´s opinion:

Reliability of the study: score 2 of the scoring system of Klimisch *et al*.(1997).

Report:	KCA 7.1.1.1/09; Iwan, J.; 1980; M-157721-01-1
Title:	Metabolism of propamocarb hydrochloride by soil microorganisms. Behaviour in sterilized and non-sterilized German standard soil 2.2 - Report of progress no. 2
Report No.:	R+S 48/80- PA 66752.73/2; A85481
Document No.:	M-157721-01-1
Guideline(s):	None
Guideline deviation(s):	None
GLP/GEP:	**No**

Comment: key elements in design and conduct reported as for actual guideline studies. Study regarded as scientifically valid. Major deficiencies: No day zero samples were investigated in combination with low total recovery below 90% AR for first sampling interval (day 1 after application).

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Executive Summary

Study R+S 38/79 (Doc.-No.: M-157719-01-1):

A mixed population of aerobic microorganisms capable of metabolizing [^{14}C]-propamocarb hydrochloride was developed from Gerrnan Standard Soil 2.2. Following a lag-phase of about 24 hours the carbamate was completely mineralized within 6 - 9 days as indicated by the evolution of respective quantities of CO_2. Fragments of the parent molecule seemed to be incorporated into the cells of the organisms which were partially identified as *Candida humicoia, Fusarium* spec. and 2 species of gram negative bacteria.

Study R+S 48/80 (Doc.-No.: M-157721-01-1):

To determine the impact of soil microorganisms on propamocarb hydrochloride degradation, tests were run with sterilized and non-sterilized German standard soil 2.2 according to current EPA guidelines. After 14 days of incubation, recoverable propamocarb contents of sterilized samples remained constant (60% of applied material) the initial decrease being due to adsorption. In microbially active soil extensive mineralization occurred following a lag-phase of 7 days. Degradation of propamocarb under these conditions is best described by zero-order kinetics with a half-life of about 18 days. These data strongly suggest that soil degradation of propamocarb is mediated by microorganisms. A mixed culture of bacteria and fungi capable of degrading the pesticide was identified. Intermediate metabolic products did not accumulate in any of the samples investigated.

I. Material and Methods

A. Materials

1. Test Material: Common name: propamocarb hydrochloride
Chemical name: Propyl 3-(dimethylamino) propylcarbamate hydrochloride;
Study R+S 38/79: Radiolabelled purity: > 96.0 – 98 %, specific activity 9.58 – 10.58 KBq/mg
Study R+S 48/80: Radiolabelled purity: > 95.0 %, specific activity 10 KBq/mg

2. Soil:

Characteristics of the test soils:

Parameter	Study number	
	Study R+S 38/79-PA 66 752.73/2 [1)]	**Study R+S 48/80-PA 66 752.73/2 [1)]**
Course Sand (0.200 – 2.000 mm) (%)	48.3	48.3
Fine Sand (0.020 – 0.200 mm) (%)	36.5	36.5
Silt (0.002 – 0.020 mm) (%)	6.4	6.4
Clay (< 0.002 mm) (%)	8.8	8.8
pH (0.1 M KCl)	5.6	5.6
Organic carbon (%)	2.19	2.19
Cation exchange capacity (mEq/100 g soil)	8.4	8.4
Maximum water holding capacity (g/100 g soil)	36	36
Texture (USDA)	Loamy Sand	Loamy sand

[1)] Same soil sample used for experimentation

B. Study design

In study R+S 38/79-PA 66 752.73/2 gas washing bottles were filled under sterile conditions with 100mL of Burk mineral salt solution containing 100mg/L [^{14}C]-propamocarb hydrochloride and 160mg sodium acetate. This was then inoculated with 2 mL of a mixed microorganism culture developed from German standard soil 2.2. The bottles were connected to a manifold and filtered compressed air was passed through the medium. 2 M H_2SO_4, 1 M KOH and etheylene glycol traps were used to trap volatile degradates. Cultures were kept at 25°C and sampled at 1, 3, 6, 9, and 12 days.

In study R+S 48/80-PA 66 752.73/2 50 g samples (dry weight) of German standard soil 2.2 ("Neuhofen", loamy sand) were placed into biometer flasks and treated with 9.8mg radiolabelled propamocarb hydrochloride to give a concentration of 200mg/kg. The water content in the samples was then raised to 70% of the maximum water holding capacity. A 0.1 N KOH solution was used as a means of trapping evolved $^{14}CO_2$ from the system. The samples were stored in the dark at 22 ± 2 C and analysed after 1, 3, 7, 14, 21 and 31 days.

Sterilised samples were prepared by autoclaving the soil and all glassware at 121 ºC and 2.5 bar pressure. An aqueous solution containing the radiolabelled propamocarb hydrochloride was sterilised by filtration and added to the biometer flasks in the germ-free atmosphere of a clean-bench. Upon being closed with sterilised rubber stoppers, the flasks were sealed with hot paraffin wax, stored in the dark at 22 ± 2 C and analysed after 1, 3, 7, 14, 21 and 31 days.

IV. Results and Discussion

Distribution of radioactivity in non-sterile test soil and overall mass balance, expressed as percent radioactivity:

Timepoint (d)	propamocarb hydrochloride	Fraction 1	Fraction 2	CO_2	Organic extract	NaCl-extract	Soil residue	Mass balance
1	68.8	<0.1	0.6	0.3	37.4	32.0	1.2	81.2
3	74.6	<0.1	0.8	0.6	40.8	34.5	2.4	94.4

Timepoint (d)	propamocarb hydrochloride	Fraction 1	Fraction 2	CO_2	Organic extract	NaCl-extract	Soil residue	Mass balance
7	78.5	<0.1	0.7	0.9	39.4	39.8	1.5	94.6
14	61.3	<0.1	0.5	3.6	28.7	33.1	2.0	80.3
21	36.9	0.1	0.5	17.3	15.4	22.1	3.8	76.2
31	13.1	0.2	0.4	48.8	5.6	8.1	5.9	81.9

Fraction 1 and 2 are unknown metabolites

Distribution of radioactivity in sterile test soil and overall mass balance, expressed as percent radioactivity:

Timepoint (d)	Replicate	propamocarb hydrochloride	Fraction 1	Fraction 2	CO_2	Organic extract	NaCl-extract	Soil residue	Mass balance
1	1	79.8	0.2	1.0	<0.1	44.6	36.4	2.1	91.0
	2	76.4	0.1	1.0	<0.1	44.8	32.6	3.1	88.7
3	1	75.7	0.3	1.1	<0.1	42.0	35.0	2.5	87.7
	2	75.7	0.2	1.0	<0.1	45.5	31.4	3.7	89.0
7	1	78.8	0.2	1.0	<0.1	41.3	38.7	2.0	89.4
	2	74.8	<0.1	1.0	<0.1	39.8	35.9	1.8	89.8
14	1	66.6	0.2	0.6	<0.1	27.5	39.9	2.2	76.3
	2	54.3	<0.1	0.5	<0.1	21.5	33.3	2.3	71.0
21	1	56.3	0.2	1.0	0.1	27.6	29.8	2.9	69.6
	2	63.4	0.1	2.4	<0.1	33.7	32.2	2.1	84.3
31	1	60.3	0.1	1.2	0.1	32.5	29.1	3.3	75.2
	2	61.5	0.2	1.4	<0.1	35.7	27.2	2.2	84.0

Fraction 1 and 2 are unknown metabolites

In study R+S 38/79-PA 66 752.73/2, following a lag phase of 24 hours, propamocarb hydrochloride was completely mineralised within 6-9 days as indicated by the evolution of $^{14}CO_2$. No degradation products found in the culture medium were detected in appreciable amounts (< 4 %). Besides large quantities of $^{14}CO_2$, radioactivity was also found in the pelleted tissue of the micro-organisms (5.4 - 22.5 % of applied radioactivity after 6 days). Although some of the detected radioactivity might have adhered to the surface of the microbial pellet in spite of washing, these data suggest that following oxidative metabolic processes C-1 or C-2 fragments from the carbon skeleton of the parent molecule had been introduced into natural anabolic pathways.

In study R+S 48/80-PA 66 752.73/2, after an initial period of adsorption to the soil, the percentage of applied propamocarb hydrochloride that was extractable from the sterilized soil remained constant at about 60 % of applied radioactivity on Days 14 and 31. In the non-sterile soil extensive mineralisation occurred following a lag-phase of 7 days. The lack of degradation in soil after deactivation of an otherwise “metabolically” active soil by heat sterilization illustrates that the degradation of propamocarb hydrochloride in soil is primarily mediated by soil microorganisms.

III. Conclusion

The degradation of propamocarb hydrochloride in soil is, primarily, mediated by soil microorganisms

RMS´s opinion:

Reliability of the study: score 2 of the scoring system of Klimisch *et al*.(1997).

New information submitted by the propamocarb Task Force:

In order to fulfil actual data requirements of identification for minor components observed in route of the aerobic degradation in soil, within the Annex I Renewal process, a study was initiated to characterise and, if possible, to identify the polar unknown radioactivity. The results were reported in the study KCA 7.1.1.1/10.

Report:	KCA 7.1.1.1/10; Heinemann, O.; Kasel, D.; 2015; M-529394-01-1
Title:	[1-^{14}C]propamocarb-hydrochloride: Characterisation of two unknown components observed in two aerobic soil metabolism studies
Report No.:	EnSa-14-0778
Document No.:	M-529394-01-1
Guideline(s):	OECD Test Guideline No. 307 Commission Regulation (EU) No 283/2013 in accordance with Regulation (EC) No 1107/2009 US EPA OCSPP Test Guideline No. 835.4100 / 835.4200
Guideline deviation(s):	No deviation. This is not a guideline study; neverthess, concerning quality criteria this study followed the respective guidelines.
GLP/GEP:	**Yes**

Executive Summary

Samples were generated for characterisation and identification of unknown metabolites already observed in ~~the~~ two existing aerobic soil degradation studies KCA 7.1.1.1/07 and KCA 7.1.2.1.1/15.

The test substance [1-*N*-propyl-^{14}C]-propamocarb-hydrochloride was incubated under aerobic conditions in the dark in soil Woolverstone at 20 C and in soil Sarotti at 10°C, both at 45% of maximum moisture capacity (MWHC) for 90 days in maximum.

By its design as a metabolite identification study, no full material balances were established. Total recoveries of extractable radioactivity declined from 95.3 (day zero) to 5.5% of AR (day 90) for soil Woolverstone and from 70.3 (day zero) to 24.3% (day 29) for soil Sarotti thus underlining the extensive microbial transformation of the test substance in the two soils.

Chromatographic analysis of soil extracts resulted in profiles of transformation products consisting of a number of metabolites, all occurring at trace level in the course of incubation. The patterns were therefore similar to those observed in earlier aerobic soil degradation studies conducted with the parent compound propamocarb-hydrochloride including the two unknown components observed (retention time in HPLC approx. 2.5 min, study KCA 7.1.1.1/07, and relative retention factor of approx. 0.33 to 0.36 in TLC, study KCA 7.1.2.1.1/15) in the existing tests at levels beyond the actual triggers set for identification.
Profiling of residues in actual soil extracts was performed by additional HPLC methods developed. The polar unknown fraction of soil Woolverstone could be characterized by HPLC using a Hypercarp column to result in separation into at least two components below the triggers for identification.
The unknown component observed in soil Sarotti could be identified by HPLC/MS/MS investigations including fine mass determination of the isolated HPLC fractions. The compound was identified as the metabolite ‘oxo-propamocarb’, representing a transient component regarded as an initial step in the overall transformation of propamocarb-hydrochloride in aerobic soil. The transient character of oxo-propamocarb is underlined by the fact that the compound was observed as a minor metabolite in tests performed at 10°C only, with no detection in tests at 20°C.

I. Material and Methods

A. Materials

Test Material: [1-*N*-propyl-^{14}C] propamocarb-hydrochloride (AE B066752)
Specific radioactivity: 3.75 MBq/mg (101.37 µCi/mg)
Radiochemical purity: >98% (HPLC, ^{14}C-detection)
>97.1% (TLC, ^{14}C-detection)
Chemical purity: not reported
Sample ID: KATH 6235

Soils: The soils had been freshly collected from the field followed by sieving to 2 mm.

Characteristics of test soils

Soil	Woolverstone Hall (WS)	Sarotti (ST)
Geographic Location (City / State / Country)	Woolverstone Hall / Suffolk / UK	Hattersheim/ Hassia / Germany
GPS coordinates	N 52° 00' 04.8'' W 01° 11' 16.2''	N 50° 22.9' E 06° 43.0'
Pesticide use history	not reported	not reported
Sampling depth (cm)	4-10	0-20
Collection procedures	Sample taken with spade from shelf cut into topsoil	Sample taken with shovel and placed in plastic buckets
Storage prior to shipment / length	Sieved to <10mm after collection, storage (3 d) at 5°C till shipping	Storage (5 d) at ambient temperature till shipping
Storage at test facility / length	Sieved to 2 mm and stored at ambient temperature (12 d)	Sieved to 2 mm and stored refrigerated (1 d)
Textural Class (USDA)	sandy loam	silt loam
Sand [50 µm - 2 mm] (%) Silt [2 µm - 50 µm] (%) Clay [< 2 µm] (%)	67 28 5	25 54 21
pH in Water pH in $CaCl_2$ (0.01 M) pH in KCl (1 M) pH, saturated paste	5.9 5.5 5.4 5.8	7.2 6.9 6.7 7.1
Organic Matter [A] (%)	4.1	2.4
Organic Carbon (%)	2.4	1.4
CEC (meq/100 g)	10.3	10.6
MWHC (g/100 g) at pF 0	48.0	49.0
MWHC (g/100 g) at 0.1 bar (pF 2)	20.9	22.6
Microbial biomass (mg microbial C/100 g dry soil)		
Initial (Day 0) Final	423 n.d.	523 n.d.

[A)] % organic matter = % organic carbon × 1.724
CEC: Cation exchange capacity; MWHC: Maximum Water Holding Capacity; n.d.: not determined

B. Study design

Experimental conditions: The study was designed to characterise and identify unknown extractable radioactivity observed in two soil degradation studies at 6.8% of AR (20°C, soil Woolverstone, day 90, study KCA 7.1.1.1 /07, retention time approx. 2.5 min) and at 5.5% (10°C, soil Sarotti, day 21, study KCA 7.1.2.1.1 /10, relative retention factor approx. 0.33 to 0.36) in maximum, respectively.

Samples of 50 g dry weight of soil each (soil Woolverstone) or 100 g each (soil Sarotti) were filled into glass incubation flasks and pre-equilibrated prior to treatment at approximate study conditions

(darkness, 20 C for soil Woolverstone or 10°C for soil Sarotti, 45% of MWHC moisture). At start, each sample received 250 mg test substance/kg soil (Woolverstone) or 4.8 mg/kg soil (Sarotti), doses representing field rates of 187.5 kg a.s./ha or 3.6 kg a.s./ha, respectively. Following application the samples were attached to 'static' incubation systems with traps to collect ^{14}C-carbon dioxide and other volatile components. Samples were incubated at 20 ±1 C (Woolverstone) or 10±1°C (Sarotti) and at 45% of MWHC moisture in the dark for 90 days in maximum.

Sampling: Single samples of soil Woolverstone were removed for work-up after 0, 31, 60 and 90 days of incubation. Single replicates of soil Sarotti were removed after 0, 14, 21 and 29 days of incubation. The complete samples were immediately processed by extraction performed the same day.

Analytical procedures: The investigations focused on the extractable portion of radioactivity thus no full ^{14}C-material balance was established. The entire soil sample in each test vessel was processed by a stepwise extraction procedure. For samples of soil Woolverstone the initial extraction step was performed with 150 mL aqueous acetonitrile solution (acetonitrile:water:hydrochloric acid = 70:30:1, by vol.) three times successively by shaking the soil/solvent mixture at ambient temperature for 30min. This step was followed by shaking the remaining residues in a soil/solvent mixture at ambient temperature with 150 mL aqueous methanol solution (methanol:saturated aqueous sodium chloride solution = 100:25, v/v) for 30 min. For samples of soil Sarotti the extraction was performed with 100 mL aqueous acetonitrile solution (acetonitrile:water:formic acid = 4:1:0.1, by vol.) three times successively by shaking the soil/solvent mixture at ambient temperature for 30 min. Each extraction step was followed by centrifugation and decantation of the solvent.
Following quantitation of radioactivity in extracts by LSC, analysis was performed by reversed phase HPLC and ^{14}C-flow-through detection for extracts of soil Woolverstone as the primary chromatographic method. For samples of soil Sarotti, the primary chromatographic method consisted of normal-phase TLC followed by quantification of ^{14}C-residues by bio-imaging of the separated spots after ascending development of the plates. The analytical methods thus reflected the methods reported in existing degradation studies (see KCA 7.1.1.1 /07 and KCA7.1.2.1.1 /10) for comparison with actual samples.
Moreover, new HPLC methods were developed for profiling of residues in actual soil extracts. For identification of unknown peak in soil Sarotti, HPLC was also used for the isolation of peaks of interest from soil extracts by fraction collection. Isolated fractions were investigated by HPLC/MS/MS analysis including fine mass determination. Polar fractions of soil Woolverstone were characterized by HPLC using a Hypercarp column as solid phase and ^{14}C-flow-through detection.

II. Results and Discussion

Mass balance and extractability: Investigations focused on extractability and the profile of radioactive residues in soil extracts and therefore no complete mass balances were determined.
The total extractable residues following incubation of [1-*N*-propyl-^{14}C]propamocarb-hydrochloride in the two soils were summarized in the table below. Values of extractable radioactivity decreased rapidly with time as it is indicated by the fast decline of extractable radioactivity after 31 days (Woolverstone) or 14 days (Sarotti) of incubation.

Extractability of radioactive residues was nearly quantitative for soil Woolverstone by day zero (95.3% of AR) to decrease to 5.5% after 90 days of incubation. Extractability was lower for soil Sarotti, as demonstrated by a recovery of 70.3% in day zero extracts to decline to 24.3% after 29 days of incubation. The results were, thus, in good agreement with the existing studies.

Transformation of test substance: The fast decline of extractability of radioactive residues indicated extensive transformation of the active substance to form a number of minor components occurring formally all below the EU triggers set for identification. However, the profile of transformation products formed was confirmed by the results from existing and actual HPLC profiling methods for the two components under investigation.

With the patterns of metabolites observed in the actual test being equivalent to those reported in the existing route and rate of degradation studies it was possible to assign peaks occurring in actual soil extracts to those observed in the existing studies.
For the unknown radioactivity in soil Woolverstone incubated at 20°C, the polar character could be confirmed by its elution behavior as a broadened peak at approx. 6.9 min when applying the existing HPLC analytical method. Being eluted later than in the existing study the peak was regarded as the target component since the difference in retention times of about 8 min (between polar peak and the test substance) was the same for the two tests.
The polar radioactivity could be separated into at least two components via HPLC after use of a Hypercarb column as static phase. Soil extracts of days 31, 60 and 90 were separated into two peaks showing a ratio of separated peaks of 1.6:2.8, 2.8:1.6 and 2.7:1.6, respectively. When translating these ratios into total occurrences of unknown polar components in the original study, none of the peaks qualified for identification since it resulted in a maximum occurrence of 4.4% AR for a single peak after separation. No further investigations for identification of unknown polar components were therefore performed for extracts of soil Woolverstone.
'Unknown III' observed in extracts of soil Sarotti incubated at 10°C and showing a relative retention factor of 0.36 to 0.39 in normal phase TLC could be isolated *via* fraction collection followed by structural elucidation of the isolated peak of interest by HPLC/MS/MS and NMR. Investigations by HPLC/MS/MS resulted in a fine mass determination and a molecular mass of 202.3 g/mole, corresponding to the elemental composition $C_9H_{18}N_2O_3$. NMR spectroscopic data supported the structure of 'Unknown III' to be elucidated as 'oxo-propamocarb' and the structure as shown in Figure CA 11.1.4.3-02.
Comparison of the chromatographic profiles of the present and the previous study [Fent G., Hein W. (2001): Degradation and metabolism of propamocarb-HCl (AE B066752) in one soil at 10°C, Report no. AGR 21, BCS document no. M-203301-01-1.], showed that the chromatographic pattern in the same chromatographic system as used in the previous study was similar.
In this study of Heinemann, O.; Kasel, D. (2015), M-529394-01-1, the total of other unidentified components was > 5% (5.6% AR at DAT-21 and 5.5% AR at DAT-29) and none of the single components exceeded 3.6% AR. In the previous study [Fent G., Hein W. (2001): Degradation and metabolism of propamocarb-HCl (AE B066752) in one soil at 10°C, Report no. AGR 21, BCS document no. M-203301-01-1.], a maximum occurrence of Unknown ST in soil Sarotti of 5.5% AR at DAT-21 was found.

Distribution of components in extracts of <u>soil Woolverstone</u> following application of [1-*N*-propyl-^{14}C]propamocarb-hydrochloride

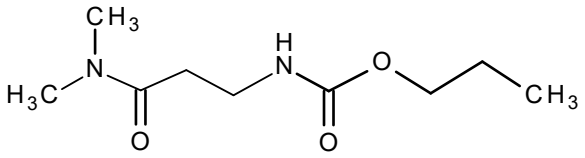
Compound	Sampling interval (days)			
	0	31	60	90
	% of initially applied radioactivity			
propamocarb	93.4	32.4	6.0	4.5
Polar unknown	0.0	2.0	1.8	1.0
Sum of other unidentified components	1.9	2.2	2.0	1.0
Total extractable	95.3	34.6	8.0	5.5

Values given as percentages of initially applied radioactivity

Distribution of components in extracts of soil Sarotti following application of [1-*N*-propyl-^{14}C]propamocarb-hydrochloride:

Compound	Sampling interval (days)			
	0	14	21	29
	% of initially applied radioactivity			
propamocarb	69.5	48.9	34.4	18.4
Unknown I	n.d.	2.8	3.6	2.3
Unknown II	n.d.	n.d.	n.d.	0.6
Oxo-propamocarb (Unknown III)	n.d.	n.d.	n.d.	0.5
Unknown IV	n.d.	n.d.	0.4	0.7
Sum of other unidentified components *	0.8	3.7	5.6	5.5
Total extractable	70.3	52.7	39.9	24.3

Values given as percentages of initially applied radioactivity.
* None of the single components exceeded 3.6% AR.



Proposed structure of Unknown III identified as oxo-propamocarb.

III. Conclusion

Following incubation of [1-*N*-propyl-^{14}C]propamocarb-hydrochloride in soils Woolverstone and Sarotti under the same conditions as for the existing studies, respectively, chromatographic investigations of extracted radioactivity showed extensive transformation. The degradation resulted in similar patterns of transformation products as observed in existing degradation studies. For polar unknown radioactivity observed in soil Woolverstone additional chromatographic investigations resulted in its separation into at least two components being each below the EU trigger for identification. For soil Sarotti an unknown component characterized by a relative retention factor of 0.33 to 0.36 in TLC was identified by HPLC analysis/fraction collection followed by HPLC/MS/MS and NMR spectroscopic investigations as oxo-propamocarb. The structure indicated one of the potential initial oxidative steps of microbial transformation in the route of degradation of the active substance in aerobic soil.
In samples of the same soil Sarotti incubated at 20°C, metabolite oxo-propamocarb was observed at trace level below 3% AR (KCA 7.1.1.1/06). Incubation at 10°C, thus, resulted in slightly higher levels just beyond 5% in the same soil underlining the transient character with no trend for increase at later sampling intervals. Moreover, oxo-propamocarb occurred at trace level in other soils, in case of its formation at all. In view of its transient characteristics, oxo-propamocarb was therefore not defined as a residue for environmental risk assessment in soil, groundwater or surface water.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Finally, additional information from aerobic soil degradation data resulted from a study performed in two US soils, in order to fulfil US EPA data requirements. The results are summarized under KCA 7.1.1.1/11.

Report:	KCA 7.1.1.1/11; Desmarteau, D. A.; 2006; M-270482-01-1
Title:	[^{14}C-propamocarb-hydrochloride]: Aerobic soil metabolism in two US soils
Report No.:	MEPRY002
Document No.:	M-270482-01-1
Guideline(s):	US EPA Subdivision N, Section 162-1
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

Executive Summary

The degradation of [1-*N*-propyl-^{14}C]propamocarb-hydrochloride was investigated in the two US soils Porterville and Aromas under aerobic conditions by incubation in the dark at 25 C ± 1°C and at 75% of the 0.33 bar (pF 2.5) moisture for 119 days in maximum.
The test was performed at a test concentration of 0.75 mg test substance/kg soil, equivalent to a nominal rate of application in the field of 562 g a.s./ha.

Total recoveries of radioactivity ranged from 90.9 to 100.0% of AR for sandy loam soil Porterville and from 95.4 to 100.1% for sandy loam Aromas.
The total extractable radioactivity decreased from 99.0% (soil Porterville) and 91.6% (soil Aromas) by day zero to 6.2% and 41.7% by day 119. The decrease of extractable radioactivity was accompanied by the formation of non-extractable residues (NER) to account for 14.8% (soil Porterville) and 17.8% (soil Aromas) after 119 days.
As a result of micro-biological degradation, mineralisation was extensive to account in maximum for 73.6% (soil Porterville) and 36.4% (soil Aromas) determined as ^{14}C-carbon dioxide at the end of the study, day 119. Formation of other organic volatile components was insignificant (≤ 0.1% AR).

Besides ^{14}C-carbon dioxide formed as the predominant transformation product, the metabolite *N*-desmethyl-propamocarb was observed in soil Portervile, at 9.7% in maximum by day 30, while the metabolite was not detected in soil Aromas. Formation of unknown components was very low and at trace level (0.5% by day 30, soil Porterville) in the course of the study.

The biotic character of degradation of [^{14}C]-propamocarb-hydrochloride in aerobic soil was again confirmed by the formation of ^{14}C-carbon dioxide as the major and terminal product of conversion along with the formation of non-extractable (bound) residues.

Following kinetic evaluation by the SFO kinetic model, the degradation of [^{14}C]-propamocarb-hydrochloride resulted in half-lives (DT_{50}) of 31.4 days for soil Porterville and 123 days for soil Aromas, associated with DT_{90} value of 104 days for soil Porterville and DT_{90} value of 409 days for soil Aromas.

I. Material and Methods

A. Materials

1. Test Material: [1-*N*-propyl-^{14}C]propamocarb-hydrochloride

Specific radioactivity:	8.52 MBq/mg (230.3 µCi/mg; 51.3 mCi/mmole)
Radiochemical purity:	98.0%
Chemical purity:	not reported
Sample/Batch ID:	BECH 1650

2. Soil: The soils had been freshly collected from the field followed by sieving to 2 mm.

Characteristics of the test soils:

Soil	Porterville	Aromas
Geographic Location (City / State / Country)	Porterville / California / US	Aromas / California / US
GPS coordinates	N 36° 00.0492‘ W 119° 04.525‘	N 36° 54.636’ W 121° 39.645’
Pesticide use history	None used last five years	Glyphosate and 2,4-D within previous 5 years, thus not same chemical class of compounds or mode of action
Sampling depth (cm)	0-15	0-15
Collection procedures	Sample taken with shovel and placed in plastic bucket	
Storage prior to test / length	Storage at 4-6°C (35 d)	Storage at 4-6°C (22 d)
Storage at test facility	Sieved to 2 mm and acclimated to study conditions	
Textural Class (USDA)	sandy loam	sandy loam
Sand [50 µm - 2 mm] (%) Silt [2 µm - 50 µm] (%) Clay [< 2 µm] (%)	61 32 7	61 24 15
pH in Water pH in $CaCl_2$ (0.01 M) pH, saturated paste	8.9 7.9 8.6	5.9 5.1 5.9
Organic Matter [A] (%)	0.6	3.9
Organic Carbon (%)	0.4	2.3
CEC (meq/100 g)	9.6	16.3
Bulk density (g/mL)	1.17	1.22
MWHC (g/100 g) at pF 0	35.2	31.0
MWHC (g/100 g) at 0.33 bar (pF 2.5)	13.0	16.9
Microbial biomass (mg microbial C/100 g dry weight of soil)		
Initial (Day 0) Final (Day 119)	28.0 25.9	25.1 12.3

A) % organic matter = % organic carbon × 1.724
CEC: Cation exchange capacity; MWHC: Maximum Water Holding Capacity

In the OECD 307 test guideline, an organic carbon content of 0.5 – 2.5% is recommended to determine the transformation pathway. Organic carbon of the soil used for the study was 0.35%, however, this content is close to acceptable organic carbon content and, besides, all other soil parameters (clay content, microbial biomass) were acceptable and the study indicated extensive degradation/mineralisation, which confirmed the viability of this soil.

B. Study design

1. Experimental conditions: Samples of 50 g dry weight of soil each were filled into glass incubation flasks and pre-equilibrated prior to treatment at approximate study conditions (darkness, 25 C, 75% of 0.33 bar moisture). At start, each sample received 0.75 mg test substance/kg soil, a dose representing a nominal field rate of 1680g a.s./ha. Following application the samples were attached to flow-through incubation systems with traps to collect ^{14}C-carbon dioxide and other volatile components. Samples were incubated at 25 ±1 C and at 75% of 0.33 bar moisture in the dark for 119 days in maximum. In addition, untreated soil samples were incubated under the same conditions for determination of soil microbial activity.

2. Sampling: Duplicate samples were removed for work-up after 0, 1, 3, 6, 14, 21, 30, 58, 91 and 119 days of incubation. Samples for determination of soil microbial biomass were investigated after 0 and 119 days of incubation. The complete samples were immediately processed by extraction performed the same day.

3. Analytical procedures: The entire soil sample of each test vessel was extracted stepwise by accelerated solvent extractor (ASE, Dionex). The extraction cycle included three successive steps with

acidified (formic acid) aqueous acetonitrile solution (100:100:1, by vol.) at 1500 psi pressure, ambient temperature and a static time of 10 min. This was followed by an aggressive extraction step at 1500 psi pressure, 100°C for 5 min and a static time of 10 min.
The ^{14}C-material balance was established for each sample by extraction, analysis of volatiles and combustion of non-extractable residues. The determination of non-extractable residues (NER) was performed by combustion/LSC of aliquots of the air-dried extracted soil. Following quantitation of radioactivity in extracts by LSC, analysis of concentrated aliquots was performed by reversed phase HPLC and ^{14}C-flow-through detection techniques as primary analytical methods. Representative samples of soil extracts were analysed by normal phase TLC. Finally, confirmation of identity of the test substance and identification of metabolite desmethyl-propamocarb was performed by isolation from soil extracts and co-elution experiments in HPLC with authentic reference material. In addition, mass spectroscopic data were compared for the test substance and metabolite desmethyl-propamocarb isolated from soil extracts and that from authentic reference material.

C. Determination of degradation kinetics: Degradation data were kinetically evaluated according to the simple first order (SFO) kinetic model by use of the software GraphPad™ PRISM® using non-linear optimization.

II. Results and Discussion

A. Data: The results of aerobic biotransformation of [1-*N*-propyl-^{14}C]propamocarb-hydrochloride after incubation in two US soils were summarized below.

Degradation of [1-*N*-propyl-^{14}C]propamocarb-hydrochloride in sandy loam soil Porterville under aerobic conditions (mean ± SD)

Component		Sampling interval (days) 0	1	3	6	14	21
propamocarb-hydrochloride	Mean*	99.0	96.0	93.9	87.0	75.4	64.7
	SD	±1.8	±1.3	±0.0	±4.1	±2.1	±2.0
N-Desmethyl-propamocarb	Mean*	0.0	0.0	0.9	3.5	6.2	8.9
	SD	±0.0	±0.0	±1.3	±1.2	±0.7	±0.1
Unknown	Mean*	0.0	0.0	0.0	0.0	0.0	0.0
	SD	±0.0	±0.0	±0.0	±0.0	±0.0	±0.0
Total extractable radioactivity	Mean*	99.0	96.0	94.9	90.5	81.6	73.6
	SD	±1.8	±1.3	±1.3	±5.3	±2.8	±2.0
Non-extractable radioactivity	Mean*	1.0	1.3	1.5	3.7	4.9	6.6
	SD	±0.4	±0.5	±0.4	±0.1	±1.5	±0.7
14CO2	Mean*	n.d.	1.4	2.9	3.8	10.8	15.6
	SD	n.a.	±0.1	±0.5	±0.8	±0.1	±0.2
Other volatiles	Mean*	n.d.	<0.1	<0.1	<0.1	<0.1	<0.1
	SD	n.a.	±0.0	±0.0	±0.0	±0.0	±0.0
Total radioactivity (%)	Mean*	100.0	98.6	99.2	98.0	97.2	95.9
	SD	±1.4	±0.8	±0.4	±2.8	±1.4	±1.0

Component		Sampling interval (days) 30	58	91	119
propamocarb-hydrochloride	Mean*	56.7	24.8	8.9	6.2
	SD	±3.1	±0.6	±0.1	±0.3
N-Desmethyl-propamocarb	Mean*	9.7	4.9	2.0	0.0
	SD	±0.7	±0.0	±0.6	±0.0
Unknown	Mean*	0.5	0.0	0.0	0.0
	SD	±0.8	±0.0	±0.0	±0.0
Total extractable radioactivity	Mean*	67.0	29.6	11.0	6.2
	SD	±3.0	±0.6	±0.7	±0.3
Non-extractable radioactivity	Mean*	7.0	14.2	16.4	14.8

	SD	±0.2	±3.3	±0.6	±1.2
14CO2	Mean*	24.3	51.3	63.5	73.6
	SD	±1.7	±0.7	±0.3	±5.9
Other volatiles	Mean*	<0.1	<0.1	<0.1	<0.1
	SD	±0.0	±0.0	±0.0	±0.0
Total radioactivity (%)	Mean*	98.3	95.1	90.9	94.6
	SD	±1.1	±3.7	±0.4	±4.5

Values given as percentages of initially applied radioactivity
SD = standard deviation; * Mean values of two replicates; n.d. = not determined; n.a. = not applicable

Degradation of [1-*N*-propyl-^{14}C]propamocarb-hydrochloride in sandy loam soil Aromas under aerobic conditions (mean ± SD)

Component		**Sampling interval** (days)					
		0	**1**	**3**	**6**	**14**	**21**
propamocarb-hydrochloride	Mean*	91.6	86.0	78.4	80.2	75.8	72.0
	SD	±0.5	±1.2	±1.3	±5.5	±0.2	±2.5
N-Desmethyl-propamocarb	Mean*	0.0	0.0	0.0	0.0	0.0	0.0
	SD	±0.0	±0.0	±0.0	±0.0	±0.0	±0.0
Unknown	Mean*	0.0	0.0	0.0	0.0	0.0	0.0
	SD	±0.0	±0.0	±0.0	±0.0	±0.0	±0.0
Total extractable radioactivity	Mean*	91.6	86.0	78.4	80.2	75.8	72.0
	SD	±0.5	±1.2	±1.3	±5.5	±0.2	±2.5
Non-extractable radioactivity	Mean*	8.4	12.4	18.0	17.5	17.3	19.3
	SD	±1.4	±1.6	±1.4	±0.6	±0.7	±2.4
14CO2	Mean*	n.d.	1.0	1.7	2.4	4.4	4.1
	SD	n.a.	±0.0	±0.0	±0.0	±0.0	±4.7
Other volatiles	Mean*	n.d.	<0.1	<0.1	<0.1	<0.1	<0.1
	SD	n.a.	±0.0	±0.0	±0.0	±0.0	±0.0
Total radioactivity (%)	Mean*	100.0	99.4	98.1	100.0	97.5	95.4
	SD	±0.9	±0.4	±0.1	±4.9	±0.9	±4.8

Component		**Sampling interval** (days)			
		30	**58**	**91**	**119**
propamocarb-hydrochloride	Mean*	73.2	64.5	51.5	41.7
	SD	±0.1	±1.0	±2.1	±0.6
N-Desmethyl-propamocarb	Mean*	0.0	0.0	0.0	0.0
	SD	±0.0	±0.0	±0.0	±0.0
Unknown	Mean*	0.0	0.0	0.0	0.0
	SD	±0.0	±0.0	±0.0	±0.0
Total extractable radioactivity	Mean*	73.2	64.5	51.5	41.7
	SD	±0.1	±1.0	±2.1	±0.6
Non-extractable radioactivity	Mean*	17.6	14.9	19.8	17.8
	SD	±1.6	±0.5	±0.4	±0.3
^{14}CO2	Mean*	9.2	17.6	26.8	36.4
	SD	±0.8	±0.8	±1.0	±0.2
Other volatiles	Mean*	<0.1	<0.1	<0.1	<0.1
	SD	±0.0	±0.0	±0.0	±0.0

Total radioactivity (%)	Mean*	100.1	97.0	98.2	95.9
	SD	±2.3	±0.7	±0.7	±0.1

Values given as percentages of initially applied radioactivity
SD = standard deviation; * Mean values of two replicates; n.d. = not determined; n.a. = not applicable

B. Mass balance: The total material balances of radioactivity showed recoveries to range from 96.1 to 100.7% AR for samples of soil Porterville and from 94.4 to 100.3% for soil Aromas. In conclusion, there were no signs for losses of radioactivity during work-up and processing.

Total material balances of radioactivity of ^{14}C-propamocarb-hydrochloride in two US soils

Soil	**Porterville**	**Aromas**
Total Recovery (% AR)	90.9 – 100.0	95.4 – 100.1
Mean (% AR)	96.8	98.2
Rel. standard deviation	2.7	1.7

Values given as percentages of initially applied radioactivity

C. Bound and extractable residues: Values of extractable radioactivity decreased moderately with time accompanied by formation of non-extractable residues as summarized in the table below to finally undergo ultimate degradation. Starting from a complete extractability (91.6 to 99.0% of AR) by day zero values decreased to 6.2 to 41.7% after 119 days of incubation.
In turn, values for non-extractable radioactivity (NER) were low starting from 1.0 to 8.4% AR by day zero to increase to 14.8 to 17.8% after 119 days of incubation.

Extractable and non-extractable residues of ^{14}C- propamocarb-hydrochloride in two US soils (mean ± SD)

Soil	**Extractable residues** (%)		**Non-extractable residues** (%)	
	(day 0)	(day 119)	(day 0)	(day 119)
Porterville	99.0 ±1.8	6.2 ±0.3	1.0 ±0.4	14.8 ±1.2
Aromas	91.6 ±0.5	41.7 ±0.6	8.4 ±1.4	17.8 ±0.3

Values given as percentages of initially applied radioactivity

D. Volatile radioactivity: ^{14}C-propamocarb-hydrochloride was significantly mineralised to ^{14}C-carbon dioxide to account for 73.6 (soil Porterville) and 36.4% of AR (soil Aromas) after 119 days of incubation. Formation of other volatile radioactivity was insignificant (≤ 0.1% AR) at any sampling interval.

E. Transformation of test substance: The active substance was extensively transformed in the course of the study to form NER and ^{14}C-carbon dioxide as predominant transformation products. No formation of other metabolites was observed in soil Aromas in the course of the study. In addition, a transformation product was found in soil Porterville accounting for 9.7% of AR in maximum (day 30). The compound was identified as *N*-desmethyl-propamocarb thus resulting from a loss of a methyl group at the nitrogen in the active substance.
The biotic character of propamocarb-hydrochloride degradation in aerobic soil is underlined by the formation of non-extractable (bound) residues being mineralized finally to carbon dioxide as the product of ultimate degradation.
Based on the new information, the proposed route of degradation of propamocarb-hydrochloride in aerobic soil was amended as summarized in the figure below.

F. Degradation kinetics: The degradation data were evaluated by use of SFO as kinetic model. The results of the kinetic evaluation were summarised in the table below.

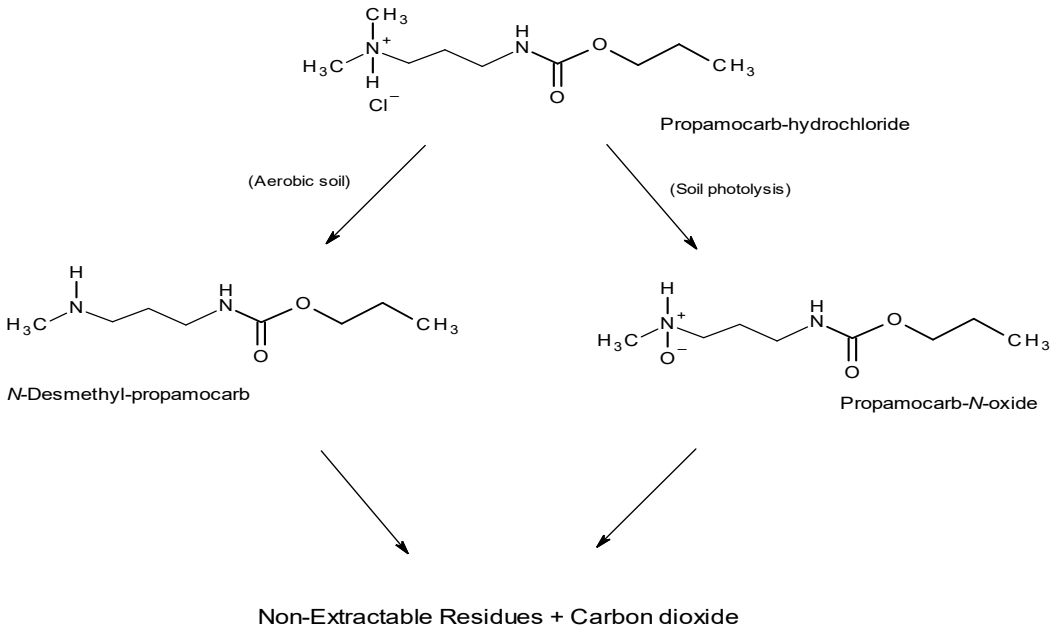
The degradation half-life of propamocarb-hydrochloride was estimated to be 31.4 days in Porterville soil associated with DT_{90}-values of 104 days. For Aromas soil, the corresponding values were 123 days for the DT_{50} and 409 days for the DT_{90}.

Kinetics of aerobic degradation of propamocarb-hydrochloride in two US soils

Soil	Kinetic model	DT_{50} (days)	DT_{90} (days)	r^2
Sandy loam Porterville	SFO	31.4	104	0.99
Sandy loam Aromas	SFO	123	409	0.94

III. Conclusion

Following incubation of radio-labeled propamocarb-hydrochloride in two aerobic soils extensive transformation was observed resulting in the observation of *N*-desmethyl-propamocarb as transformation product.
The overall basic processes of degradation were biotic in nature as demonstrated by de-methylation and the significant formation of ^{14}C-carbon dioxide in the course of the test.
Dependent on soil, the degradation of propamocarb-hydrochloride in aerobic soil was fast to moderate to result in a half-life of 31.4 days for soil Porterville and 123 days for soil Aromas.
The degradation data were kinetically re-evaluated under KCA7.1.2.1.1/01 and KCA7.1.2.1.2/01 for comparison with EU trigger endpoints and to derive input values for modelling in environmental exposure assessments.
The proposed route of degradation of propamocarb-hydrochloride in aerobic soil including soil photolysis was amended accordingly as illustrated in the figure below**.**



Amended route of degradation of propamocarb-hydrochloride in aerobic soil

RMS´s opinion:

Reliability of the study: score 2 of the scoring system of Klimisch *et al*.(1997).

The existing studies and the new information were evaluated kinetically according to actual FOCUS Guidance in order to derive values, for the half-lives and the DT_{90} for comparison with trigger endpoints

and half-lives for modeling endpoints. The re-evaluation, detailed in KCA 7.1.2.1.1/16, superseded the existing kinetic evaluations.

Report:	KCA 7.1.2.1.1/16; Oberdoerster, C.; Boiselle, N.; Hoerold, C.; 2015b; M-541770-01-1
Title:	Kinetic evaluation of the degradation of propamocarb-hydrochloride and its metabolite N-desmethyl-propamocarb in soil under aerobic laboratory conditions
Report No.:	EnSa-14-1331
Document No.:	M-541770-01-1
Guideline(s):	"Generic Guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". EC Document Reference: None, version 1.1, 2015 amending "Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference Sanco/10058/2005 version 2.0, 2006
Guideline deviation(s):	not applicable
GLP/GEP:	**No**

For the active substance propamocarb-hydrochloride degradation data as referenced under KCA7.1.2.1.1/01 to KCA7.1.2.1.1/08 and KCA7.1.2.1.1/15 were kinetically evaluated according to actual FOCUS Guidance to derive values for the half-life and the DT_{90} in aerobic soil from studies performed at 15 to 25°C for modelling and trigger endpoints.
A total of eight aerobic soil degradation studies under conditions of the laboratory was considered to consist of 17 data sets in total following application of [1-*N*-propyl-^{14}C]- or [2-*N*-propyl-^{14}C]-propamocarb-hydrochloride to different soils.
At the study KCA7.1.2.1.1/15, throughout the study incubation, the soil was in contact with air via the flow-through test system apparatus. The test systems were maintained in a dark environmental chamber at a controlled temperature of 25 ± 1 °C (average = 25.2 °C, range 25.1-25.4 °C). The moisture content of each soil was maintained at 75 ± 10% of ⅓ bar moisture by adding water at 34 and 84 days post-treatment. The microbial biomass at the start of the study (day 0) was 28.0 µg/g (dry basis) in the Porterville soil and 25.1 µg/g (dry basis) in the Aromas soil. The microbial biomass at the end of the study (day 119) was 25.9 µg/g (dry basis) in the Porterville soil and 12.3 µg/g (dry basis) in the Aromas soil. Therefore, both soils sustained their viability
The calculations of half-lives in soil followed a stepwise approach. For identification of best fits to the measured data, the SFO kinetic model was applied as the initial step. This was followed by application of bi-phasic models, i.e. FOMC or DFOP, in case of unacceptable fits according to the criteria set. The resulting best fits served as the basis to derive non-normalized half-lives for comparison against trigger endpoints. In a next step, values for the DT_{50} were normalized to reference conditions (20°C, pF2 moisture).

Trigger endpoints: Non-normalised values of the DT_{50} and the DT_{90} for tests performed at 15º to 25°C were derived from SFO best fits for all data sets with results summarized in Table CA 8.1.2.1.1-01.
Non-normalised half-lives of propamocarb-hydrochloride ranged from 7.9 days for German loamy sand soil (KCA 7.1.2.1.1/03) to 136.7 days for Minnesota clay loam soil (KCA 7.1.2.1.1/06), while values for the DT_{90} ranged from 26.1 days to 454.2 days for the same soils, respectively.

Comparison against EU triggers: Summary of results of kinetic evaluation of degradation for propamocarb-hydrochloride in aerobic soil in the laboratory:

Parameter	**propamocarb-hydrochloride**
20°C, Non-normalised DT_{50}, range (days)	7.9 – 136.7
Worst case DT_{50} (days)	**136.7**
20°C, Non-normalised DT_{90}, range (days)	26.1 – 454.2
Worst case DT_{90} (days)	**454.2**

Modelling endpoints: SFO was confirmed to be considered as the visually and statistically best acceptable kinetic model for deriving modelling endpoints for all soil data sets. Values were normalized, by comparison of study incubation conditions, to reference conditions (20°C, pF2 moisture), which results are summarised in Table CA 8.1.2.1.1-02.
For use as modelling endpoint, the **overall mean** normalised half-life of propamocarb-hydrochloride was estimated to 23.1 days.

Modelling endpoints: Normalised laboratory DT_{50} values for propamocarb-hydrochloride in aerobic soil, for use as input in environmental exposure assessments

Parameter	**propamocarb-hydrochloride**
Normalised (20°C, pF2) DT_{50}, range (days)	8.4 – 149.1
Geometric mean (days)	**23.1**

I. Material and Methods

The degradation data were kinetically evaluated following FOCUS guidance [FOCUS, 2006, amended 2011][3] with the software KinGUI2.
The actual kinetic evaluation considered those data sets that were considered reliable and valid by the RMS during the assessment for Annex I inclusion.
The kinetic evaluation relied on a total set of eight aerobic soil degradation studies performed with the active substance at 15 to 25°C to result in 17 data sets in total including re-assessment of reliability. The data sets along with the characteristics of soils were summarised in the table below.
The two potential data sets excluded within the Annex I inclusion process were from studies KCA 7.1.1.1/08 and KCA 7.1.1.1/09. Moreover, one of two data sets of study KCA 7.1.2.1.1/05 was excluded due to reasons detailed below.
For the data set of study KCA 7.1.1.1/08, the reason for exclusion was the fact that the investigations were performed in cultural media with microbial populations derived from soil instead of the use of fully 'native' soil. Design and results were thus not comparable to those of a standard aerobic soil study.
For the data set of study KCA 7.1.1.1/09, the reason for exclusion was that no samples were taken for analysis at day zero. This fact was accompanied by a low total recovery below 90% AR for first sampling interval (day 1 after application). The design and results were thus not comparable to actual standard aerobic soil studies.
The reason to exclude one of the two data sets of study KCA 7.1.1.1/05 was the fact that the study design included investigations of degradation following a repeated application. In view of actual standards in design of soil degradation studies this was a significant deviation since degradation after repeated application was not independent of the first application. Considering the structure of the active substance it cannot be excluded that enhanced microbial degradation was induced by the first application. Again, this is in contradiction with actual standards in soil degradation testing requiring soils at least being free of residues of the same class as the test substance.
For the two data sets resulting from tests at 10°C (KCA 7.1.2.1.1/07 and KCA 7.1.2.1.1/05), the reason for exclusion was the incubation at this non-standard test temperature combined with the fact that degradation data were available in the same soil at the test temperature of 20°C. The data sets were kinetically re-evaluated as summarized separately in detail below, i.e. after the evaluation of studies performed at 15 to 25°C.
The kinetic evaluation derived DT50 values according to the respective decision flowchart for the determination of trigger endpoints and for use as input parameters in modelling.

- All data sets were evaluated using simple first order (SFO), first order multi-compartment (FOMC) and double first order in parallel (DFOP) kinetics with free optimisation of parameters.
- The kinetic evaluations and the statistical calculations were conducted with KinGUI (v2.0) using iteratively re-weighted least-square (IRLS) optimization.

[3] FOCUS (2006): "Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". Report of the FOCUS Work Group on Degradation Kinetics, EC Document Reference Sanco/10058/2005 version 2.0

- The measured values were taken into account as reported and thus treated as individual replicates. All sets with their data points were weighted equally.
- For day zero samples, total residues of propamocarb-hydrochloride were set to the amount recovered.

For the evaluation of results the following was considered in addition:

- In a first and major step the assessment of fits was made on the basis of visual inspection. The visual inspection focused on residuals to be minimal compared to the measured data and should randomly distributed around zero. Systematic variations of the residuals can be regarded as an indication for an inappropriate kinetic model. However, in case of sufficiently small, but systematic deviations, a fit may be still qualified to be visually acceptable.
- The quantitative statistical measure for the quality of a fit was expressed in terms of chi square (χ^2) with the latter to be a minimum.
- For a check of parameter significance the evaluation included a test to identify the probability that a parameter is not significantly different from zero, here expressed in terms of a t-test.
- The identification of the most appropriate kinetic model was based on visual inspection and the scaled error (χ^2). Since most exposure models use SFO, this is the kinetic model of choice. If case the SFO fit was visually acceptable and the scaled error χ^2 did not significantly exceed 15 %, the SFO fit and its parameters were regarded as acceptable.
- In case the value of χ^2 was significantly higher than 15 %, other kinetic models were tested and/or model parameters were fixed based on available information (e.g. initial amount). The model with the smaller error is finally chosen as the appropriate model. For metabolite fits also higher values of χ^2 were accepted.
- In case the measured residues of the compound applied were below 10 % at study end, the Gustafson-Holden (FOMC) model was applied as an alternative. Provided the FOMC fit was visually acceptable and significantly better than the SFO fit with a χ^2 error significantly below 15%, the FOMC fit and its parameters was accepted. An equivalent single first-order half-life was 'back-calculated' on the basis of $DT_{90\ FOMC}$ / 3.32, while the $DT_{90\ FOMC} = \beta\ (10^{1/\alpha} - 1)$. The equivalent SFO-curve then meets the FOMC-curve at the time $DT_{90\ FOMC}$ thus over-predicting the residues at earlier time points as a conservative element.
- In case the measured residues at study end were higher than 10 % of the applied amount, the dual first order in parallel (DFOP) or the hockey stick (HS) model were considered. If the respective fit was acceptable applying the criteria discussed above, the fitted parameter values were considered. Then, a very conservative equivalent single first-order half-life was calculated from the lower of the two kinetic rates. In effect the resulting equivalent SFO-curve over-predicts the residues at all time points.
- In case none of the alternative models had led to a significantly improved fit, the SFO model was chosen, when visually acceptable. The purpose of these rules is to finally avoid over-parameterised models just based on a marginally better fit.
- The value for the scaled error χ^2 of 15 % should not be handled as a threshold and thus as a strict and absolute cut-off criterion since this value is most appropriate only under optimal experimental conditions. While the value of χ^2 may exceed 15 %, the model fit may still describe reasonably well the degradation behaviour. In particular for metabolites it may be justified to accept higher values, due to generally low measurements compared to the mean of all measurements, which strongly influences the results of the χ^2 test.

Degradation studies performed with propamocarb-hydrochloride in aerobic soil under laboratory conditions, including characteristics of soils

Study	Soil	Soil texture	Test temperature (°C)	Test moisture (%w/w)	Sand (%)	Clay (%)	Org. carbon (%)	pH ($CaCl_2$)	CEC (meq / 100 g)
KCA 7.1.2.1.1/01	(LS2.2)	loamy sand	25	27	86.7	5	2.4	6.6	11.2
KCA 7.1.2.1.1/02	California	loamy sand	25	22.5	88.4	4.1	1.1	5.2	5.0

KCA 7.1.2.1.1/03	German	loamy sand	25	34.1	85.4	6.6	2.3	6.6	n.a.
KCA 7.1.2.1.1/04	LS2.2	loamy sand	15	27	86.7	5	2.4	6.6	11.2
	SL2.3	sandy loam	15	23.3	75.7	8.9	0.9	5.7	6.0
KCA 7.1.2.1.1/05	LS2.2	loamy sand	25	27	86.7	5	2.4	6.6	11.2
KCA 7.1.2.1.1/06	Minnesota	clay loam	20	22.8	25.3	32.2	3.15	5.8	24
	Sarotti	silt loam	20	16.2	12.1	17.7	1.3	7.4	13
	Abington	sandy loam	20	19.8	61.6	16.4	1.86	7.4	18
	Borstel	loamy sand	20	12.2	77.5	4.0	1.04	5.8	8
KCA 7.1.2.1.1/07	A, B6*	sandy loam	20	12.2	54	11	2.5	6.7	14.6
	B, B7	clay loam	20	14.4	24	20	4.5	6.2	17.8
	C, B8	clay loam	20	14.4	33	34	2.7	7.3	22.2
	D, B9	sandy loam	20	12.2	75	12	1.3	4.9	11.1
	F, B6*	sandy loam	20	12.2	54	11	2.5	6.7	14.6
KCA 7.1.2.1.1/15	Aromas	sandy loam	25	9.8	61	15	2.3	5.1	16.3
	Porterville	sandy loam	25	12.7	61	7	0.4	7.9	9.6

*: Variation of application rate

II. Results and Discussion

Trigger endpoint determination:

According to the decision criteria, the bi-phasic models FOMC and DFOP showed no improvement over SFO kinetics. SFO kinetics was determined to be the best-fit for all data sets.

The resulting non-normalised values for the DT_{50} and the DT_{90} derived are summarised in the table below.

Trigger evaluation: Non-normalised DT_{50} values for propamocarb-hydrochloride in aerobic soils at 15°C to 25°C under laboratory conditions

Soil	Label position	Model	DT_{50} (days)	DT_{90} (days)	Chi^2 (%)	t-test/ confidence interval	VA[a)]
LS2.2, loamy sand, 25°C (Study 1)	1-*N*-propyl	SFO	13.2	43.7	17.8	k = 0.006	+
California, loamy sand, 25°C (Study 2)	1-*N*-propyl	SFO	30.0	99.7	16.3	k = 0.012	+
German, loamy sand, 25°C (Study 3)	1-*N*-propyl	SFO	7.9	26.1	19.0	k = 0.002	+
LS2.2, loamy sand, 25°C (Study 4)	1-*N*-propyl	SFO	17.0	56.5	17.2	k = 0.001	O
SL2.3, sandy loam, 20°C (Study 4)	1-*N*-propyl	SFO	22.0	73.0	18.7	k = 0.001	-*
LS2.2, loamy sand, 25°C (Study 5)	1-*N*-propyl	SFO	11.2	37.2	14.6	k = 0.001	++
Minnesota, clay loam, 20°C (Study 6)	1-*N*-propyl	SFO	136.7	454.2	3.4	k < 0.001	+
Sarotti, silt loam, 20°C (Study 6)	1-*N*-propyl	SFO	11.7	38.9	9.3	k < 0.001	+
Abington sandy loam, 20°C (Study 6)	1-*N*-propyl	SFO	11.2	37.1	10.1	k < 0.001	+
Borstel, loamy sand, 20°C (Study 6)	1-*N*-propyl	SFO	29.8	99	12.4	k < 0.001	+
A, B6, Woolverstone, sandy loam, 20°C (Study 7)	2-*N*-propyl	SFO	22.6	75	13.2	k < 0.001	+
B, B7, Quarter, clay loam, 20°C (Study 7)	2-*N*-propyl	SFO	23.4	77.8	9.8	k < 0.001	O
C, B8, Empingham, clay loam, 20°C (Study 7)	2-*N*-propyl	SFO	17.8	59	15.1	k < 0.001	O
D, B9, Baylham, sandy loam, 20°C (Study 7)	2-*N*-propyl	SFO	87.7	291.5	7.0	k < 0.001	+

F, B6, Woolverstone, sandy loam, 20°C (Study 7)	2-*N*-propyl	SFO	14.1	46.8	8.4	k < 0.001	++
Aromas sandy loam, 25°C (Study 8)	1-*N*-propyl	SFO	123.2	409.3	3.4	k < 0.001	++
Porterville sandy loam, 25°C (Study 8)	1-*N*-propyl	SFO	31.4	104.4	3.8	k < 0.001	++

Study 1: KCA 7.1.1.1 /01 and KCA 7.1.2.1.1 /01; Study 2: KCA 7.1.1.1 /02 and KCA 7.1.2.1.1 /02; Study 3: KCA 7.1.1.1 /03 and KCA 7.1.2.1.1 /03; Study 4: KCA 7.1.1.1 /04 and KCA 7.1.2.1.1 /04; Study 5: KCA 7.1.1.1 /05 and KCA 7.1.2.1.1 /05; Study 6: KCA 7.1.1.1 /06 and KCA 7.1.2.1.1 /06; Study 7: KCA 7.1.1.1 /07 and KCA 7.1.2.1.1 /07; Study 8: KCA 7.1.1.1 /11, KCA 7.1.2.1.1 /15 and KCA 7.1.2.1.2 /01;

[a)] VA = Visual Assessment (++ = excellent, + = good, O = acceptable, - = not acceptable)

* SFO fit statistically acceptable and visually poor. Worst case since fit resulted in overestimation of residues for later sampling intervals. Fits from FOMC and DFOP statistically worse in terms of values for Chi^2 and t-test.

Modelling endpoint determination:

The FOCUS Kinetics modelling endpoint flowchart [FOCUS, 2006] was used to evaluate the datasets. The SFO kinetic model was considered visually and statistically acceptable for deriving modelling endpoints for all data sets, thus, with no improvement when applying bi-phasic kinetic models like FOMC or DFOP.

It should be noted that the evaluation of the biphasic fits resulted in identical DT50 and chi2 error values for example in the studies of Brühl and Celorio (1978-1980). Further inspection showed a statistically non valid t-test for the g-factor for the DFOP model. As the g factor for the biphasic fits is either 1 or < 0.001, a biphasic plot could not be fitted as you have either a fast phase (g=1) and no slow phase and vice versa, therefore, the plots look like the SFO plots, as they describe a single phase.

Consequently, the SFO fits were chosen for either trigger and modelling endpoint, as biphasic fits were not appropriate.

For the use in environmental modeling, the degradation half-lives were normalised to reference conditions regarding soil moisture (100% field capacity) and temperature (20°C). The parameters used in the laboratory tests and the respective correction factors calculated were summarised in the table below.

Correction factors for soil temperature and moisture content:

Soil	Temperature (°C)	Correction factor Temperature	Incubation moisture (%w/w)	pF2 moisture (%w/w)	Correction factor Moisture	Total correction factor
LS2.2, loamy sand, (Study 1)	25	1.6062	27.0	14	1.0000	1.6062
California, loamy sand (Study 2)	25	1.6062	22.5	14	1.0000	1.6062
German, loamy sand (Study 3)	25	1.6062	34.1	14	1.0000	1.6062
LS2.2, loamy sand (Study 4)	15	0.6226	27.0	14	1.0000	0.6226
SL2.3, sandy loam (Study 4)	15	0.6226	23.3	19	1.0000	0.6226
LS2.2, loamy sand (Study 5)	25	1.6062	27.0	14	1.0000	1.6062
Minnesota, clay loam (Study 6)	20	1.0000	22.8	28	0.8652	0.8652
Sarotti, silt loam (Study 6)	20	1.0000	16.2	26	0.7190	0.7190
Abington sandy loam (Study 6)	20	1.0000	19.8	14	1.0000	1.0000
Borstel, loamy sand (Study 6)	20	1.0000	12.2	14	0.9088	0.9088
A, B6, Woolverstone, sandy loam (Study 7)	20	1.0000	12.2	19	0.7313	0.7313
B, B7, Quarter, clay loam (Study 7)	20	1.0000	14.4	28	0.6278	0.6278
C, B8, Empingham, clay loam (Study 7)	20	1.0000	14.4	28	0.6278	0.6278

D, B9, Baylham, sandy loam (Study 7)	20	1.0000	12.2	19	0.7313	0.7313
F, B6, Woolverstone, sandy loam (Study 7)	20	1.0000	12.2	19	0.7313	0.7313
Porterville sandy loam (Study 8)	25	1.6062	12.7	19	0.7532	1.2099
Aromas sandy loam (Study 8)	25	1.6062	9.8	19	0.6269	1.0069

Study 1: KCA 7.1.1.1 /01 and KCA 7.1.2.1.1 /01; Study 2: KCA 7.1.1.1 /02 and KCA 7.1.2.1.1 /02;
Study 3: KCA 7.1.1.1 /03 and KCA 7.1.2.1.1 /03; Study 4: KCA 7.1.1.1 /04 and KCA 7.1.2.1.1 /04;
Study 5: KCA 7.1.1.1 /05 and KCA 7.1.2.1.1 /05; Study 6: KCA 7.1.1.1 /06 and KCA 7.1.2.1.1 /06
Study 7: KCA 7.1.1.1 /07 and KCA 7.1.2.1.1 /07;
Study 10: KCA 7.1.1.1 /11, KCA 7.1.2.1.1 /15 and KCA 7.1.2.1.2 /01

The resulting normalised half-lives are summarised in the table below.

Normalised (20°C and pF2) DT_{50} values for propamocarb-hydrochloride as modelling endpoints:

Soil	Kinetics	Trigger DT_{50} (days)	Trigger DT_{90} (days)	Non-normalised DT_{50} estimate for modelling (days)	DT_{50} [20°C and pF2] (days)
LS2.2, loamy sand, (Study 1)	SFO	13.2	43.7	13.2	21.1
California, loamy sand (Study 2)	SFO	30.0	99.7	30.0	48.2
German, loamy sand (Study 3)	SFO	7.9	26.1	7.9	12.6
LS2.2, loamy sand (Study 4)	SFO	17.0	56.5	17.0	10.6
SL2.3, sandy loam (Study 4)	SFO	22.0	73.0	22.0	13.7
LS2.2, loamy sand (Study 5)	SFO	11.2	37.2	11.2	18.0
Minnesota, clay loam (Study 6)	SFO	136.7	454.2	136.7	118.3
Sarotti, silt loam (Study 6)	SFO	11.7	38.9	11.7	8.4
Abington sandy loam (Study 6)	SFO	11.2	37.1	11.2	11.2
Borstel, loamy sand (Study 6)	SFO	29.8	99	29.8	27.1
A, B6, Woolverstone, sandy loam (Study 7)	SFO	22.6	75	22.6	(16.5)
F, B6, Woolverstone, sandy loam (Study 7)	SFO	14.1	46.8	14.1	(10.3)
Geometric mean A/F, B6 (used for calculation of overall mean)					13.0 *
B, B7, Quarter, clay loam (Study 7)	SFO	23.4	77.8	23.4	14.7
C, B8, Empingham, clay loam (Study 7)	SFO	17.8	59	17.8	11.2
D, B9, Baylham, sandy loam (Study 7)	SFO	87.7	291.5	87.7	64.2
Aromas sandy loam (Study 8)	SFO	123.2	409.3	123.2	149.1
Porterville sandy loam (Study 8)	SFO	31.4	104.4	31.4	31.6
Geometric mean					**23.1**

Study 1: KCA 7.1.1.1 /01 and KCA 7.1.2.1.1 /01
Study 2: KCA 7.1.1.1 /02 and KCA 7.1.2.1.1 /02
Study 3: KCA 7.1.1.1 /03 and KCA 7.1.2.1.1 /03
Study 4: KCA 7.1.1.1 /04 and KCA 7.1.2.1.1 /04
Study 5: KCA 7.1.1.1 /05 and KCA 7.1.2.1.1 /05
Study 6: KCA 7.1.1.1 /06 and KCA 7.1.2.1.1 /06

Study 7: KCA 7.1.1.1 /07 and KCA 7.1.2.1.1 /07
Study 8: KCA 7.1.1.1 /11, KCA 7.1.2.1.1 /15 and KCA 7.1.2.1.2 /01
* The geometric mean value was used for calculation of overall mean as the soil incubation conditions were the same

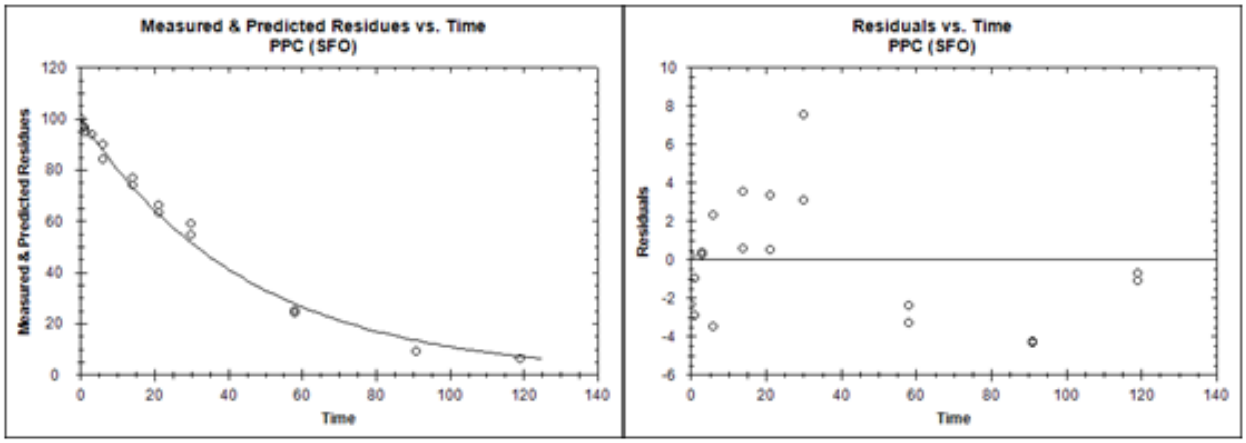
Visual assessment and the figures of the pathway fit propamocarb-hydrochloride + N-desmethyl-propamocarb with the fit of the kinetic analysis (which support the validity of the endpoints):

Trigger endpoints:

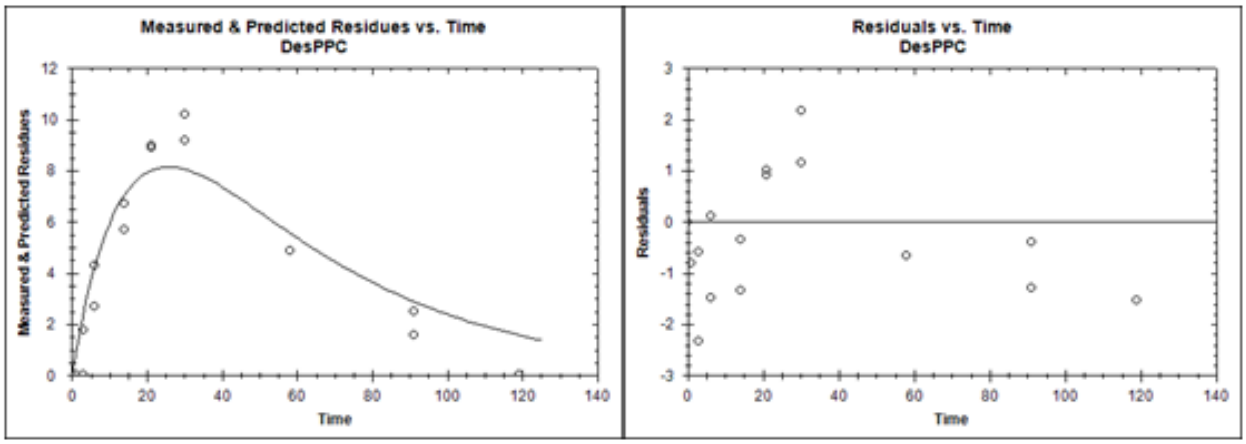
5.1.8 Desmarteau, 2006

Table 22: **Porterville**: **Trigger endpoints** and statistical parameters of propamocarb-hydrochloride (9.3.12)

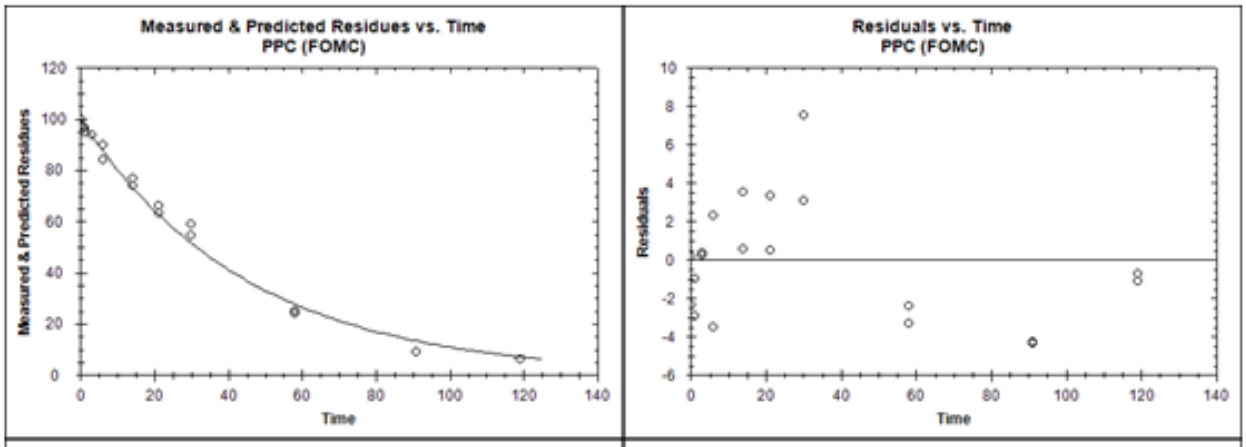
Substance	Fitted parameters	Type of kinetic	X^2 error [%]	p (t-test)	Visual fit	DT_{50} [d]	DT_{90} [d]
PPC-HCl	M_0: 100.10 k: 0.0221	SFO	3.43	k < 0.001	++	**31.42**	104.4
	M_0: 100.1 α: 28260.0 β: 1281000	FOMC	3.60	-	++	31.42	104.4
► SFO fit better than FOMC (Chi^2), SFO provides very good fit							
► **Conclusion**: DT50 is well described using SFO kinetics							
N-desmethyl-PPC (pathway fit)	M_0: 0 k: 0.0624	SFO	22.00	k < 0.001	o	**11.11**	36.91
	M_0: 0 α: 551100 β: 24800000	FOMC	22.00	-	o	11.11	36.91
► SFO fit better than FOMC (Chi^2), SFO provides acceptable fit							
► **Conclusion**: DT50 is well described using SFO kinetics							


Measured & Predicted Residues vs. Time
PPC (SFO)
Measured & Predicted Residues
Time

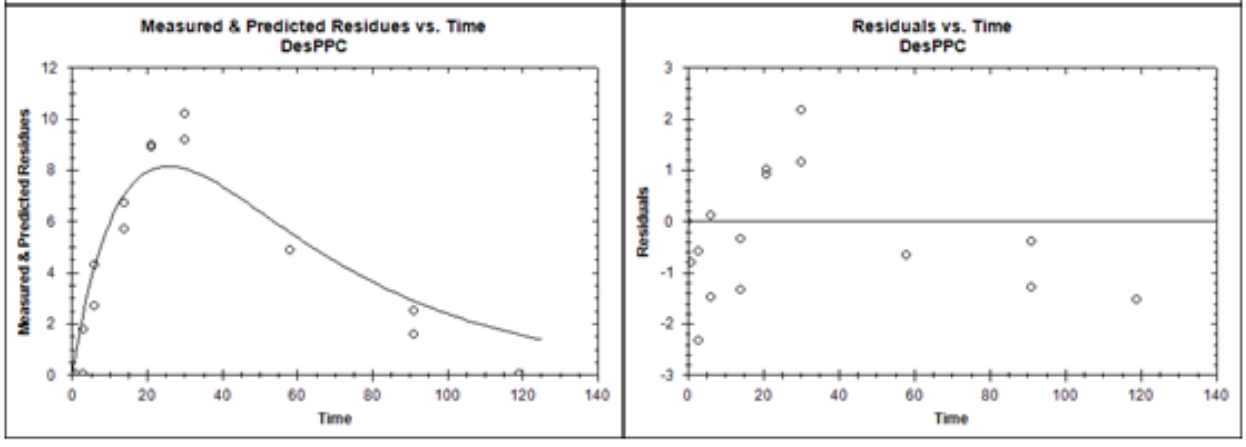
Residuals vs. Time
PPC (SFO)
Residuals
Time


Measured & Predicted Residues vs. Time
DesPPC
Measured & Predicted Residues
Time

Residuals vs. Time
DesPPC
Residuals
Time


Measured & Predicted Residues vs. Time
PPC (FOMC)
Measured & Predicted Residues
Time

Residuals vs. Time
PPC (FOMC)
Residuals
Time

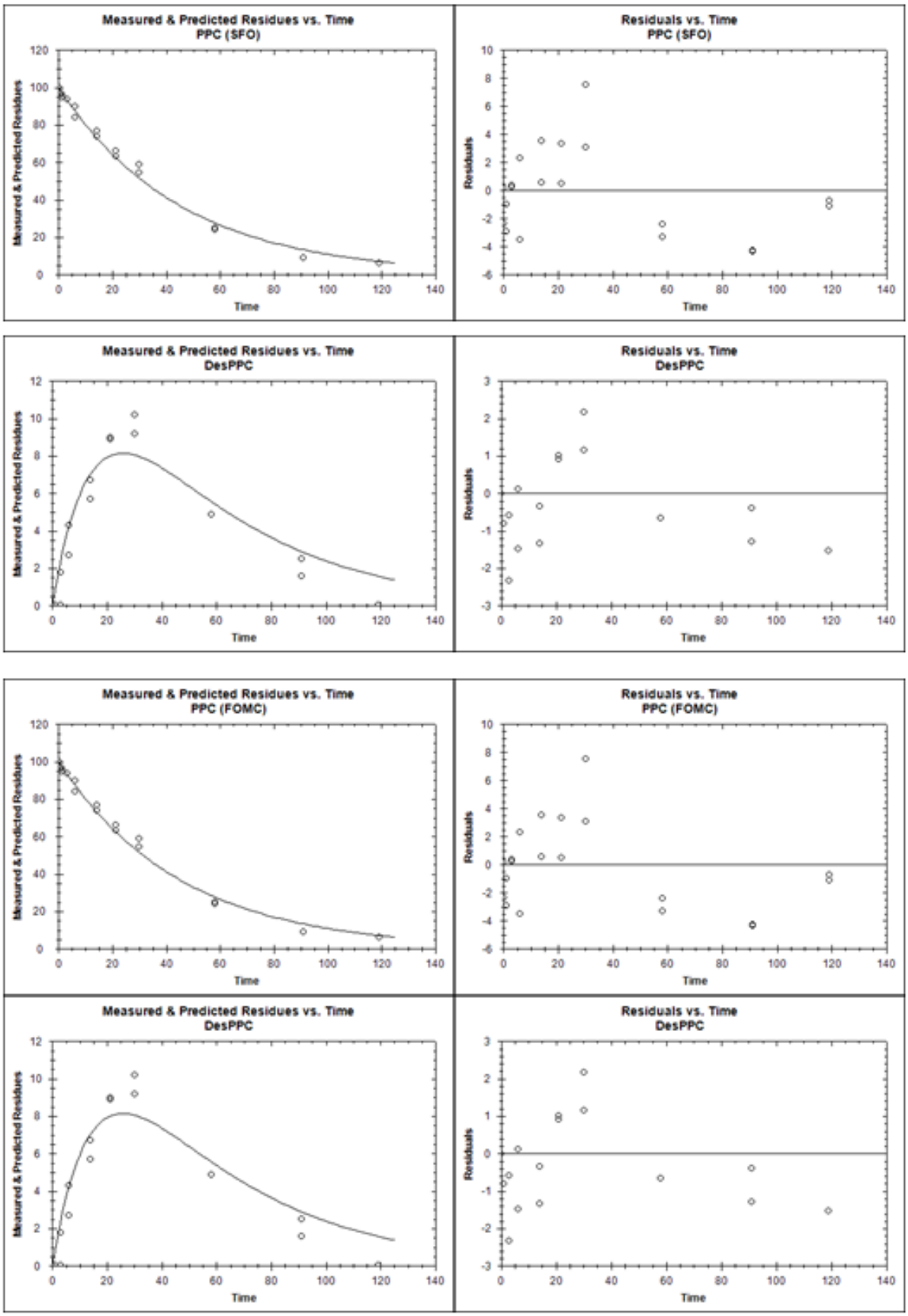

Measured & Predicted Residues vs. Time
DesPPC
Measured & Predicted Residues
Time

Residuals vs. Time
DesPPC
Residuals
Time

Modelling endpoints:

Table 40: **Porterville**: **Modelling endpoints** and statistical parameters of propamocarb-hydrochloride (9.4.11)

Substance	Fitted parameters	Type of kinetic	X^2 error [%]	p (t-test)	Visual fit	DT_{50} [d]	DT_{90} [d]
PPC-HCl	M_0: 100.10 k: 0.0221	SFO	3.43	k < 0.001	++	**31.42**	104.4
	M_0: 100.1 α: 28260.0 β: 1281000	FOMC	3.60	-	++	31.42	104.4
► SFO provides very good fit							
► **Conclusion**: DT50 is well described using SFO kinetics							
N-desmethyl-PPC (pathway fit)	M_0: 0 k: 0.0624 ff: 0.4035	SFO	22.00	k < 0.001 ff <0.001	o	**11.11**	36.91
	M_0: 0 α: 551100 β: 24800000	FOMC	22.00	-	o	11.11	36.91
► SFO fit better than FOMC (Chi²), SFO provides acceptable fit, a formation fraction could be derived							
► **Conclusion**: DT50 is well described using SFO kinetics, the formation fraction of 0.4035 is acceptable							


Measured & Predicted Residues vs. Time
PPC (SFO)
Measured & Predicted Residues
Time
Residuals vs. Time
PPC (SFO)
Residuals
Time
Measured & Predicted Residues vs. Time
DesPPC
Measured & Predicted Residues
Time
Residuals vs. Time
DesPPC
Residuals
Time
Measured & Predicted Residues vs. Time
PPC (FOMC)
Measured & Predicted Residues
Time
Residuals vs. Time
PPC (FOMC)
Residuals
Time
Measured & Predicted Residues vs. Time
DesPPC
Measured & Predicted Residues
Time
Residuals vs. Time
DesPPC
Residuals
Time

III. Conclusion

The evaluation of aerobic soil degradation data of tests performed at 15°C to 25°C according to actual FOCUS kinetic guidance resulted in values for non-normalised half-lives and the DT_{90} of the active substance propamocarb-hydrochloride for comparison with EU trigger endpoints.
Degradation was found to be adequately described by SFO as kinetic model for all data sets to fit with experimental data.
Values of non-normalised half-lives from best fits to measured data were found to range from 7.9 days for German loamy sand to 136.7 days for a Minnesota clay loam soil. The corresponding DT_{90} ranged from 26.1 days to 454.2 days for the same soils, respectively.
The evaluation according to FOCUS kinetic guidance resulted in values for half-lives of the active substance propamocarb-hydrochloride in aerobic soil for use as modelling input parameters in environmental risk assessments.
The approach for fitting with experimental data resulted in the use of the SFO kinetic model to derive non-normalised values for the DT_{50} then normalised for moisture (pF2) and temperature (20°C).
The values derived from laboratory tests are regarded as suitable and reliable for use in environmental exposure assessments.
It should be noted that the evaluation of the biphasic fits resulted in identical DT50 and chi^2 error values for example in the studies of Brühl and Celorio (1978-1980). Further inspection showed a statistically non valid t-test for the g-factor for the DFOP model. As the g factor for the biphasic fits is either 1 or < 0.001 a biphasic plot could not be fitted as you have either a fast phase (g=1) and no slow phase and vice versa, therefore the plots look like the SFO plots, as they describe a single phase.
Consequently the SFO fits were chosen for either trigger and modelling endpoint, as biphasic fits were not appropriate.
The study was performed according to the instructions of the valid guideline FOCUS kinetics report (2014) with the respective data and the model KinGUI 2.1.
For the active substance propamocarb-hydrochloride, a normalised geometric mean half-life of 23.1 days was calculated as modelling endpoint.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Data on the rate of degradation at 10°C had been generated in studies KCA 7.1.2.1.1/07, KCA 7.1.2.1.1/08, and KCA 7.1.2.1.1/09

Report:	KCA 7.1.2.1.1/08; Fent, G.; Hein, W.; 2001; M-203301-01-1
Title:	Degradation and metabolism of propamocarb-HCL (AE B066752) in one soil at 10 degrees C
Report No.:	AGR21; C012749
Document No.:	M-203301-01-1
Guideline(s):	SETAC Procedures for Assessing the Environmental Fate and Ecotoxicity of Pesticides Part 1 1.1, March 1995
Guideline deviation(s):	None
GLP/GEP:	**Yes**

Comment: key elements in design and conduct reported as for actual guideline studies. Study regarded as scientifically valid.

Executive Summary

The route of degradation of propamocarb hydrochloride was investigated in a laboratory study at 10°C ± 2°C using a loamy silt soil under aerobic conditions. Soil samples were kept incubated in the dark.

A laboratory investigation using a loamy silt test soil (Sarotti) indicate that propamocarb hydrochloride, applied at a rate of 4.8 g/kg dry soil, corresponding to a field rate of 3.6 kg a.s./ha, degrades readily

under aerobic experimental conditions at a temperature of 10°C. Carbon dioxide was the principal degradation product, reaching a maximum of 57.9% (or 59.8% of the average day 120 sampling point). NER bound to soil also increased slightly during the study duration, whilst the amount of radioactivity extracted from the soil decreased over time. Extracted radioactivity consisted principally of propamocarb hydrochloride.

In addition, up to six unidentified polar metabolites were observed during the study with one individual component of up to 5.5% (for characterisation and identification of component > 5% AR see study KCA 7.1.1.1/10). No recognisable pattern of formation was determined for all the metabolites observed in the study indicating that the metabolites are transient in nature.

Despite the lower incubation temperature propamocarb hydrochloride showed similar CO_2 formation and a high degradation potential in the Sarotti soil, which was comparable to an experiment conducted at 20°C (study C012748 – AGR20).

I. Material and Methods

A. Materials

1. Test Material: Common name: propamocarb hydrochloride
Chemical name: propyl 3-(dimethylamino) propylcarbamate hydrochloride
Radiolabelled purity: > 99.0%
Lot # IS1795-21
Specific activity 8.76 MBq/mg
Non-radiolabelled purity: 744.0 g/L
Lot # 934578

2. Soil:

Characteristics of test soil

Soil		**Sarotti**
Origin		Germany
Sampling date		Oct. 07, 1999
Sampling depth		0-20 cm
Soil texture[1),2)]		Loamy silt
Sand (%)[2)]	(63 µm - 2 mm)	12.1
Silt (%)[2)]	(2 µm – 63 µm)	70.2
Clay (%)[2)]	(< 2 µm)	17.7
pH ($CaCl_2$) [3)]		7.383
Organic substance [2)] org. Substance (%) org. Carbon (%)		 2.24 1.30
Cation exchange capacity [2)] (meq/100 g)		 13
Nitrogen content [2)] (mg/100 g)		 110
Lime content [2)] (in % $CaCO_3$)		 0.9
Maximum water holding capacity (g H_2O/100 g dry soil)		 40.57
Internal SLFA soil number		91

Note: 1)According to DIN 19682
2) Determined by Lufa Speyer, Obere Langgasse 40, 67436 Speyer (report dated Feb. 17, 2000)
3) Determined by the Test Facility

B. Study design

1. Experimental conditions: The test system was connected with soda lime traps and oil-wetted glass wool for the adsorption of volatile organics and $^{14}CO_2$. The soil samples were treated with propamocarb hydrochloride at an application rate of 0.48mg/100g dry soil, corresponding to a rate equivalent to 3.61kg a.s/ha. The temperature was held at 10 C ± 2°C, in dark conditions, and the moisture content of the soil samples was set to 45% of the MWHC, corresponding to a soil moisture content of 18.25g water/100g dry soil. Gas exchange was kept aerobic. Microbial biomass was tested in the soil simultaneously to the application and at the end of the incubation period according to the Anderson and Domsch method[4].

2. Sampling: Sampling of the soil test systems were undertaken at intervals of 0 h (immediately after application), 7, 14, 21, 28, 35, 43, 56, 84, and 120 days. At each sampling point duplicate sub-samples were removed for analysis. At each sampling date the units were flushed with air in order to transfer all organic volatiles into the trapping system.

3. Analytical procedures: Each soil sample was exhaustively extracted 3 times with 100 mL acetonitrile/water (4:1 v/v; pH< 4 with formic acid). However, if non-extractable radioactivity was greater than 10% of the applied after the first extraction then further extraction was undertaken using acetonitrile/water (4:1 v/v). If radioactivity in the second extract exceeded 2% of the applied radioactivity the extract was concentrated and subsequently analysed by TLC. Radioactivity of extracts was determined by Liquid Scintillation Counting (LSC). Soil samples that were not directly analysed were stored at ≤ -18°C.

The soda lime trap was dissolved in 70 mL of 6 M HCl to release the $^{14}CO_2$, which was then transferred to LSC vials by a stream of CO_2 free air. The vials were then directly measured by LSC. Volatiles were extracted from the quartz wool with 40 mL acetone. Two 10 mL aliquots of the extract were subsequently measured by LSC.

Investigation of non-extractable residues (NER) was conducted on extracted soil samples. Residues were dried directly after extraction, however, previously stored soil residues that were frozen at ≤ -18 C were dried after thawing for determination of NER. The soil residue was then homogenised in a mill and 2-4 soil aliquots were combusted, which was followed by radioactivity measurements by LSC.

The identification and determination of radiochemical purity of ^{14}C-propamocarb hydrochloride was done by High Performance Liquid Chromatography (HPLC). However, HPLC proved to be not suitable for the determination of the identity and quantity of the propamocarb hydrochloride in the soil extracts. Therefore Thin Layer Chromatography (TLC) was employed to determine the distribution of the radioactivity in the soil extracts.

II. Results and Discussion

A. Data: A decrease in the soil microbial biomass was observed during the incubation of the test soil over 120 days. Results of microbial biomass investigations conducted on Day 0 and day 120 are summarised in the table below. The reduction in biomass over the study period is considered to be typical owing to limited nutrient supply from the closed system nature of the experimental apparatus.

Microbial biomass in the Sarotti soil at the beginning and the end of the incubation period

Soil	Microbial Carbon Day 0 (mg C/kg)		Microbial Carbon Day 120 (mg C/kg)	
	Replicate 1	Replicate 2	Replicate 1	Replicate 2
Sarotti	426.82	427.13	368.86	381.52

[4] Anderson, J. P. E. and Domsch, K. H. (1978): A physiological method for the quantitative measurement of microbial biomass in soils. Soil. Biol. Biochem., 10, 215-221.

Distribution and radioactive material balance in the Sarotti soil during 120 days incubation with propamocarb hydrochloride

Sampling Date	(% of total applied radioactivity) [1]						
	$^{14}CO_2$	Quartz wool	Extracted radioactivity			NER	Material balance
			1st extract	2nd extract	Total		
0a [2]	-	-	61.8	20.3	82.1	14.6	96.7
0b [2]	-	-	61.3	21.8	83.1	13.9	97.0
7	1.4	0.0	63.3	13.0	76.3	19.8	97.5
14	4.9	0.0	58.8	12.5	71.3	15.0	91.2
21	10.3	0.1	51.1	11.4	62.5	17.1	90.0
28	16.5	< 0.1	43.7	10.4	54.1	22.6	93.2
35	24.9	< 0.1	31.3	8.4	39.7	22.3	86.9
43	31.7	< 0.1	23.1	6.4	29.5	23.5	84.7
56	40.0	< 0.1	10.9	6.9	17.8	19.5	77.3
84	55.3	< 0.1	5.5	4.1	9.6	21.0	85.9
120	57.9	< 0.1	4.4	3.4	7.7	20.3	85.9
120, R1	61.6	< 0.1	3.3	4.3	7.6	21.8	91.0

Note: - = Not Determined; [1] Applied radioactivity was 52.649 kBq; [2] Applied radioactivity was 53.629 kBq

Summary of results characterising the extracted radioactivity from the Sarotti soil

Sampling Date	(% of total radioactivity applied)					
	propamocarb hydrochloride			Sum of unknown metabolites		
	1st extract	2nd extract	Total	1st extract	2nd extract	Total
0a	59.6	19.3	78.9	2.2	1.1	3.3
0b	58.7	20.6	79.3	2.6	1.2	3.8
7	57.5	11.5	69.0	5.8	1.6	7.4
14	48.1	11.4	59.5	10.7	1.2	11.9
21	42.1	9.9	52.0	9.0	1.5	10.5
28	35.1	8.9	44.0	8.7	1.5	10.2
35	23.9	7.1	31.0	7.5	1.3	8.8
43	15.6	5.3	20.9	7.5	1.1	8.6
56	6.2	4.7	10.9	4.8	2.1	6.9
84	1.8	2.4	4.2	3.7	1.7	5.4
120	1.2	1.8	3.0	3.2	1.6	4.8
120, R1	0.8	1.6	2.4	2.5	2.7	5.2

B. Mass balance: The radioactive recovery from all the individual test vessels ranged from 77.3% to 97.5% of the applied radioactivity, demonstrating that radioactivity was lost from the test system from approximately day 35 (dropping below 90%). The mean recovery rate for all test systems was determined to be 89.7% of the applied radioactivity. The losses from the test system appeared to correlate with periods of increased mineralisation of the test substance, therefore, it may be expected that the trapping system for $^{14}CO_2$ was not quantitative during that period of the study. On Day 120 the reserve test system (R1) was sampled in order to provide another data set for that sampling point.
C. Bound and extractable residues: The amount of radioactivity extractable from the soil decreased from 83.1% to 7.6% after 120 days. The highest extraction yields were achieved with the first extraction procedure, while the following extraction resulted in minor portions of overall extracted radioactivity.
In contrast the formation of NER increased slightly from 13.9% on Day 0 to 20.3% on Day 120. Soil organic matter fractionation between humin, humic acid, and fulvic acid was not investigated in this study.
D. Volatile radioactivity: Overall the principal degradation product formed was $^{14}CO_2$, which increased to 57.9% of applied radioactivity after 120 days.

E. Transformation of test substance: Chromatographic results of metabolites from soil extracts are provided in Table 11.1.4.3-54. For the Sarotti test soil the major portion of applied radioactivity was assigned to be unchanged propamocarb hydrochloride. However, over the period of experimentation the

portion of propamocarb hydrochloride determined from the soil extracts continuously decreased, down to 3.0% by Day 120 from 79.0% of applied radioactivity on Day 0. Over the incubation period the sum of six un-identified metabolites exceeded values of 10% of the applied radioactivity on Days 14, 21, and 28. However, no single metabolite accounted for more than 5.5% of the applied radioactivity in the Sarotti soil (for characterisation and identification see study KCA 7.1.1.1/10). At the final sampling point of the incubation period 57.9% (or 59.8% of the average day 120 sampling point) of applied radioactivity was released as $^{14}CO_2$.

III. Conclusion

Similarly to the incubation at 20°C, propamocarb hydrochloride showed rapid and nearly complete degradation at the lower test temperature of 10°C within the 120-day test period. Likewise, the major route of degradation resulted in the conversion to and release of $^{14}CO_2$. No single metabolite was formed exceeding 5.5% of the applied radioactivity (for characterisation and identification see study KCA 7.1.1.1/10), indicating that metabolites being formed at low temperatures still remained transient in nature.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Report:	KCA 7.1.2.1.1/09; Fent, G.; Hein, W.; 2001; M-203303-01-1
Title:	Degradation and metabolism of propamocarb-HCl (AE B066752) in four subsoil horizons of one soil
Report No.:	AGR22; C012750
Document No.:	M-203303-01-1
Guideline(s):	SETAC Procedures for Assessing the Environmental Fate and Ecotoxicity of Pesticides Part 1 1.1, March 1995
Guideline deviation(s):	none
GLP/GEP:	**yes**

Comment: key elements in design and conduct reported as for actual guideline studies. Study regarded as scientifically valid. However, subsoils used for tests in contrast to guideline requirements. Results from subsoils thus excluded from risk assessment.

Executive Summary

A laboratory investigtion using a Borstel test soil indicate that propamocarb hydrochloride, applied at a rate of 0.48 mg/100 g dry soil, degrades under aerobic experimental conditions at depths of 20, 40, 60, and 90cm at a temperature of 10°C. The degree of degradation was partially a function of soil depth. Carbon dioxide and NER were the principal degradation products formed. However, with increasing soil depth the formation of $^{14}CO_2$ decreased to amounts that were almost negligible and a greater portion of the test substance was bound as NER. Up to nine unidentified polar metabolites were observed during the study. The maximum value for a single component never exceeded 5.5% of the applied radioactivity at two consecutive sampling intervals.

I. Material and Methods

A. Materials

1. Test Material: Common name: propamocarb hydrochloride
Chemical name: propyl 3-(dimethylamino) propylcarbamate hydrochloride
Radiolabelled purity: > 99.0%
Lot # IS1795-21
Specific activity 8.76 MBq/mg
Non-radiolabelled purity: 744.0 g/L
Lot # 934578

2. Soil:

Characteristics of test soils

Soil No.	**I**	**II**	**III**	**IV**
Name = Origin	**Borstel**			
Country	**Germany**			
Sampling date	**Nov. 18, 1999**			
Sampling depth	**20 cm**	**40 cm**	**60 cm**	**90 cm**
Horizon	**Bhv**	**Bv**	**Cv**	**C**
Soil texture [1),2)]	**Loamy sand**	**Loamy sand**	**Clay sand**	**Sand**
Sand (%) [2)]	72.6	80.6	90.5	96.7
Silt (%) [2)]	20.4	13.2	4.3	0.0
Clay (%) [2)]	7.0	6.2	5.2	3.3
Maximum water holding capacity [3)] ($g\ H_2O/100\ g$ dry soil)	42.87	29.68	30.16	30.29
pH ($CaCl_2$) [3)]	6.29	6.34	6.37	6.40
Nitrogen content [2)] (mg/100 g)	20	10	10	10
CEC (meq/100 g dry soil) [2)]	5	5	4	3
Organic substance [2)]				
Org. substance (%)	0.96	0.41	0.31	0.03
Org. carbon (%)	0.56	0.24	0.18	0.02
Lime content (% $CaCO_3$) [2)]	< 0.1	< 0.1	< 0.1	< 0.1
Internal SLFA soil number	100	101	102	103

Note: 1) According to DIN 19682
2) Determined by Lufa Speyer, Obere Langgasse 40, 67436 Speyer (reports dated 10.05.00 and 25.09.00)
3) Determined by the Test Facility

B. Study design

1. Experimental conditions: The test system consisted of 300 mL Erlenmeyer flasks, which were connected with soda lime traps and oil-wetted glass wool for the adsorption of volatile organics and $^{14}CO_2$. Soil samples were treated with propamocarb hydrochloride at an application rate of 0.04 mg/100 g dry soil, corresponding to a rate equivalent to 3.61 kg a.s/ha. The temperature was held at 10° C ± 2°C, under dark conditions, and the moisture content of the soil samples was set to 45 % of the MWHC corresponding to soil moisture contents of

19.3 g water/100 g dry soil for the 20 cm horizon, 13.4 g water/100 g dry soil for the 40 cm horizon, 13.6 g water/100 g dry soil for the 60 cm horizon, 13.6 g water/100 g dry soil for the 90 cm horizon. Gas exchange was kept aerobic. Microbial biomass was tested in the sub-soil horizons simultaneously to the application and at the end of the incubation period according to the Anderson and Domsch method

2. Sampling: Soil sampling was undertaken at intervals of 0 h (immediately after application), 7, 14, 21, 28, 35, 45 (49 for soil from 40 cm soil depth), 56, 84, and 120 days. On Day 45 one test system was sampled, however, the soil II was lost. A reserve test system of soil II was sampled on Day 49. At each sampling point duplicate sub-samples were removed for analysis. At each sampling date the units were flushed with air in order to transfer all organic volatiles into the trapping system.

3. Analytical procedures: Each soil sample was exhaustively extracted 3 times with 100 mL acetonitrile/water (4:1 v/v; pH < 4 with formic acid). The extract was concentrated and subsequently analysed by TLC. Radioactivity of extracts was determined by Liquid Scintillation Counting (LSC). Soil samples that were not directly analysed were stored at ≤ -18°C.

The soda lime trap was dissolved in 70 mL of 6 M HCl to release the $^{14}CO_2$, which was then transferred to LSC vials by a stream of CO_2 free air. The vials were then directly measured by LSC. Volatiles were extracted from the quartz wool with 40 mL acetone. Two 10 mL aliquots of the extract were subsequently measured by LSC.

Investigation of non-extractable residues (NER) was conducted on extracted soil samples. Residues were dried directly after extraction, however, previously stored soil residues that were frozen at <-18°C were dried after thawing for determination of NER. The soil residue was then homogenised in a mill and 4-6 soil aliquots were combusted, which was followed by radioactivity measurements by LSC. This process was repeated except that combustion of 2-4 soil aliquots was followed by LSC.

The identification and determination of radiochemical purity of [^{14}C]-Propamocarb hydrochloride was done using High Performance Liquid Chromatography (HPLC). However, HPLC showed to be not suitable for the determination of the identity and quantity of the propamocarb hydrochloride in the soil extracts. Instead Thin Layer Chromatography (TLC) was utilised to determine the distribution of the radioactivity in the soil extracts.

II. Results and Discussion

A. Data:

Results of the microbial biomass tests are summarised below. In the sub-soil samples of the Borstel soil low amounts of microbial biomass are observed in the soil in comparison to the soil surface layers (see study M-203298-01-1). Microbial biomass did not decrease significantly with depth, although some evidence for depletion of microbial biomass during the incubation may be observed. However, this is similar to microbial biomass investigations in the study M-203298-01-1 and study M-203301-01-1.

Microbial biomass in the Borstel soil at different soil depths at the beginning and the end of the incubation period

Soil	Microbial Carbon Day 0 (mg C/kg)		Microbial Carbon Day 120 (mg C/kg)	
	Replicate 1	Replicate 2	Replicate 1	Replicate 2
Borstel 20 cm	45.84	49.92	35.09	34.98
Borstel 40 cm	58.67	39.35	27.79	36.49
Borstel 60 cm	37.03	37.88	23.93	25.00
Borstel 90 cm	31.61	44.85	24.74	27.79

Distribution and radioactive material balance at depths of 20, 40, 60, and 90 cm in a Borstel test soil after application with Propamocarb hydrochloride

Sampling date (d)	(% of total applied radioactivity) [1)]				
	$^{14}CO_2$	Quartz wool	Extracted radioactivity	NER	Material balance
Borstel 20 cm					
0a	-	-	100.0	4.8	104.8
0b	-	-	98.9	5.1	104.0
7	2.0	<0.1	90.6	11.3	103.9
14	4.1	0.0	85.7	13.9	103.7
21	5.9	<0.1	80.1	15.1	101.1
28	9.1	<0.1	75.4	16.2	100.7
35	12.1	0.0	69.9	18.2	100.2
45	11.9	0.0	68.4	17.3	97.6
56	20.7	0.0	54.8	21.2	96.7
84	31.2	0.0	44.3	21.9	97.4
120	36.7	<0.1	27.9	26.9	91.5
Borstel 40 cm					
0a	**-**	**-**	**97.9**	**5.8**	**103.7**
0b	-	-	97.8	6.0	103.8
7	1.2	<0.1	86.6	14.2	102.0
14	2.5	0.0	87.8	16.1	106.4
21	3.9	<0.1	80.5	16.4	100.8
28	5.9	0.0	79.0	17.5	102.4
35	4.8	0.0	77.9	18.1	100.8

49	8.1	0.0	71.8	18.3	98.2
56	10.4	<0.1	67.9	18.6	96.9
84	17.0	0.0	60.0	21.2	98.2
120	22.1	<0.1	52.2	22.0	96.3
Borstel 60 cm					
0a	-	-	94.2	12.1	106.3
0b	-	-	91.2	12.0	103.2
7	0.8	0.0	79.9	23.6	104.3
14	1.8	0.0	76.3	26.1	104.2
21	2.5	0.0	73.2	26.1	101.8
28	3.0	0.0	72.6	27.7	103.3
35	3.7	0.0	70.5	29.2	103.4
45	4.8	0.0	73.4	26.2	104.4
56	5.6	0.0	68.8	27.9	102.3
84	7.2	0.0	64.5	30.1	101.8
120	6.6	0.0	60.8	29.7	97.1
Borstel 90 cm					
0a	-	-	94.0	10.8	104.8
0b	-	-	92.2	11.5	103.7
7	0.7	0.0	73.3	28.5	102.5
14	1.2	0.0	69.8	31.0	102.0
21	1.4	0.0	67.6	32.0	101.0
28	1.7	0.0	70.3	34.2	106.2
35	1.7	0.0	67.4	35.9	105.0
45	1.8	0.0	69.9	31.5	103.2
56	2.0	0.0	64.8	34.9	101.7
84	1.7	<0.1	61.9	36.8	100.4
120	2.1	<0.1	60.4	36.8	99.3

Note: - = Not Determined
1) Applied radioactivity was 33.326 kBq.

Distribution and radioactive material balance at depths of 20, 40, 60, and 90 cm in a Borstel test soil after application with propamocarb hydrochloride

Sampling Date (d)	% of total radioactivity applied	
	propamocarb hydrochloride	Sum of unknown Metabolites
Borstel 20 cm		
0a	90.9	9.1
0b	89.1	9.7
7	83.5	7.2
14	78.5	7.3
21	75.2	4.8
28	69.7	5.6
35	63.0	6.9
45	63.5	4.9
56	51.3	3.5
84	41.6	2.7
120	25.7	2.2

Borstel 40 cm		
0a	90.3	7.7
0b	91.4	6.4
7	80.5	6.1
14	82.3	5.5
21	75.4	5.0
28	73.0	6.0
35	71.8	6.2
49	68.1	3.7
56	63.6	4.3
84	57.0	3.0
120	50.1	2.1
Borstel 60 cm		
0a	87.1	7.2
0b	84.3	6.8
7	74.6	5.2
14	70.7	5.5
21	67.5	5.7
28	65.4	7.3
35	63.0	7.6
45	69.5	3.8
56	65.4	3.4
84	61.8	2.6
120	59.7	1.2
Borstel 90 cm		
0a	83.3	10.7
0b	81.8	10.5
7	68.7	4.6
14	63.8	6.1
21	61.4	6.2
28	62.4	7.9
35	59.4	8.0
45	67.2	2.7
56	62.8	2.0
84	59.4	2.4
120	58.1	2.4

B. Mass balance: Overall, a good radioactive recovery was established in all individual test vessels ranging from 91.5% to 106.4%. The mean recovery for all investigated test systems was 101.7 %.

C. Bound and extractable residues: The amount of radioactivity extractable from the soil depths decreased during the incubation period but remained above 50%, with the exception of the test system containing subsoil from 20cm. In the 20cm subsoil sample 27.9% of the applied radioactivity was still extractable after 120 days. However, 52.2%, 60.8%, and 60.4 % of the applied radioactivity was still extractable in the soils from the 40, 60, and 90cm horizon, respectively. The first extraction procedure achieved high extraction yields allowing for no further extraction. In contrast, the formation of NER increased over the incubation period. After 120 days of incubation 26.9%, 22.0%, 29.7%, and 36.8% of the applied radioactivity were found in the NER fraction for the 20, 40, 60, and 90 cm subsoil horizon, respectively.

D. Volatile radioactivity: The amount of $^{14}CO_2$ released during the incubation period decreased with increasing soil depth. After 120 days the amount of applied radioactivity determined as $^{14}CO_2$ in 20cm and 40cm horizon was 36.7% and 22.1%, respectively. In contracts the amount of $^{14}CO_2$ determined for the 60cm and 90cm soil horizon was considerably lower, being 6.6% and 2.1% of the applied radioactivity, respectively.

E. Transformation of test substance: In all four soil horizons the amount of propamocarb hydrochloride identified in the soil extracts was decreasing with time. The highest mineralisation was observed in the 20 cm horizon, in which 25.7% of the applied radioactivity was present as propamocarb

hydrochloride by Day 120. In the 40, 60, and 90 cm horizons 50.1%, 59.7%, and 58.1% of the radioactivity was assigned to unchanged propamocarb hydrochloride by Day 120, respectively. Therefore, it might be expected that the mineralisation potential of soils to propamocarb hydrochloride could decrease with depth.

Up to nine unknown metabolites were seen in the soil extracts. After 120 days the sum of unidentified extractable residue ranged from 1.2 to 2.4% of the radioactivity applied in all soils. The maximum value for a single component never exceeded 5.5% of the applied radioactivity at two consecutive sampling intervals.

III. Conclusion

The route of degradation of propamocarb hydrochloride was investigated in a laboratory study under aerobic conditions at 10°C using four subsoil horizons from one soil (Borstel test soil) giving additional information regarding the metabolism of propamocarb hydrochloride at different depths in the soil profile. The mineralisation of propamocarb hydrochloride in the test soils decreased with depth.

RMS´s opinion:

Reliability of the study: score 2 of the scoring system of Klimisch *et al*.(1997).

Information on the rate of degradation in aerobic soil at a temperature of 10°C can be derived from existing data in:

- one German soil (10°C, moisture at 45% MWHC) after application of 1-*N*-propyl-^{14}C-labeled propamocarb-hydrochloride (KCA 7.1.2.1.1/08);
- one UK soil (10°C, moisture at 45% MWHC) after application of 2-*N*-propyl-^{14}C-labeled propamocarb-hydrochloride (KCA 7.1.2.1.1/07);
- one German soil (10°C, moisture at 45% MWHC) after application of 1-*N*-propyl-^{14}C-labeled active substance to sub-soils (KCA 7.1.2.1.1/09).

This data requirement had been addressed under Point 7.1.1.2 of the Dossier submitted.
The evaluation revealed that the active substance propamocarb-hydrochloride was degraded at 10°C to result in values of the DT_{50} in aerobic soil of 25.3 days (study KCA 7.1.2.1.1/07) and 47.2 days (study KCA 7.1.2.1.1/08), respectively. The corresponding values of the DT_{90} were 84.1 days and 156.9 days. The values served for comparison with trigger endpoints.
Being part of a non-standard approach in testing, soil degradation data had been additionally submitted from tests in four sub-soils of the same German soil at 10°C and at 45% MWHC following application of 1-*N*-propyl-^{14}C-labeled active substance (KCA 7.1.2.1.1/09). Considering the fact that the use of top soils sampled from the plough layer of agricultural soils is standard in aerobic soil testing, the results of the test were regarded as supplemental information. This is in line with current requirements of OECD Guideline 307.

The existing data of studies KCA 7.1.2.1.1/07 and KCA 7.1.2.1.1/08 were re-evaluated following actual FOCUS kinetic guidance [FOCUS, 2006, 2011] as reported in KCA 7.1.2.1.1/16.

Report:	KCA 7.1.2.1.1/16; Oberdoerster, C.; Boiselle, N.; Hoerold, C.; 2015b; M-541770-01-1
Title:	Kinetic evaluation of the degradation of propamocarb-hydrochloride and its metabolite N-desmethyl-propamocarb in soil under aerobic laboratory conditions
Report No.:	EnSa-14-1331
Document No.:	M-541770-01-1
Guideline(s):	"Generic Guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". EC Document Reference: None, version 1.1, 2015 amending "Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference Sanco/10058/2005 version 2.0, 2006
Guideline deviation(s):	not applicable
GLP/GEP:	**no**

For the active substance propamocarb-hydrochloride degradation data as referenced under KCA 7.1.2.1.1/07 and KCA 7.1.2.1.1/08 were kinetically re-evaluated according to FOCUS Guidance to derive values for the half-life and the DT_{90} in aerobic soil for trigger endpoints.
A total of two aerobic soil degradation studies under conditions of the laboratory was considered to result in two data sets in total following application of [1-*N*-propyl-^{14}C]- or [2-*N*-propyl-^{14}C]-propamocarb-hydrochloride.
A stepwise approach was made for the calculation of normalised half-lives in soil. The initial step consisted of best fits to the measured data following the SFO kinetic model. This was followed by application of bi-phasic models, i.e. FOMC or DFOP, in case of unacceptable fits according to the criteria set. The resulting best fits served as the basis to derive half-lives for comparison against trigger endpoints.

For trigger endpoints, non-normalised values of the DT_{50} and the DT_{90} were derived from SFO best fits in the two soils as summarized in the table below.
Non-normalised half-lives of propamocarb-hydrochloride at 10°C ranged from 0.5 days to 8.1 days while values for the DT_{90} ranged from 5.0 days to 87.1 days.

Comparison against EU triggers: Kinetic evaluation of degradation for propamocarb-hydrochloride in aerobic soil at 10°C in the laboratory

Parameter	propamocarb-hydrochloride
10°C, Non-normalised DT_{50}, range (days)	25.3 – 47.2
Worst case DT_{50} (days)	**47.2**
10°C, Non-normalised DT_{90}, range (days)	84.2 – 156.9
Worst case DT_{90} (days)	**156.9**

I. Material and Methods

The degradation data were kinetically evaluated following FOCUS guidance [FOCUS, 2006, amended 2011][5] with the software KinGUI2.
The actual kinetic re-evaluation considered those data sets that were considered reliable and valid by the RMS during the assessment for Annex I inclusion:
The two aerobic soil degradation studies containing information on tests performed at 10°C with the active substance resulted in two data sets in total being subject to re-assessment on reliability followed by kinetic evaluation. The data sets including characteristics of soils were summarised in the table below.

[5] FOCUS (2006) "Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration" Report of the FOCUS Work Group on Degradation Kinetics, EC Document Reference Sanco/10058/2005 version 2.0

The kinetic evaluation derived non-normalised DT50 values for comparison against EU trigger values. The assessment followed the same respective decision flowcharts and the criteria outlined as summarized earlier for KCA 7.1.2.1.1/09 in more detail for the set of studies performed at 15 to 25°C.

Aerobic soil degradation data performed with propamocarb-hydrochloride at 10°C under laboratory conditions, including characteristics of soils

Study	Soil	Soil texture	Test temperature (°C)	Test moisture (%w/w)	Sand (%)	Clay (%)	Org. carbon (%)	pH ($CaCl_2$)	CEC (meq / 100 g)
KCA 7.1.2.1.1/07	E, B6	sandy loam	10	12.2	54	11	2.5	6.7	14.6
KCA 7.1.2.1.1/08	Sarotti	silt loam	10	16.2	12.1	17.7	1.3	7.4	13

*: Variation of application rate

II. Results and Discussion

For trigger endpoint determination the bi-phasic models FOMC and DFOP showed no improvement over SFO kinetics when following the decision criteria. SFO kinetics was thus determined to be the best-fit for the two data sets.
The resulting non-normalised values for the DT_{50} and the DT_{90} derived were summarised in the table below.

Trigger evaluation: Non-normalised DT_{50} values for propamocarb-hydrochloride in aerobic soil at 10°C under laboratory conditions

Soil	Label position	Model	DT_{50} (days)	DT_{90} (days)	Chi^2 (%)	t-test/ confidence interval	Visual[a)]
E, B6, Woolverstone sandy loam, 10°C (Study 1)	2-N-propyl	SFO	47.2	156.9	10.7	k < 0.001	+
Sarotti, silt loam, 10°C (Study 2)	1-*N*-propyl	SFO	25.3	84.2	9.0	k < 0.001	++

Study 1: KCA 7.1.1.1 /07 and KCA 7.1.2.1.1 /07; Study 2: KCA 7.1.1.1 /08 and KCA 7.1.2.1.1 /08
a) VA = Visual Assessment (++ = excellent, + = good, O = acceptable, - = not acceptable)

III. Conclusion

The evaluation according to FOCUS kinetic guidance resulted in values for half-lives and the DT_{90} of the parent compound propamocarb-hydrochloride at 10°C for comparison with EU trigger endpoints.
The approach for fitting with experimental data resulted in the use of the monophasic kinetic model SFO for calculation.
Values of non-normalised half-lives at 10°C from best fits to measured data were 25.3 days for silt loam soil Sarotti and 47.2 days for sandy loam soil E (B6, Woolverstone). The corresponding DT_{90} were 84.2 days for soil Sarotti and 156.9 days for soil E (B6, Woolverstone).

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Assessment of the potential pH dependency of the rate of degradation in soil of the active substance and its metabolites.

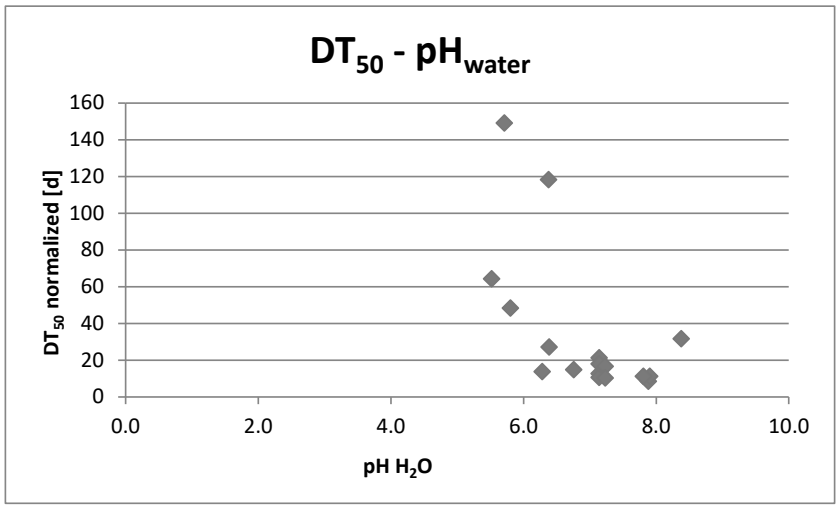
The pH dependency of the degradation of propamocarb-hydrochloride, *N*-desmethyl-propamocarb and propamocarb-*N*-oxide is tested using the Kendall rank correlation test. The Input Decision tool v3.3 of

Federal Environment Agency (UBA) is used. The normalised $DegT_{50}$ values of the soils and the corresponding pH values (as shown in Document N2, List of endpoints, M-544296-01-1) are tested. Measured pH_{CaCL2} values were calculated to pH_{H2O}values by Input Decision tool.

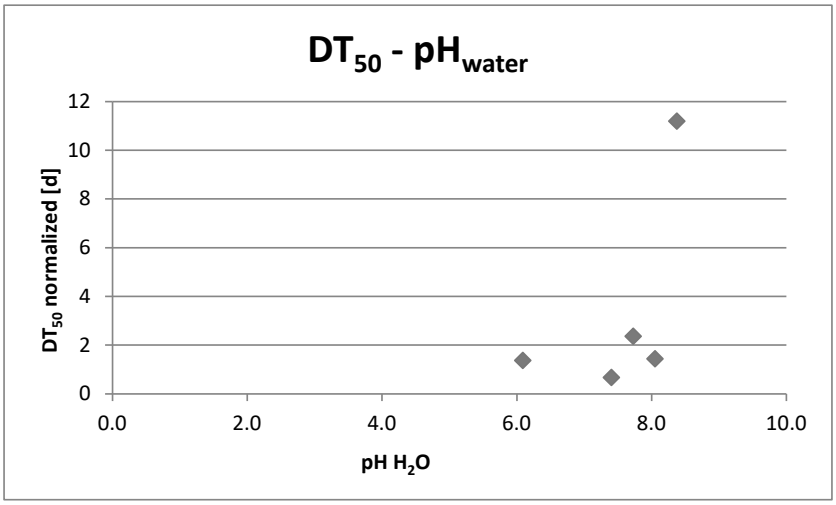
Correlation parameters for $DegT_{50}$ values and pH values

Compound	Kendall tau (stringency of the correlation)	p (level of significance)
propamocarb-hydrochloride	-0.491	0.008
N-desmethyl-propamocarb	0.600	0.221
propamocarb-*N*-oxide	-0.667	0.308

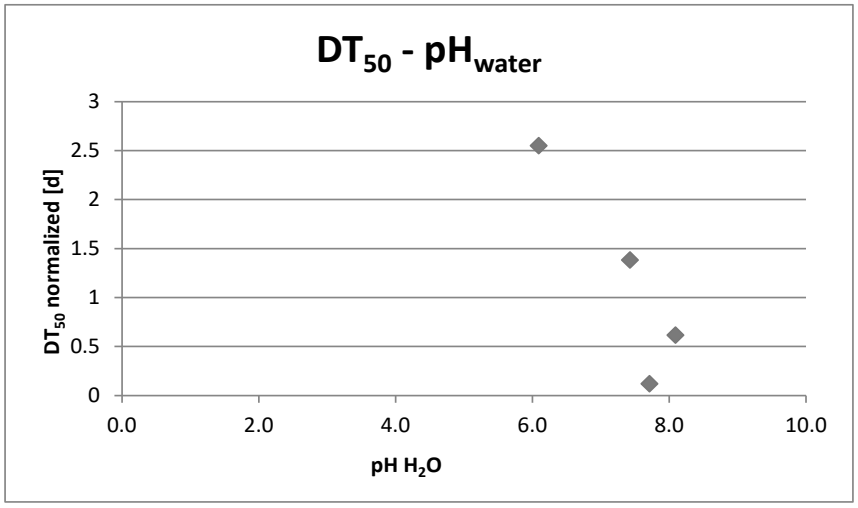
Correlation between DT_{50} values and pH - propamocarb-hydrochloride



Correlation between DT_{50} values and pH - *N*-desmethyl-propamocarb



Correlation between DT_{50} values and pH - propamocarb-*N*-oxide



There is no significant correlation between the pH value and the degradation rates. Therefore, it is concluded that the degradation of propamocarb-hydrochloride and its metabolites is not pH-dependent.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Aerobic degradation of metabolites, breakdown and reaction products

Information on the rate of degradation, in aerobic soils, for metabolites of propamocarb-hydrochloride can be derived from laboratory studies performed under the following conditions:

- two US soils under standard conditions (25°C, moisture at 75% of water holding capacity (MWHC) at 0.33 bar) and application of 1-*N*-propyl-^{14}C-labeled active substance (KCA 7.1.2.1.2/01);
- four soils under standard conditions (20°C, moisture at 33 to 50% MWHC and application of 1-*N*-propyl-^{14}C-labelled N-desmethyl-propamocarb (KCA 7.1.2.1.2 /02).
- four soils under standard conditions (20°C, moisture at 33 to 50% MWHC) following application of 1-*N*-propyl-^{14}C-labelled propamocarb-N-oxide (KCA 7.1.2.1.2 /03);

In view of the fact that the degradation of propamocarb-hydrochloride in aerobic soils proceeded predominantly via the formation of non-extractable residues (NER) and ^{14}C-carbon dioxide, no transformation product had been observed at a level of > 10% AR.

Based on a data request by US EPA, information on route of aerobic degradation (KCA 7.1.1.1/11) had been generated from two US soils. The investigations resulted in the observation of the metabolite N-desmethyl-propamocarb at maximum values of 9.7% AR after 30 days of incubation.

Report:	KCA 7.1.2.1.2/01; Desmarteau, D. A.; 2006; M-270482-01-1
Title:	[14C-Propamocarb-hydrochloride]: Aerobic soil metabolism in two US soils
Report No.:	MEPRY002
Document No.:	M-270482-01-1
Guideline(s):	US EPA Subdivision N, Section 162-1
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

Besides the potential information on rate of degradation of *N*-desmethyl-propamocarb to be found in one soil of study KCA 7.1.2.1.2/01, additional degradation data were generated by dosing ^{14}C-labeled *N*-desmethyl-propamocarb separately to four soils (KCA 7.1.2.1.2/02).
In addition, metabolite propamocarb-*N*-oxide was observed in the existing soil photolysis study KCA 7.1.1.3/01 at a maximum value of 8.7 % AR in irradiated samples after 30.66 days. Following actual data requirements of Commission Regulation (EU) No. 283/2013 amending Regulation (EC) No. 1107/2009, metabolite propamocarb-*N*-oxide was thus triggered for consideration in environmental risk assessment. Additional data on rate of degradation were therefore generated by dosing ^{14}C-labeled propamocarb-*N*-oxide separately to four soils (KCA 7.1.2.1.2/03).
The kinetic evaluations were performed in KCA 7.1.2.1.2/04 and KCA 7.1.2.1.2/05 for metabolite N-desmethyl-propamocarb and in KCA 7.1.2.1.2/06 for propamocarb-N-oxide in order to derive trigger and modeling endpoints for input into environmental risk assessments.

Report:	KCA 7.1.2.1.2/02; Walther, D.; 2015a; M-530922-01-1
Title:	[14C]N-desmethyl-propamocarb: Rate of degradation in four soils incubated under aerobic conditions
Report No.:	D96215
Document No.:	M-530922-01-1
Guideline(s):	OECD Test Guideline No. 307 US EPA OPPTS Test Guideline No. 835.4100 Regulation (EC) No. 1107/2009 Commission Regulation (EU) No 283/2013
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

Executive Summary

The degradation rate of the N-desmethyl-propamocarb was investigated in four soils under aerobic conditions at 20°C and at moisture in the dark of 16% (g water/100 g soil) for soil LS2.2, 21.0% for soil Laacher Hof AXXa, 26.0% for soil Fraunhofer 06A and 24.5% for soil Attenschwiller moisture. These moisture levels correspond to pF 2.0 - 2.5. The soil moisture was adjusted, during the study, to 16 g water/100 g soil for soil I (Speyer 2.2), 21.0 g water/100 g soil for soil II (Laacher Hof AXXa), 26.0 g water/100 g soil for soil III (Fraunhofer 06A) and 24.5 g water/100 g soil for soil IV (Attenschwiller). These moisture levels correspond to pF 2.0–2.5. The MWHC was determined to be 48.86 g/100g dry soil for soil Speyer 2.2, 48.06 g/100g for soil Laacher Hof AXXa, 57.36 g/100g for soil Fraunhofer 06A and 49.28 g/100g for soil Attenschwiller. The study was performed with 1-*N*-propyl-^{14}C-labelled *N*-desmethyl-propamocarb hydrochloride for a maximum incubation period of 7 days (soils soil LS2.2, Laacher Hof AXXa and Attenschwiller) or 10 days (soil Fraunhofer 06A).
The nominal application rate was 0.61 mg ^{14}C-test substance/kg soil, based on a maximum occurrence of 9.7% AR in a study performed with the active substance propamocarb-hydrochloride and a single treatment rate in the field of 2200 g a.s./ha.
Values for ^{14}C-N-desmethyl-propamocarb extractable from soil decreased from 100.6% (day zero) to 2.8% (day 7) in soil LS 2.2, from 98.3% to 2.5% in soil Laacher Hof AXXa, from 94.7% to 10.0% in soil Fraunhofer 06A and from 93.6% to 5.0% in soil Attenschwiller.

Best fit degradation kinetics to measured data were obtained by applying the SFO model for all soils. The resulting values for the DT_{50} and DT_{90} of N-desmethyl-propamocarb in aerobic soil were summarised in the table below.

Best fit DT_{50} and DT_{90} values of N-desmethyl-propamocarb in aerobic soil

Soil	DT_{50} [days]	DT_{90} [days]	Chi² error	Visual assessment	Kinetic model
LS2.2	1.40	4.63	12.72	A	SFO
Laacher Hof AXXa	0.78	2.61	4.64	A	SFO
Fraunhofer 06A	3.40	11.3	2.45	A	SFO
Attenschwiller	1.81	6.02	11.61	A	SFO

Visual assessment of fit to be acceptable (A) or unacceptable (U)

I. Material and Methods

A. Materials

1. Test Material: [1-*N*-propyl-^{14}C]*N*-desmethyl-propamocarb hydrochloride (BCS-AW 15480)
Specific radioactivity: 5.15 MBq/mg (139.2 µCi/mg)
Radiochemical purity: 95.6% (TLC)
Sample ID: KML 9854

2. Soils: The test soils originated from the EU and reflected a range of physico-chemical characteristics as summarized in the table below. The soils had been collected fresh from the field and were passed through a 2 mm sieve.

Characteristics of test soils

	Soil			
	Speyer 2.2 (Soil I)	**Laacher Hof AXXa (Soil II)**	**Fraunhofer 06A (Soil III)**	**Attenschwiller (Soil IV)**
Geographic location (city / state / country)	Speyer, Rhineland Palatinate Germany	Monheim / North Rhine-Westphalia / Germany	Schmallenberg / North Rhine-Westphalia / Germany	Attenschwiller / Alsace / France
GPS Coordinates	N 49° 19' E 08° 20'	N 51° 05' E 06° 54'	N 51° 09' E 08° 18'	N 47° 34' E 07° 30'
Textural class [A)]	loamy sand	sandy loam	silty clay	silt loam
Sand (%)a)	7.9	11.8	44.5	17.1
Silt (%)a)	16.3	16.7	44.6	68.0
Clay (%)a)	75.8	71.5	10.9	14.9
pH - water	n.d.	7.5	n.d.	8.2
- 0.01 M CaCl2	5.5	6.9	7.2	7.6
Organic matter (%)[B)]	2.8	2.5	4.8	2.8
Organic carbon (%)	1.6	1.5	2.8	1.7
Carbonate as CaCO3 (%)	0.3	3.2	2.0	18.0
Microbial biomass (mg microbial C / 100 g soil)				
- Initial (DAT-0)	22.8	47.2	54.6	43.7
- Final	24.1	48.4	56.9	47.9
Cation exchange capacity (meq/100 g)	10.0	9.5	30.1	13.5
Water holding capacity at zero bar (pF 1) (%) 6	48.9	48.1	57.4	49.3
Water holding capacity at zero bar (pF 2) (%)	14.8	25.2	39.9	32.2
Water holding capacity at 0.33 bar (pF 2.5) (%)	14.1	20.8	36.2	29.3

n.a. not analysed; n.d. = not determnined; [A)] USDA classification ; [B)] % organic matter = % organic carbon x 1.724

6 Equivalent to the Maximum Water Holding Capacity (MWHC)

B. Study design

1. Experimental conditions: Samples of 100 g dry weight of soil each were filled into glass incubation flasks with each sample to receive 0.61 mg test substance/kg soil, a dose representing a field rate of 213 g test substance/ha derived from 2200 g a.s. propamocarb-hydrochloride/ha and a maximum occurrence of 9.7% in study KCA 7.1.2.1.2/01. Following application the samples were attached to 'flow through' systems with traps to collect each ^{14}C-carbon dioxide and other volatile components. Samples were incubated at 20 ±1°C and a moisture content of 33% (Soil I, Speyer 2.2), 44% (Soil II, Laacher Hof AXXa), 45% (Soil III, Fraunhofer 06A) and 50% (soil IV, Attenschwiller) of the MWHC in the dark for 7 days (Soils I, II and IV) or 10 days (Soil III) in maximum. In addition, untreated soil samples were incubated under the same conditions for determination of soil microbial activity.

2. Sampling: Duplicate samples were removed for work-up after 0, 1, 2, 3, 5 and 7 days of incubation. Additional samples were taken by day 10 for Soil IV, Attenschwiller, and after 4 hours and 6 hours for Soil II, Laacher Hof AXXa). Samples for determination of soil microbial biomass were investigated after 0 days and at the end of incubation. The complete samples were immediately processed by extraction.

3. Analytical procedures: The entire soil sample in each test vessel was extracted four times successively each with 100 mL acidified (formic acid) aqueous acetonitrile solution (80:20:1, by vol.) by ultra-sonication for 5 min followed by shaking the soil/solvent mixture at ambient temperature for 30 min. The ambient-extracted soil (included all sampling intervals for soil III, starting by day 1 and the following for Soils I, II and IV) was additionally Soxhlet-extracted for 4 hours. Ambient and Soxhlet extracts were combined and sub-samples concentrated and centrifuged prior to analysis.
The ^{14}C-material balance was established for each sample by extraction, analysis of volatiles and combustion of non-extractable residues. Following quantitation of radioactivity in extracts by LSC, analysis was performed by normal phase TLC as primary chromatographic method followed by reversed phase HPLC and ^{14}C-flow-through detection techniques as confirmatory method for selected time points. The determination of non-extractable residues (NER) was performed by combustion/LSC of aliquots of the air-dried extracted soil.

C. Determination of degradation kinetics: The kinetic evaluation was performed for the test substance *N*-desmethyl-propamocarb with the software KinGUI II following FOCUS kinetic guidance (2011) to obtain best fits to the measured data.

II. Results and Discussion

A. Data: The results of aerobic biotransformation of [1-*N*-propyl-^{14}C]*N*-desmethyl-propamocarb after incubation in four soils are summarized in the tables below.

Degradation of [1-*N*-propyl-^{14}C]*N*-desmethyl-propamocarb in loamy sand soil LS 2.2 under aerobic conditions:

		Sampling interval (days)					
Component		**0**	**1**	**2**	**3**	**5**	**7**
N-desmethyl-propamocarb	Mean*	100.6	74.9	41.0	16.1	2.4	2.8
	SD	±1.0	±0.4	±0.1	±2.8	±0.2	±0.7
Unknown M1	Mean*	-	-	-	-	1.5	-
	SD	-	-	-	-	±0.1	-
Unknown M2	Mean*	2.3	2.9	2.2	3.0	1.0	1.2
	SD	±0.2	±0.2	±0.0	±0.2	±0.3	±0.4
Unknown M3	Mean*	-	1.5	2.4	3.9	2.8	3.6
	SD	-	±0.0	±0.3	±0.4	±0.8	±0.3

Unknown M4	Mean*	-	1.5	3.8	2.8	2.3	1.5
	SD	-	±0.3	±0.3	±0.7	±0.2	±0.1
Total extractable	Mean*	102.9	80.7	49.4	25.9	10.0	9.1
Radioactivity	SD	±0.8	±0.8	±0.1	±2.9	±0.6	±0.0
Non-extractable	Mean*	1.4	7.7	9.7	22.7	21.3	24.5
Radioactivity	SD	±0.0	±0.4	±0.0	±1.1	±1.6	±0.7
14CO2	Mean*	n.d.	9.5	31.0	49.1	57.9	57.8
	SD	n.a.	±1.5	±0.1	±1.7	±4.7	±4.2
Other volatiles	Mean*	n.d.	<0.1	<0.1	<0.1	<0.1	<0.1
	SD	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Total recovery (%)	Mean*	104.3	97.9	90.0	97.7	96.1**	96.3**
	SD	±0.8	±1.9	±0.2	±0.3	n.a.	n.a.

Values given as percentages of initially applied radioactivity; n.d.: not determined; n.a.: not applicable
SD = standard deviation; * Mean values of duplicate samples analysed; ** Replicate excluded from mean of total recovery due to loss of volatile radioactivity (82.4%, day 5 and 86.5%, day 7)

Degradation of [1-*N*-propyl-^{14}C]*N*-desmethyl-propamocarb in sandy loam soil Laacher Hof AXXa under aerobic conditions:

		Sampling interval (days)							
Component		**0**	**0.17**	**0.25**	**1**	**2**	**3**	**5**	**7**
N-desmethyl-propamocarb	Mean*	98.3	83.5	84.9	42.0	15.0	5.6	2.5	2.5
	SD	±0.9	±0.5	±5.7	±2.6	±1.0	±0.0	±0.3	±0.7
Unknown M1	Mean*	-	-	-	-	-	-	-	-
	SD	-	-	-	-	-	-	-	-
Unknown M2	Mean*	2.3	2.3	2.6	2.7	1.2	-	0.9	1.2
	SD	±0.0	±0.1	±0.5	±0.1	±0.1	-	±0.6	±0.5
Unknown M3	Mean*	-	-	-	2.5	3.7	4.1	2.4	1.9
	SD	-	-	-	±0.0	±0.1	±0.3	±0.3	±0.1
Unknown M4	Mean*	-	0.4	0.7	2.5	2.5	1.9	2.1	1.3
	SD	-	±0.4	±0.7	±0.2	±0.1	±0.4	±0.3	±0.1
Total extractable radioactivity	Mean*	100.5	86.2	88.1	49.6	22.4	11.5	7.9	7.0
	SD	±1.0	±0.8	±5.5	±2.6	±1.0	±0.6	±0.4	±0.0
Non-extractable radioactivity	Mean*	2.2	2.5	3.9	14.8	15.2	24.1	22.1	22.4
	SD	±0.0	±0.2	±0.2	±0.6	±0.4	±0.3	±0.2	±0.6
14CO2	Mean*	n.d.	1.1	2.0	22.6	49.0	54.3	58.5	61.7
	SD	n.a.	±0.1	±0.1	±1.5	±0.1	±0.3	±3.6	±0.1
Other volatiles	Mean*	n.d.	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
	SD	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Total recovery (%)	Mean*	102.8	89.9	94.2	87.2	86.6	90.0	88.6	91.1
	SD	±1.0	±0.6	±5.8	±0.4	±0.5	±0.1	±3.4	±0.6

Values given as percentages of initially applied radioactivity; n.d.: not determined; n.a.: not applicable
SD = standard deviation; * Mean values of duplicate samples analysed

Degradation of [1-*N*-propyl-^{14}C]*N*-desmethyl-propamocarb in silty clay soil Fraunhofer 06A under aerobic conditions

Component		Sampling interval (days)						
		0	1	2	3	5	7	10
N-desmethyl-propamocarb	Mean*	94.7	80.8	64.4	53.9	35.4	22.2	10.0
	SD	±1.6	±0.0	±1.7	±0.7	±2.2	±1.9	±3.3
Unknown M1	Mean*	-	-	0.8	-	0.8	0.5	0.4
	SD	-	-	±0.1	-	±0.1	±0.1	±0.1
Unknown M2	Mean*	2.6	1.6	1.9	2.7	1.9	2.3	1.3
	SD	±0.1	±1.7	±0.2	±0.3	±0.1	±0.4	±0.0
Unknown M3	Mean*	-	-	-	-	0.7	1.1	1.2
	SD	-	-	-	-	±0.2	±0.2	±0.4
Unknown M4	Mean*	-	-	1.6	0.9	1.5	1.1	1.0
	SD	-	-	±0.1	±0.4	±0.2	±0.2	±0.1
Total extractable radioactivity	Mean*	97.2	82.5	68.7	57.5	40.3	27.2	14.0
	SD	±1.6	±1.7	±1.8	±0.8	±2.1	±1.6	±3.7
Non-extractable radioactivity	Mean*	4.6	10.4	8.8	20.2	19.9	23.4	24.2
	SD	±1.0	±1.2	±0.9	±10	±0.4	±0.0	±0.4
14CO2	Mean*	n.d.	4.7	11.6	20.6	37.5	46.8	45.9
	SD	n.a.	±0.7	±1.2	±0.7	±1.4	±3.1	±18.4
Other volatiles	Mean*	n.d.	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
	SD	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Total recovery (%)	Mean*	101.9	97.6	89.1	98.3	97.7	97.4	98.7**
	SD	±0.6	±0.1	±2.0	±0.5	±0.3	±1.5	n.a.

Values given as percentages of initially applied radioactivity; n.d.: not determined; n.a.: not applicable
SD = standard deviation; * Mean values of duplicate samples analysed; ** Replicate (69.7%) excluded from mean of total recovery due to loss of volatile radioactivity

Degradation of [1-*N*-propyl-^{14}C]*N*-desmethyl-propamocarb in silt loam soil Attenschwiller under aerobic conditions:

Component		Sampling interval (days)					
		0	1	2	3	5	7
N-desmethyl-propamocarb	Mean*	93.6	77.9	51.1	27.1	7.0	5.0
	SD	±1.7	±0.9	±1.8	±0.8	±0.0	±0.0
Unknown M1	Mean*	-	-	1.0	0.8	1.3	-
	SD	-	-	±1.0	±0.1	±1.0	-
Unknown M2	Mean*	3.2	3.3	2.0	2.0	1.4	1.2
	SD	±1.0	±0.0	±0.3	±0.3	±0.3	±0.0
Unknown M3	Mean*	-	-	-	1.3	1.1	1.5
	SD	-	-	-	±0.0	±0.2	±0.1
Unknown M4	Mean*	-	-	2.4	2.6	3.0	1.6
	SD	-	-	±0.3	±0.2	±0.0	±0.1
Total extractable radioactivity	Mean*	96.8	81.2	56.5	33.8	13.8	9.2
	SD	±0.7	±0.8	±0.8	±1.2	±0.6	±0.1
Non-extractable radioactivity	Mean*	2.2	8.0	10.2	24.9	27.1	27.0
	SD	±0.0	±0.6	±0.1	±0.4	±0.7	±0.9
14CO2	Mean*	n.d.	6.3	19.2	35.5	53.8	49.9

	SD	n.a.	±0.0	±4.4	±1.9	±1.4	±11.0
Other volatiles	Mean*	n.d.	<0.1	<0.1	<0.1	<0.1	<0.1
	SD	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Total recovery (%)	Mean*	99.0	95.5	89.6**	94.3	94.7	96.4**
	SD	±0.7	±0.3	n.a.	±1.1	±1.5	n.a.

Values given as percentages of initially applied radioactivity; n.d.: not determined; n.a.: not applicable
SD = standard deviation; * Mean values of duplicate samples analysed; ** Replicate excluded from duplicate mean of total recovery due to loss of volatile radioactivity (82.3%, day 2 and 75.9%, day 7)

B. Mass balance: The total recovery of radioactivity was complete to range from 90.0 to 104.3% of AR for loamy sand soil LS2.2, 86.6 to 102.8% for sandy loam soil Laacher Hof AXXa, 89.1 to 101.9% for silty clay soil Fraunhofer 06A and 89.6 to 99.0% for soil Attenschwiller. The results are summarised in more detail in the table below. For some single replicates at some sampling intervals total recoveries of radioactivity were below 90% AR. The losses could be assigned to leaks in trapping of ^{14}C-carbon dioxide within the flow-through incubation systems.

Total material balances of radioactivity of ^{14}C-*N*-desmethyl-propamocarb in four aerobic soils:

Soil	LS2.2	Laacher Hof AXXa	Fraunhofer 06A	Attenschwiller
Total Recovery (% AR)	90.0 - 104.3	86.6 - 102.8	89.1 - 101.9	89.6 - 99.0
Mean (% AR)*	95.1	91.3	95.1	92.6
Rel. standard deviation*	6.7	5.6	8.3	6.9

Values given as percentages of initially applied radioactivity; *Value includes low recovery samples

C. Bound and extractable residues: Values of extractable radioactivity decreased rapidly with time accompanied by formation of non-extractable residues to finally undergo ultimate degradation as summarized in the table below. Starting from a nearly complete extractability given by day zero (96.8 to 102.9%) values decreased to 7.0 to 14.0% after the maximum incubation period of 7 days (soils LS2.2, Laacher Hof AXXa and Attenschwiller) or 10 days (soil Fraunhofer).
In turn, values for non-extractable radioactivity (NER) were low by day zero starting from 1.4 to 4.6% to increase to 22.4 to 27.0% after 7 (soils LS2.2, Laacher Hof AXXa and Attenschwiller) or 10 days (soil Fraunhofer) of incubation.

Extractable and non-extractable residues of ^{14}C-*N*-desmethyl-propamocarb in four aerobic soils

Soil	Extractable residues (%)		Non-extractable residues (%)	
	Day 0	End	Day 0	End
LS2.2	102.9	9.1 (day 7)	1.4	24.5 (day 7)
Laacher Hof AXXa	100.5	7.0 (day 7)	2.2	22.4 (day 7)
Fraunhofer 06A	97.2	14.0 (day 10)	4.6	24.2 (day 10)
Attenschwiller	96.8	9.2 (day 7)	2.2	27.0 (day 7)

Values given as percentages of initially applied radioactivity

D. Volatile radioactivity: Mineralization of ^{14}C-*N*-desmethyl-propamocarb to ^{14}C-carbon dioxide was significant to range from 45.9% to 61.7% of AR in all test soils after 7 (soils LS2.2, Laacher Hof AXXa and Attenschwiller) or 10 days (soil Fraunhofer) of incubation. Formation of other volatile radioactivity was insignificant at any sampling interval (≤ 0.1% AR).

E. Transformation of test substance: ^{14}C-carbon dioxide was formed as the predominant transformation product observed in the course of the study. Other components were observed at minor level to occur at a maximum of 4.1% of AR for a single component in all soils in the course of the study. The biotic character of N-desmethyl-propamocarb degradation in aerobic soil is underlined by the formation of carbon dioxide including non-extractable (bound) residues that could not be converted fully during the runtime of the study.

F. Degradation kinetics: The kinetic evaluation of degradation was performed by fitting of data to the kinetic models SFO, FOMC and DFOP for the test substance using the software KinGui II. The application of the SFO kinetic model resulted in best fits to measured data while the use of bi-phasic models did not result in better fits. The results of the kinetic evaluation were summarized in the table below.
The degradation half-life of *N*-desmethyl-propamocarb in four aerobic soils was estimated to 0.78 days to 3.40 days associated with DT_{90}-values ranging from 2.61 days to 11.3 days on the basis of best fits derived from the SFO kinetic model for all soils.

Kinetics of aerobic degradation of *N*-desmethyl-propamocarb in four aerobic soils:

Kinetic model	Soil	M_0	Parameter	Prob > t [A)]	CI [A)]	DT_{50} (days)	DT_{90} (days)	χ^2-error	VA
SFO	Soil I	105.5	k = 0.497	1.00×10^{-7}	n.a.	1.40	4.63	12.72	A
	Soil II	99.8	k = 0.884	1.00×10^{-11}	n.a.	0.78	2.61	4.64	A
	Soil III	96.7	k = 0.204	0.4×10^{-12}	n.a.	3.40	11.3	2.45	A
	Soil IV	99.7	k = 0.382	0.15×10^{-6}	n.a.	1.81	6.02	11.61	A
FOMC	Soil I	110.6	α = 1292	0.392	incl zero	1.13	3.77	18.11	A
			β = 2114	0.392					
	Soil II	99.9	α = 819	0.401	incl zero	0.78	2.60	4.95	A
			β = 924	0.401					
	Soil III	100.4	α = 5491	0.200	incl zero	2.97	9.86	5.53	U
			β = 23503	0.200					
	Soil IV	104.9	α = 43460	0.003	incl zero	1.49	4.94	16.05	U
			β = 93319	0.003					
DFOP	Soil I	105.5	k1 = 0.497	0.408	n.a.	1.40	4.63	16.01	A
			k2 = 0.227	0.500					
	Soil II	99.9	k1 = 0.902	0.365	n.a.	0.78	2.63	5.28	A
			k2 = 0.7×10^{-6}	0.500					
	Soil III	96.7	k1 = 0.205	0.0008	n.a.	3.40	11.28	2.91	A
			k2 = 0.131	0.5×10^{-5}					
	Soil IV	99.7	k1 = 0.3829	0.128	n.a.	1.81	6.02	14.61	A
			k2 = 0.120	0.461					

[A)] In order to assess the fitted degradation rates as statistically acceptable, Prob > t (i.e. the p-value) should be < 0.05 for all models, except FOMC. Since the two FOMC parameters α and β are shape parameters rather than degradation rates, the confidence interval (CI) was used for evaluation: to be statistically acceptable, the confidence interval should not include zero.
Soil I = LS2.2; Soil II = Laacher Hof AXXa; Soil III = Fraunhofer 06A; Soil IV = Attenschwiller
Best fits were marked bold; n.a. = not applicable
VA = Visual Acceptability: A = Acceptable; U = Unacceptable

II. Conclusions

Following application of ^{14}C-*N*-desmethyl-propamocarb to four soils, degradation was rapid to form ^{14}C-carbon dioxide and non-extractable residues as predominant transformation products underlining the biotic character of conversion of this compound in aerobic soil.
The degradation resulted in half-lives of 0.78 days to 3.40 days following best fits according to the SFO kinetic model.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

The study above was kinetically re-evaluated as reported in KCA 7.1.2.1.2/05 in order to derive trigger and modeling endpoints for use as input parameters.

Report:	KCA 7.1.2.1.2/03; Walther, D.; 2015b; M-530457-01-1
Title:	[14C]propamocarb-N-oxide: Rate of degradation in four soils incubated under aerobic conditions
Report No.:	D96204
Document No.:	M-530457-01-1
Guideline(s):	OECD Test Guideline No. 307 • US EPA OPPTS Test Guideline No. 835.4100 • Regulation (EC) No. 1107/2009 • Commission Regulation (EU) No 283/2013
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

Executive Summary

The degradation rate of the metabolite propamocarb-N-oxide was investigated in four soils under aerobic conditions at 20°C at 16% (g water/100 g soil) (soil LS2.2), 21.0% (soil Laacher Hof AXXa), 26.0% (soil Fraunhofer 06A) and 24.5% (soil Attenschwiller) moisture of MWHC in the dark. These moisture levels correspond to pF 2.0–2.5. The study was performed with 1-*N*-propyl-^{14}C-labelled propamocarb-N-oxide hydrochloride for a maximum incubation period of 7 days (soils Laacher Hof AXXa and Attenschwiller) or 10 days (soil LS2.2 and Fraunhofer 06A).
The nominal application rate was 0.5 mg ^{14}C-test substance/kg soil, based on a maximum occurrence of 8.7% AR in a study performed with the active substance propamocarb-hydrochloride and a single treatment rate in the field of 2200 g a.s./ha.
Values for ^{14}C-propamocarb-N-oxide extractable from soil decreased from 95.0% (day zero) to 8.3% (day 10) in soil LS 2.2, from 93.7% to 1.9% in soil Laacher Hof AXXa, from 84.7% to 0.8% in soil Fraunhofer 06A and from 83.7% to 1.2% in soil Attenschwiller.

Best fit degradation kinetics to measured data were obtained by applying the SFO model for soils LS 2.2 and Laacher Hof AXXa and the FOMC model for soils Fraunhofer 06A and Attenschwiller. The resulting values for the DT_{50} and DT_{90} of propamocarb-N-oxide in aerobic soil were summarised in the table below.

Best fit DT_{50} and DT_{90} values of propamocarb-N-oxide in aerobic soil:

Soil	DT50 [days]	DT90 [days]	Chi² error	Visual assessment	Kinetic model
LS2.2	2.63	8.75	2.662	A	SFO
Laacher Hof AXXa	1.63	5.43	4.678	A	SFO
Fraunhofer 06A	0.02	0.72	4.856	A	FOMC
Attenschwiller	0.36	2.66	8.83	A	FOMC

Visual assessment of fit to be acceptable (A) or unacceptable (U)

I. Material and Methods

A. Materials

1. Test Material: [1-*N*-propyl-^{14}C]propamocarb-*N*-oxide hydrochloride (BCS-AU81087)

Specific radioactivity:	4.65 MBq/mg (125.7 µCi/mg)
Radiochemical purity:	>96% (TLC)
Sample ID:	KML 9853

2. Soils: The test soils originated from the EU and reflected a range of physico-chemical characteristics as summarized in the table below. The soils had been collected fresh from the field and were passed through a 2 mm sieve.

Characteristics of the test soils:

	Soil			
	Speyer 2.2 (Soil I)	**Laacher Hof AXXa (Soil II)**	**Fraunhofer 06A (Soil III)**	**Attenschwiller (Soil IV)**
Geographic location (city / state / country)	Speyer, Rhineland Palatinate Germany	Monheim / North Rhine-Westphalia / Germany	Schmallenberg / North Rhine-Westphalia / Germany	Attenschwiller / Alsace / France
GPS Coordinates	N 49° 19' E 08° 20'	N 51° 05' E 06° 54'	N 51° 09' E 08° 18'	N 47° 34' E 07° 30'
Textural class A)	loamy sand	sandy loam	silty clay	silt loam
Sand (%)a)	7.9	11.8	44.5	17.1
Silt (%)a)	16.3	16.7	44.6	68.0
Clay (%)a)	75.8	71.5	10.9	14.9
pH - water	n.d.	7.5	n.d.	8.2
- 0.01 M CaCl2	5.5	6.9	7.2	7.6
Organic matter (%)B)	2.8	2.5	4.8	2.8
Organic carbon (%)	1.6	1.5	2.8	1.7
Carbonate as CaCO3 (%)	0.3	3.2	2.0	18.0
Microbial biomass (mg microbial C / 100 g soil)				
- Initial (DAT-0)	22.8	47.2	54.6	43.7
- Final	24.1	48.4	56.9	47.9
Cation exchange capacity (meq/100 g)	10.0	9.5	30.1	13.5
Water holding capacity at zero bar (pF 1) (%)7	48.9	48.1	57.4	49.3
Water holding capacity at zero bar (pF 2) (%)	14.8	25.2	39.9	32.2
Water holding capacity at 0.33 bar (pF 2.5) (%)	14.1	20.8	36.2	29.3

n.a. = not analysed; n.d. = not determined

A) USDA classification

B) % organic matter = % organic carbon x 1.724

B. Study design

1. Experimental conditions: Samples of 100 g dry weight of soil each were filled into glass incubation flasks with each sample to receive 0.5 mg test substance/kg soil, a dose representing a nominal field rate of 190 g test substance/ha derived from 2200 g a.s. propamocarb-hydrochloride/ha and a maximum occurrence of 8.7% in soil photolysis study KCA 7.1.1.3/01. Following application the samples were attached to 'flow through' systems with traps to collect each ^{14}C-carbon dioxide and other volatile components. Samples were incubated at 20 ± 1 C and a moisture content of 33% (Soil I, Speyer 2.2), 44% (Soil II, Laacher Hof AXXa), 45% (Soil III, Fraunhofer 06A) and 50% (soil IV, Attenschwiller) in the dark for 7 days (Soils I, II and IV) or 10 days (Soil III) in maximum. The soil moisture was adjusted, during the study, to 16 g water/100 g soil for soil I (Speyer 2.2), 21.0 g water/100 g soil for soil II (Laacher Hof AXXa), 26.0 g water/100 g soil for soil III (Fraunhofer 06A) and 24.5 g water/100 g soil for soil IV (Attenschwiller). These moisture levels correspond to pF 2.0–2.5. The MWHC was determined to be 48.86 g/100g dry soil for soil Speyer 2.2, 48.06 g/100g for soil Laacher Hof AXXa, 57.36 g/100g for soil Fraunhofer 06A and 49.28 g/100g for soil Attenschwiller. In addition, untreated soil samples were incubated under the same conditions for determination of soil microbial activity.

2. Sampling: Duplicate samples were removed for work-up after 0, 1, 2, 3, 5 and 7 days of incubation. Additional samples were taken by day 10 for Soil I (LS2.2) and Soil III (Fraunhofer 06A), and after 0.25 days for Soil II (Laacher Hof AXXa), Soil III (Fraunhofer 06A) and Soil IV (Attenschwiller). Samples

7 Equivalent to the Maximum Water Holding Capacity (MWHC)

for determination of soil microbial biomass were investigated after 0 days and at the end of incubation. The complete samples were immediately processed by extraction.

3. Analytical procedures: The entire soil sample in each test vessel was extracted four times successively with 100 mL acidified (formic acid) aqueous acetonitrile solution (80:20:1, by vol.) by shaking the soil/solvent mixture at ambient temperature for 30 min. The ambient-extracted soil was additionally Soxhlet-extracted with the same solvent (300 mL) for 4 hours. Ambient extracts (included all sampling intervals for soil III, starting by day 1 and the following for Soils I, II and IV) and Soxhlet extracts were combined and sub-samples concentrated and centrifuged prior to analysis.
The ^{14}C-material balance was established for each sample by extraction, analysis of volatiles and combustion of non-extractable residues. Following quantitation of radioactivity in extracts by LSC, analysis was performed by normal phase TLC as primary chromatographic method followed by reversed phase HPLC and ^{14}C-flow-through detection techniques as confirmatory method for selected time points. The determination of non-extractable residues (NER) was performed by combustion/LSC of aliquots of the air-dried extracted soil.
C. Determination of degradation kinetics: The kinetic evaluation was performed for the test substance propamocarb-*N*-oxide with the software KinGUI II following FOCUS kinetic guidance (2011) to obtain best fits to the measured data.

II. Results and Discussion

A. Data: The results of aerobic biotransformation of [1-*N*-propyl-^{14}C]propamocarb-*N*-oxide after incubation in four soils are summarized in the tables below.

Degradation of [1-*N*-propyl-^{14}C]propamocarb-*N*-oxide in loamy sand soil LS 2.2 under aerobic conditions:

Component		Sampling interval (days)						
		0	1	2	3	5	7	10
propamocarb-N-oxide	Mean*	95.0	69.3	55.6	44.1	23.9	14.9	8.3
	SD	±0.5	±2.1	±1.0	±0.8	±2.8	±1.7	±1.0
Unknown M1	Mean*	0.8	0.5	1.8	0.9	2.3	2.0	1.9
	SD	±0.0	±0.3	±0.0	±0.5	±0.2	±0.3	±0.3
Unknown M2	Mean*	0.7	1.4	2.8	2.2	2.7	2.3	1.7
	SD	±0.1	±0.2	±0.6	±0.1	±0.1	±0.1	±0.2
Unknown M3	Mean*	0.3	1.0	2.1	0.4	0.9	1.1	0.9
	SD	±0.2	±0.1	±0.2	±0.2	±0.1	±0.	±0.2
Unknown M4	Mean*	-	6.8	4.9	8.1	7.7	8.0	2.8
	SD	-	±0.3	±0.2	±0.0	±0.5	±0.5	±0.9
Unknown M6	Mean*	-	7.5	9.9	8.7	3.5	3.3	1.4
	SD	-	±0.3	±0.3	±0.4	±0.5	±0.2	±0.1
Unknown M7	Mean*	-	2.2	2.6	2.0	1.6	1.4	2.0
	SD	-	±0.1	±0.7	±2.0	±0.9	±0.8	±0.1
Total extractable radioactivity	Mean*	96.8	88.6	79.6	66.3	42.6	33.0	18.9
	SD	±0.6	±2.7	±0.0	±2.7	±4.2	±2.9	±0.5
Non-extractable radioactivity	Mean*	1.5	5.1	8.9	11.3	18.2	19.0	22.1
	SD	±0.1	±0.0	±0.3	±0.7	±0.9	±0.7	±0.0
$14CO_2$	Mean*	n.d.	4.0	13.1	19.2	34.8	43.3	54.7
	SD	n.a.	±0.4	±0.4	±0.5	±2.9	±0.3	±0.1
Other volatiles	Mean*	n.d.	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
	SD	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.

Total recovery (%)	Mean*	98.4	97.7	101.6	96.8	95.6	95.3	95.7
	SD	±0.6	±2.4	±0.1	±1.5	±0.5	±2.5	±0.6

Values given as percentages of initially applied radioactivity; n.d.: not determined; n.a.: not applicable
SD = standard deviation; * Mean values of duplicate samples analysed

Degradation of [1-*N*-propyl-^{14}C]propamocarb-*N*-oxide in sandy loam soil Laacher Hof AXXa under aerobic conditions:

Component		**Sampling interval** (days)						
		0	**0.25**	**1**	**2**	**3**	**5**	**7**
propamocarb-N-oxide	Mean*	93.7	81.1	57.3	43.4	23.6	13.5	1.9
	SD	±0.3	±1.2	±0.6	±0.8	±0.1	±3.0	±0.4
Unknown M1	Mean*	0.5	0.5	0.4	0.6	2.1	1.9	2.0
	SD	±0.2	±0.0	±0.1	±0.2	±0.3	±0.0	±0.2
Unknown M2	Mean*	1.1	0.5	1.2	1.4	2.2	2.2	1.9
	SD	±0.0	±0.1	±0.0	±0.2	±0.1	±0.0	±0.4
Unknown M3	Mean*	0.6	1.4	1.1	0.9	1.2	0.9	1.6
	SD	±0.1	±0.1	±0.3	±0.2	±0.1	±0.2	±0.1
Unknown M4	Mean*	-	3.4	8.0	3.0	6.6	1.9	3.1
	SD	-	±0.5	±0.3	±0.1	±0.5	±0.4	±0.5
Unknown M6	Mean*	-	5.9	7.4	7.1	4.9	1.9	0.8
	SD	-	±0.4	±0.2	±0.1	±0.0	±0.4	±0.1
Unknown M7	Mean*	-	-	1.8	2.8	1.8	1.4	0.8
	SD	-	-	±0.3	±0.3	±1.3	±0.4	±0.1
Total extractable radioactivity	Mean*	96.0	92.8	77.2	59.2	42.4	23.7	12.2
	SD	±0.5	±0.5	±0.9	±0.6	±1.4	±3.2	±0.7
Non-extractable radioactivity	Mean*	2.6	3.6	8.5	15.9	19.7	24.0	24.6
	SD	±0.0	±0.4	±0.2	±0.4	±0.4	±0.6	±0.2
14CO2	Mean*	n.d.	1.7	5.8	23.2	33.2	45.6	51.9
	SD	n.a.	±0.0	±1.7	±1.2	±1.5	±2.3	±4.6
Other volatiles	Mean*	n.d.	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
	SD	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Total recovery (%)	Mean*	98.5	98.1	91.6	98.4	95.4	93.5	88.6**
	SD	±0.5	±0.8	±1.1	±1.1	±0.4	±4.9	±4.1

Values given as percentages of initially applied radioactivity; n.d.: not determined; n.a.: not applicable
SD = standard deviation; * Mean values of duplicate samples analysed; **Low total recovery for two replicates due to losses in determination of ^{14}C-carbon dioxide for replicate B of day 7 (47.3% AR) in comparison to replicate A (56.5%)

Degradation of [1-*N*-propyl-^{14}C]propamocarb-*N*-oxide in silty clay soil Fraunhofer 06A under aerobic conditions:

Component		Sampling interval (days)							
		0	**0.25**	**1**	**2**	**3**	**5**	**7**	**10**
propamocarb-N-oxide	Mean*	84.7	13.8	8.4	6.0	4.5	2.3	2.0	0.8
	SD	±0.0	±1.0	±0.0	±0.6	±1.3	±0.0	±0.3	±0.2
Unknown M1	Mean*	0.4	-	0.4	-	0.5	0.5	0.8	0.6
	SD	±0.4	-	±0.0	-	±0.6	±0.4	±0.1	±0.0
Unknown M2	Mean*	0.4	0.2	0.8	0.5	1.1	1.4	0.9	0.8
	SD	±0.4	±0.2	±0.1	±0.2	±0.3	±0.1	±0.1	±0.1
Unknown M3	Mean*	0.2	0.4	0.9	0.1	0.3	0.2	0.4	0.6
	SD	±0.2	±0.2	±0.0	±0.0	±0.3	±0.2	±0.1	±0.0
Unknown M4	Mean*	1.7	1.4	1.6	0.6	0.9	0.5	0.5	0.5
	SD	±0.6	±0.3	±0.1	±0.0	±0.3	±0.1	±0.1	±0.2
Unknown M6	Mean*	1.1	69.7	61.4	53.8	45.6	28.0	14.6	5.9
	SD	±0.4	±2.3	±2.0	±1.5	±0.2	±0.5	±0.1	±1.4
Unknown M7	Mean*	3.9	-	4.1	2.0	1.3	0.6	1.2	1.2
	SD	±1.5	-	±0.2	±1.7	±1.3	±0.1	±0.1	±0.1
Total extractable radioactivity	Mean*	92.4	85.6	77.6	63.0	54.2	33.4	20.5	10.4
	SD	±0.2	±3.3	±2.1	±0.7	±1.7	±0.8	±0.1	±1.6
Non-extractable radioactivity	Mean*	6.2	7.9	13.1	16.0	18.1	22.9	23.2	22.5
	SD	±0.1	±2.2	±0.8	±0.0	±0.1	±0.4	±0.3	±0.1
14CO2	Mean*	n.d.	0.5	3.9	15.7	22.6	36.4	47.9	61.7
	SD	n.a.	±0.1	±0.1	±1.0	±0.7	±1.4	±0.9	±1.3
Other volatiles	Mean*	n.d.	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
	SD	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Total recovery (%)	Mean*	98.6	94.1	94.7	94.8	95.0	92.7	91.6	94.7
	SD	±0.4	±1.2	±1.4	±1.6	±1.0	±1.0	±0.7	±0.3

Values given as percentages of initially applied radioactivity; n.d.: not determined; n.a.: not applicable
SD = standard deviation; * Mean values of duplicate samples analysed

Degradation of [1-*N*-propyl-^{14}C]propamocarb-*N*-oxide in silt loam soil Attenschwiller under aerobic conditions

Component		Sampling interval (days)						
		0	**0.25**	**1**	**2**	**3**	**5**	**7**
propamocarb-N-oxide	Mean*	83.7	51.5	16.7	16.2	7.5	3.8	1.2
	SD	±0.1	±2.5	±0.7	±1.2	±1.4	±0.5	±0.3
Unknown M1	Mean*	1.0	0.2	1.1	0.7	0.5	1.1	0.9
	SD	±0.1	±0.2	±0.4	±0.4	±0.3	±0.1	±0.1
Unknown M2	Mean*	0.9	1.3	1.1	1.3	1.8	1.8	1.0
	SD	±0.1	±0.8	±0.2	±0.1	±0.1	±0.2	±0.1
Unknown M3	Mean*	0.4	0.8	0.4	0.9	1.1	1.6	1.0
	SD	±0.1	±0.2	±0.1	±0.3	±0.0	±0.2	±0.1
Unknown M4	Mean*	0.6	2.1	2.8	1.1	1.5	2.0	0.7

	SD	±0.1	±0.2	±0.4	±0.3	±0.1	±0.4	±0.1
Unknown M6	Mean*	-	36.2	49.1	33.2	19.6	5.9	2.1
	SD	-	±2.5	±2.9	±0.3	±0.2	±0.4	±0.1
Unknown M7	Mean*	3.3	1.1	6.3	2.3	2.2	1.1	1.7
	SD	±1.0	±1.2	±0.6	±0.4	±0.3	±0.1	±0.2
Total extractable radioactivity	Mean*	91.9	93.3	77.7	55.7	34.4	17.2	8.6
	SD	±0.8	±0.2	±2.2	±0.6	±1.1	±0.9	±0.6
Non-extractable radioactivity	Mean*	1.0	1.7	8.9	16.1	23.7	27.3	25.7
	SD	±0.1	±0.2	±0.3	±0.7	±0.7	±0.5	±0.1
14CO2	Mean*	n.d.	0.9	3.1	20.2	35.8	51.1	59.5
	SD	n.a.	±0.2	±2.8	±0.1	±0.7	±3.2	±1.5
Other volatiles	Mean*	n.d.	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
	SD	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Total recovery (%)	Mean*	92.9	96.0	89.7	92.0	93.9	95.6	93.8
	SD	±0.9	±0.2	±0.9	±0.0	±0.3	±2.8	±0.7

Values given as percentages of initially applied radioactivity; n.d.: not determined; n.a.: not applicable
SD = standard deviation; * Mean values of duplicate samples analysed

The full and fast degradation of the photolysis metabolite propamocarb-N-oxide could be observed during the study duration. In the last sampling day the amount of the test substance is lower than 10% of applied. This is in accordance with the OECD 307 test guideline, where it is stated that a termination of the test is possible after 120 days or when at least 90% of the test substance is transformed but only if at least 5% CO2 is formed. The later was the case. In addition, the study was initiated to address the current data requirements and to estimate the soil degradation rate of the relevant soil photolysis metabolite propamocarb-N-oxide. However, the study should not be seen as a full pathway study. All during this study, formed transient minor metabolites were not detected in relevant amounts in any soil degradation study of propamocarb-hydrochloride (all < 5% of applied active substance).

B. Mass balance: The total recovery of radioactivity was complete to range from 95.3 to 101.6% of AR for loamy sand soil LS2.2, 88.6 to 98.5% for sandy loam soil Laacher Hof AXXa, 91.6 to 98.6% for silty clay soil Fraunhofer 06A and 89.7 to 96.0% for soil Attenschwiller. The results are summarised in more detail in the table below. For some single replicates at some sampling intervals total recoveries of radioactivity were be below 90% AR. The losses could be assigned to leaks in trapping of ^{14}C-carbon dioxide within the flow-through incubation systems.

Total material balances of radioactivity of ^{14}C-propamocarb-*N*-oxide in four aerobic soils:

Soil	LS2.2	Laacher Hof AXXa	Fraunhofer 06A	Attenschwiller
Total Recovery (% AR)	95.3 - 101.6	88.6 - 98.5	91.6 - 98.6	89.7 - 96.0
Mean (% AR)*	97.3	94.8	94.5	93.4
Rel. standard deviation*	2.6	4.5	2.2	2.4

Values given as percentages of initially applied radioactivity; *Values include low recovery samples

C. Bound and extractable residues: Values of extractable radioactivity decreased rapidly with time accompanied by formation of non-extractable residues to finally undergo ultimate degradation as summarized in Table 11.1.4.3-79. Starting from a nearly complete extractability given by day zero (91.9 to 96.8%) values decreased to 8.6 to 18.9% after the maximum incubation periods of 7 days or 10 days, respectively. In turn, values for non-extractable radioactivity (NER) were low by day zero starting from 1.0 to 6.2% to increase to 22.1 to 25.7% at the end of incubation.

Extractable and non-extractable residues of ^{14}C- propamocarb-*N*-oxide in four aerobic soils

Soil	Extractable residues (%)		Non-extractable residues (%)	
	Day 0	End	Day 0	End
LS2.2	96.8	18.9 (day 10)	1.5	22.1 (day 10)
Laacher Hof AXXa	96.0	12.2 (day 7)	2.5	24.6 (day 7)
Fraunhofer 06A	92.4	10.4 (day 10)	6.2	22.5 (day 10)
Attenschwiller	91.9	8.6 (day 7)	1.0	25.7 (day 7)

Values given as percentages of initially applied radioactivity

D. Volatile radioactivity: Mineralization of ^{14}C- propamocarb-*N*-oxide to ^{14}C-carbon dioxide was significant to range from 51.9% to 61.7% of AR in all test soils after 7 (soils Laacher Hof AXXa and Attenschwiller) or 10 days (soils LS2.2 and Fraunhofer) of incubation. Formation of other volatile radioactivity was insignificant at any sampling interval (≤ 0.1% AR).

E. Transformation of test substance: ^{14}C-carbon dioxide was formed as the major transformation product in the course of the study. Other components were observed at maximum levels of 69.7% of AR (Unknown M6, day 0.25, soil Fraunhofer), 8.1% (Unknown M4, day 3, soil LS2.2) and 6.3% (Unknown M7, day 1, soil Attenschwiller). The transient character of the components observed was indicated by their decline to values of 5.9% AR (Unknown M6, day 10, soil Fraunhofer) and significantly below after 7 or 10 days, respectively. Additional components were observed at trace level each accounting below 3% AR in maximum in all soils in the course of the study. The biotic character of degradation in aerobic soil was underlined by the formation of non-extractable (bound) residues that could not be converted fully to carbon dioxide during the short total runtime of the study.

F. Degradation kinetics: The kinetic evaluation of degradation was performed by fitting of data to the kinetic models SFO, FOMC and DFOP for the test substance using the software KinGui II. The application of the SFO kinetic model resulted in best fits to measured data while the use of bi-phasic models did not result in better fits.

The degradation half-life of propamocarb-N-oxide in four aerobic soils was estimated to 0.02 days to 2.63 days associated with DT_{90} values ranging from 0.72 days to 8.75 days when applying the SFO kinetic model as best fits for soils LS2.2 and Laacher Hof AXXa and the kinetic model FOMC for soils Fraunhofer and Attenschwiller.

The results of the kinetic evaluation were summarized in the table below.

Kinetics of aerobic degradation of propamocarb-N-oxide in four aerobic soils

Kinetic model	Test Item	M_0	Parameter	Prob > t [A)]	CI [A)]	DT_{50} [days]	DT_{90} [days]	χ^2-error	VA
SFO	Soil I	93.6	k = 0.263	1.29×10^{-13}	n.a.	2.63	8.75	2.662	A
	Soil II	91.8	k = 0.424	1.53×10^{-11}	n.a.	1.63	5.43	4.678	A
	Soil III	84.7	k = 7.202	9.32×10^{-7}	n.a.	0.10	0.32	21.45	U
	Soil IV	80.1	k = 1.3905	1.47×10^{-5}	n.a.	0.50	1.66	17.76	U
FOMC	Soil I	94.5	α = 1050	n.a.	incl. zero	2.55	8.46	3.156	A
			β = 3965	n.a.					
	Soil II	93.4	α = 1266	n.a.	incl. zero	1.51	5.02	5.84	A
			β = 2755	n.a.					
	Soil III	84.7	α = 0.510	n.a.	excl. zero	0.02	0.72	4.856	A
			β = 0.008	n.a.					
	Soil IV	84.0	α = 1.2189	n.a.	excl. zero	0.36	2.66	8.83	A
			β = 0.4747	n.a.					
DFOP	Soil I	94.1	k1 = 0.279	2.71×10^{-5}	n.a.	2.58	9.16	2.923	A
			k2 = 1.49×10^{-6}	0.5					

	Soil II	91.8	k1 = 0.424	2.51×10^{-4}	n.a.	1.63	5.43	5.568	A
			k2 = 0.192	6.55×10^{-11}					
	Soil III	84.7	k1 = 11.98	7.34×10^{-9}	n.a.	0.07	0.89	1.59	A
			k2 = 0.285	3.51×10^{-7}					
	Soil IV	84.1	k1 = 2.98	5.51×10^{-13}	n.a.	0.35	3.06	7.64	A
			k2 = 0.334	0.00125					

[A]) In order to assess the fitted degradation rates as statistically acceptable, Prob > t (i.e. the p-value) should be < 0.05 for all models except FOMC. Since the two FOMC parameters α and β are shape parameters rather than degradation rates, the confidence interval (CI) was used for evaluation: to be statistically acceptable, the confidence interval should not include zero.
Soil I = LS2.2; Soil II = Laacher Hof AXXa; Soil III = Fraunhofer 06A; Soil IV = Attenschwiller
Best fits were marked bold; n.a. = not applicable; VA = Visual Acceptability: A = Acceptable; U = Unacceptable

III. Conclusion

Following application of ^{14}C-propamocarb-*N*-oxide to four soils degradation was rapid to form ^{14}C-carbon dioxide and non-extractable residues as predominant transformation products underlining the biotic character of conversion of this compound in aerobic soil.
The degradation resulted in half-lives of 0.78 to 3.40 days following best fits from SFO for two soils or the FOMC multi-compartment model for the other two.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Report:	KCA 7.1.2.1.2/04; Oberdoerster, C.; Boiselle, N.; Hoerold, C.; 2015a; M-541770-01-1
Title:	Kinetic evaluation of the degradation of propamocarb-hydrochloride and its metabolite N-desmethyl-propamocarb in soil under aerobic laboratory conditions
Report No.:	EnSa-14-1331
Document No.:	M-541770-01-1
Guideline(s):	"Generic Guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". EC Document Reference: None, version 1.1, 2015 amending "Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference Sanco/10058/2005 version 2.0, 2006
Guideline deviation(s):	not applicable
GLP/GEP:	**no**

Executive Summary
For metabolite *N*-desmethyl-propamocarb degradation data were kinetically evaluated according to FOCUS Guidance coming from one soil in a study performed with ^{14}C-labeled active substance (KCA 7.1.2.1.2/01). The data were evaluated to derive trigger and modelling endpoints for use as input parameters for environmental risk assessments.
The calculations of half-lives in soil followed a stepwise approach. For identification of best fits to the measured data the SFO kinetic model was applied as the initial step. This was followed by application of bi-phasic models, i.e. FOMC or DFOP, in case of unacceptable fits according to the criteria set. The resulting best fits served as the basis to derive non-normalized half-lives for comparison against trigger endpoints. In a next step, values for the DT_{50} were normalized to reference conditions (20°C, pF2 moisture).

Trigger endpoints: Non-normalised values of the DT_{50} and the DT_{90} were derived from an 'all-SFO' combined best fit with the active substance with results summarized in the table below.
The non-normalised half-life of *N*-desmethyl-propamocarb was 11.1 days for Porterville loamy sand soil while the value for the DT_{90} was 36.9 days for the same soil.

Comparison against EU triggers: Summary of results of kinetic evaluation of degradation for *N*-desmethyl-propamocarb in aerobic soil in the laboratory

Parameter	*N*-Desmethyl-propamocarb
20°C, Non-normalised DT_{50}, range (days)	11.1
Worst case DT_{50} (days)	11.1
20°C, Non-normalised DT_{90}, range (days)	36.9
Worst case DT_{90} (days)	36.9

Modelling endpoints: The 'all-SFO' approach in combination with the active substance was confirmed as the visually and statistically best acceptable kinetic model for deriving the modelling endpoint. The value was normalised by comparison of study incubation conditions to reference conditions (20°C, pF2 moisture) with results summarised in the table below.
For use as modelling endpoint, the overall mean normalised half-life of N-desmethyl propamocarb was estimated to 11.2 days.

Modelling endpoints: Normalised laboratory DT_{50} values for *N*-desmethyl propamocarb in aerobic soil for use as input in environmental exposure assessments

Parameter	N-Desmethyl-propamocarb
Normalised (20°C, pF2) DT_{50}, range (days)	11.2
Geometric mean	n.a.

I. Material and Methods

For metabolite *N*-desmethyl-propamocarb the kinetic analysis was performed in combination with parent compound data as referenced under KCA 7.1.2.1.2/01. The evaluation considered degradation data of *N*-desmethyl propamocarb in soil under aerobic conditions of the laboratory from a study following application of 1-*N*-propyl-^{14}C-labelled active substance to two US soils. However, metabolite N-desmethyl propamocarb was observed just in one soil, i.e. Porterville loamy sand.
The degradation data were kinetically evaluated following FOCUS Guidance [FOCUS 2006, amended 2011] with the software KinGui2 including the use of iteratively re-weighted least-square (IRLS) optimisation.
The kinetic evaluation derived DT_{50} values according to the respective flowcharts for the determination of trigger endpoints and for use as input parameters in modelling.
In following the actual FOCUS guidance, the particular criteria applied were essentially the same as described for the evaluation of the active substance earlier (see KCA 7.1.2.1.1).
The data sets along with the characteristics of soils was summarised in the table below.

Degradation study performed with propamocarb-hydrochloride in aerobic soil under laboratory conditions including characteristics of soils

Study	Soil	Soil texture	Test temperature (°C)	Test moisture (%w/w)	Sand (%)	Clay (%)	Org. carbon (%)	pH ($CaCl_2$)	CEC (meq / 100 g)
KCA 7.1.2.1.2/01	Aromas	sandy loam	25	9.8	61	15	2.3	5.1	16.3
	Porterville	sandy loam	25	12.7	61	7	0.4	7.9	9.6

Following input of propamocarb-hydrochloride and N-desmethyl propamocarb degradation data (KCA 7.1.2.1.2/01) into KinGUI2 SFO kinetics were applied to all datasets according to the flowcharts.

II. Results and Discussion

Trigger endpoint determination:
According to the decision criteria, the bi-phasic models FOMC and DFOP showed no improvement over SFO kinetics. SFO kinetics was determined to be the best-fit for all data sets.
The resulting non-normalised values for the DT_{50} and the DT_{90} derived are summarised in the table below.

Trigger evaluation: Non-normalised DT_{50}-values for *N*-desmethyl-propamocarb in aerobic soil under laboratory conditions (combined parent/metabolite evaluation)

Soil	Label position	DT_{50} (days)	DT_{90} (days)	formation fraction	Chi^2 (%)	t-test/ confidence interval	VA[a)]
Aromas sandy loam, 25°C (Study 1)	1-*N*-propyl	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Porterville sandy loam, 25°C (Study 1)	1-*N*-propyl	11.1	36.9	0.40	22.0	k < 0.001	O

Study 1: KCA 7.1.2.1.2/01; n.a. = not applicable
[a)] VA = Visual Assessment (++ = excellent, + = good, O = acceptable, - = not acceptable)

Modelling endpoint determination:
The FOCUS Kinetics modelling endpoint flowchart [FOCUS, 2006, 2011] was used to evaluate the datasets. The SFO kinetic model was considered visually and statistically acceptable for deriving modelling endpoints for all data sets thus with no improvement when applying bi-phasic kinetic models like FOMC or DFOP.
For the use in environmental modelling the degradation half-lives were normalised to reference conditions regarding soil moisture (100% field capacity) and temperature (20°C). The parameters used in the laboratory tests and the respective correction factors calculated were summarised in the table below.

Correction factors for soil temperature and moisture content

Soil	Tempe-rature (°C)	Correction factor Temperature	Incubation moisture (%w/w)	pF2 moisture (%w/w)	Correction factor Moisture	Total correction factor
Porterville sandy loam (Study 8)	25	1.6062	9.8	19	0.6269	1.0069
Aromas sandy loam (Study 8)	25	1.6062	12.7	19	0.7532	1.2099

Study 1: KCA 7.1.2.1.2/01

The resulting normalised half-lives were summarised the table below.

Normalised (20°C and pF2) DT_{50} values for N-desmethyl propamocarb as modelling endpoints:

Soil	Kinetic model	Trigger DT_{50} (days)	Trigger DT_{90} (days)	Non-normalised DT_{50} estimate for modelling (days)	DT_{50} [20°C and pF2] (days)
Aromas sandy loam (Study 8)	n.a.	n.a.	n.a.	n.a	n.a.
Porterville sandy loam (Study 8)	SFO	11.1	36.9	11.1	11.2

Geometric mean					n.a.

Study 1: KCA 7.1.2.1.2/01

III. Conclusions

The evaluation of aerobic soil degradation data according to actual FOCUS kinetic guidance resulted in a non-normalised half-life of 11.1 days and a DT_{90} of 36.9 days for the metabolite N-desmethyl propamocarb for comparison with EU trigger endpoints.
Degradation was found to be adequately described by SFO as kinetic model for all data sets to fit with experimental data.
The approach for fitting with experimental data resulted in the use of the SFO kinetic model to derive non-normalised values for the DT_{50} then normalised for moisture (pF2) and temperature (20°C). The evaluation resulted in a normalized half-life of 11.1 days for use as modelling input parameter in environmental risk assessments.
The value derived is regarded as suitable and reliable for use in environmental exposure assessments.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

The total data on rate of degradation of metabolite N-desmethyl propamocarb in soil to derive a normalised geometric mean as modelling endpoint is summarized after the following kinetic evaluation.

Report:	KCA 7.1.2.1.2/05; Oberdoerster, C.; Hoerold, C.; 2015a; M-541686-01-1
Title:	Kinetic evaluation of the degradation of N-desmethyl-propamocarb in soil under aerobic laboratory conditions
Report No.:	EnSa-15-0519
Document No.:	M-541686-01-1
Guideline(s):	"Generic Guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". EC Document Reference: None, version 1.1, 2015 amending "Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference Sanco/10058/2005 version 2.0, 2006
Guideline deviation(s):	not applicable
GLP/GEP:	**no**

For metabolite *N*-desmethyl-propamocarb degradation data, the kinetic evaluation was performed according to FOCUS Guidance coming from four soils in a study performed with separately dosed ^{14}C-labeled N-desmethyl propamocarb to soil (KCA 7.1.2.1.2/02).
The data were evaluated to derive trigger and modelling endpoints for use as input parameters for environmental risk assessments.
The calculations of half-lives in soil followed a stepwise approach. For identification of best fits to the measured data, the SFO kinetic model was applied as the initial step. This was followed by application of bi-phasic models, i.e. FOMC or DFOP, in case of unacceptable fits according to the criteria set. The resulting best fits served as the basis to derive non-normalized half-lives for comparison against trigger endpoints. In a next step, values for the DT_{50} were normalized to reference conditions (20°C, pF2 moisture).

Trigger endpoints: Non-normalised values of the DT_{50} and the DT_{90} were derived from an SFO best fits, with results summarized in the table below.
The non-normalised half-lives of *N*-desmethyl-propamocarb ranged from 0.76 days for Laacher Hof AXXa sandy loam soil to 3.19 days for Fraunhofer 06A soil while the corresponding values for the DT_{90} were from 3.22 days to 12.14 days for the same soils.

Comparison against EU triggers: Summary of results of kinetic evaluation of degradation for *N*-desmethyl- propamocarb in aerobic soil in the laboratory

Parameter	*N*-Desmethyl-propamocarb
20°C, Non-normalised DT_{50}, range (days)	0.76 – 3.19
Worst case DT_{50} (days)	3.19
20°C, Non-normalised DT_{90}, range (days)	3.22 – 12.14
Worst case DT_{90} (days)	12.14

For completeness, includes values derived from active substance study

Modelling endpoints: The kinetic model SFO was the visually and statistically best acceptable kinetic model for deriving the modelling endpoint for all soils. The values were normalised by comparison of study incubation conditions to reference conditions (20°C, pF2 moisture) with results summarised in the table below.
For use as modelling endpoint and considering the results of a study performed with the active substance, the overall geometric mean normalised half-life of N-desmethyl propamocarb was estimated to 2.03 days.

Modelling endpoints: Normalised laboratory DT_{50}-values for *N*-desmethyl propamocarb in aerobic soil for use as input in environmental exposure assessment

Parameter	N-Desmethyl-propamocarb
Normalised (20°C, pF2) DT_{50}, range (days)	0.67 – 2.36
Geometric mean	1.32
Normalised (20°C, pF2) DT_{50}, range (days)	0.67 – 11.1*
Geometric mean	2.03*

*For completeness, includes value derived from active substance study

I. Material and Methods

The evaluation considered degradation data of *N*-desmethyl propamocarb in soil under aerobic conditions of the laboratory from a study following separately dosed 1-*N*-propyl-^{14}C-labelled *N*-desmethyl-propamocarb to four soils (KCA 7.1.2.1.2/02).
The degradation data were kinetically evaluated following FOCUS Guidance [FOCUS 2006, amended 2011] with the software KinGui2 including the use of iteratively re-weighted least-square (IRLS) optimisation.
The kinetic evaluation derived DT_{50} values according to the respective flowcharts for the determination of trigger endpoints and for use as input parameters in modelling.
In following the actual FOCUS guidance, the particular criteria applied were essentially the same as described for the evaluation of the active substance earlier (see KCA 7.1.2.1.1).
The data sets along with the characteristics of soils was summarised in the table below.

Degradation study performed with N-desmethyl propamocarb in aerobic soil under laboratory conditions including characteristics of soils

Study	Soil	Soil texture	Test temperature (°C)	Test moisture (%w/w)	Sand (%)	Clay (%)	Org. carbon (%)	pH ($CaCl_2$)	CEC (meq / 100 g)
KCA 7.1.2.1.2/02	Speyer 2.2.	loamy sand	20	16	75.8	7.9	1.61	5.5	10.0
	Laacher Hof AXXa	sandy loam	20	21	71.5	11.8	1.47	6.9	9.46
	Fraunhofer 06A	silty clay	20	26	10.9	44.5	2.76	7.2	30.12
	Atten-schwiller	silt loam	20	25	14.9	17.1	1.65	7.6	13.53

Following input of N-desmethyl propamocarb degradation data (KCA 7.1.2.1.2/02) into KinGUI2 SFO kinetics were applied to all datasets according to the flowcharts.

II. Results and Discussion

Trigger endpoint determination:
According to the decision criteria, the bi-phasic models FOMC and DFOP showed no improvement over SFO kinetics. SFO kinetics was determined to be the best-fit for all data sets. The resulting non-normalised values for the DT_{50} and the DT_{90} derived are summarised in the table below.

Trigger evaluation: Non-normalised DT_{50}-values for *N*-desmethyl-propamocarb in aerobic soil under laboratory conditions (evaluation of metabolite separately dosed)

Soil	Label position	DT_{50} (days)	DT_{90} (days)	formation fraction	Chi^2 (%)	t-test/ confidence interval	VA[a)]
Speyer 2.2, loamy sand, 20°C	1-*N*-propyl	1.36	4.51	n.a.	11.6	k < 0.001	O
Laacher Hof AXXa sandy loam, 20°C	1-*N*-propyl	0.76	2.52	n.a.	4.3	k < 0.001	+
Fraunhofer 06A, silty clay, 20°C	1-*N*-propyl	3.19	10.60	n.a.	1.5	k < 0.001	++
Attenschwiller, silt loam, 20°C	1-*N*-propyl	1.73	5.76	n.a.	9.8	k < 0.001	O

Study: KCA 7.1.2.1.2/02; n.a. = not applicable
[a)] VA = Visual Assessment (++ = excellent, + = good, O = acceptable, - = not acceptable)

Modelling endpoint determination:
The FOCUS Kinetics modelling endpoint flowchart [FOCUS, 2006, 2011] was used to evaluate the datasets. The SFO kinetic model was considered visually and statistically acceptable for deriving modelling endpoints for all data sets thus with no improvement when applying bi-phasic kinetic models like FOMC or DFOP.
For the use in environmental modelling the degradation half-lives were normalised to reference conditions regarding soil moisture (100% field capacity) and temperature (20°C). The parameters used in the laboratory tests and the respective correction factors calculated were summarised in the table below.

Correction factors for soil temperature and moisture content

Soil	Tempe-rature (°C)	Correction factor Temperature	Incubation moisture (%w/w)	pF2 moisture (%w/w)	Correction factor Moisture	Total correction factor
Speyer 2.2, loamy sand (Study 1)	20	1.00	16	14.79	1.00	1.000
Laacher Hof AXXa sandy loam (Study 1)	20	1.00	21	25.17	0.881	0.881
Fraunhofer 06A, silty clay (Study 1)	20	1.00	26	39.93	0.741	0.741
Attenschwiller, silt loam (Study 1)	20	1.00	25	32.15	0.827	0.827

Study 1: KCA 7.1.2.1.2 /02

The resulting normalised half-lives were summarised the table below.

Normalised (20°C and pF2) DT_{50} values for *N*-desmethyl propamocarb as modelling endpoints

Soil	Kinetic model	Trigger DT_{50} (days)	Trigger DT_{90} (days)	Non-normalised DT_{50} estimate for modelling (days)	DT_{50} [20°C and pF2] (days)
Speyer 2.2, loamy sand (Study 1)	SFO	1.36	4.51	1.36	1.36
Laacher Hof AXXa sandy loam (Study 1)	SFO	0.76	2.52	0.76	0.67
Fraunhofer 06A, silty clay (Study 1)	SFO	3.19	10.60	3.19	2.36
Attenschwiller, silt loam (Study 1)	SFO	1.73	5.76	1.73	1.43
Geometric mean, four soils					1.32
Porterville sandy loam (Study 2)	SFO	11.1	36.9	11.1	11.1*
Overall geometric mean					2.03*

Study 1: KCA 7.1.2.1.2 /02; Study 2: KCA 7.1.2.1.2 /01
*For completeness, includes value derived from active substance study

III. Conclusion

For comparison with EU trigger endpoints the evaluation of aerobic soil degradation data according to actual FOCUS kinetic guidance resulted in non-normalised half-lives for metabolite N-desmethyl propamocarb to range from 0.76 days to 11.1 days and values of the DT_{90} of ranging from 2.52 days to 36.9 days.
Degradation was found to be adequately described by SFO as kinetic model for all data sets to fit with experimental data.

For use as modelling input parameter in environmental risk assessments the evaluation resulted in a normalized geometric mean half-life of 2.03 days for the total of data sets available.
The approach for fitting with experimental data resulted in the use of the SFO kinetic model to derive non-normalised values for the DT_{50} then normalised for moisture (pF2) and temperature (20°C).

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Report:	KCA 7.1.2.1.2/06; Oberdoerster, C.; Hoerold, C.; 2015b; M-541685-01-1
Title:	Kinetic evaluation of the degradation of propamocarb-N-oxide in soil under aerobic laboratory conditions
Report No.:	EnSa-15-0518
Document No.:	M-541685-01-1
Guideline(s):	"Generic Guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". EC Document Reference: None, version 1.1, 2015 amending "Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration". Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference Sanco/10058/2005 version 2.0, 2006
Guideline deviation(s):	not applicable
GLP/GEP:	**No**

For metabolite propamocarb-*N*-oxide degradation data the kinetic evaluation was performed according to FOCUS Guidance coming from four soils in a study performed with separately dosed ^{14}C-labeled propamocarb-*N*-oxide to soil (KCA 7.1.2.1.2/03).

The data were evaluated to derive trigger and modelling endpoints for use as input parameters for environmental risk assessments.
The calculations of half-lives in soil followed a stepwise approach. For identification of best fits to the measured data the SFO kinetic model was applied as the initial step. This was followed by application of bi-phasic models, i.e. FOMC or DFOP, in case of unacceptable fits according to the criteria set. The resulting best fits served as the basis to derive non-normalized half-lives for comparison against trigger endpoints. In a next step, values for the DT_{50} were normalized to reference conditions (20°C, pF2 moisture).

Trigger endpoints: Non-normalised values of the DT_{50} and the DT_{90} were derived from an SFO best fit for one soil while use of FOMC (one soil) or DFOP (two soils) resulted in best fits to measured data. The results were summarized in the table below.
The non-normalised half-lives of propamocarb-*N*-oxide ranged from 0.06 days for Fraunhofer silty clay soil to 2.37 days for the Speyer 2.2 loamy sand. The values for the DT_{90} were from 0.46 days to 9.14 days for the same soils.

Comparison against EU triggers: Summary of results of kinetic evaluation of degradation for propamocarb-N-oxide in aerobic soil in the laboratory

Parameter	**propamocarb-*N*-oxide**
20°C, Non-normalised DT_{50}, range (days)	0.06 – 2.37
Worst case DT_{50} (days)	2.37
20°C, Non-normalised DT_{90}, range (days)	0.46 – 9.14
Worst case DT_{90} (days)	9.14

Modelling endpoints: Non-normalised values of the DT_{50} and the DT_{90} were derived from SFO best fits for two soils while use of FOMC (two soils) resulted in visually and statistically best acceptable kinetic models for deriving the modelling endpoint. The values were normalised by comparison of study incubation conditions to reference conditions (20°C, pF2 moisture) with results summarised in the table below.
For use as modelling endpoint, the geometric mean normalised half-life of propamocarb-*N*-oxide was estimated to 1.60 days.

Modelling endpoints: Normalised laboratory DT_{50}-values for propamocarb-N-oxide in aerobic soil for use as input in environmental exposure assessment

Parameter	propamocarb-*N*-oxide
Normalised (20°C, pF2) DT_{50}, range (days)	0.12 – 2.55
Geometric mean	1.60

I. Material and Methods

The evaluation considered degradation data of propamocarb-*N*-oxide in soil under aerobic conditions of the laboratory from a study following separately dosed 1-*N*-propyl-^{14}C-labelled propamocarb-*N*-oxide to four soils (KCA 7.1.2.1.2/03).
The degradation data were kinetically evaluated following FOCUS Guidance [FOCUS 2006, amended 2011] with the software KinGui2. The latter included the use of iteratively re-weighted least-square (IRLS) optimisation.
The kinetic evaluation derived DT_{50} values according to the respective flowcharts for the determination of trigger endpoints and for use as input parameters in modelling.
In following the actual FOCUS guidance, the particular criteria applied were essentially the same as described for the evaluation of the active substance earlier (see KCA 7.1.2.1.1).

The data sets along with the characteristics of soils was summarised in the table below.

Degradation study performed with propamocarb-N-oxide in aerobic soil under laboratory conditions including characteristics of soils

Study	Soil	Soil texture	Test temperature (°C)	Test moisture (%w/w)	Sand (%)	Clay (%)	Org. carbon (%)	pH ($CaCl_2$)	CEC (meq / 100 g)
KCA 7.1.2.1.2/03	Speyer 2.2.	loamy sand	20	16	75.8	7.9	1.61	5.5	10.0
	Laacher Hof AXXa	sandy loam	20	21	71.5	11.8	1.47	6.9	9.46
	Fraunhofer 06A	silty clay	20	26	10.9	44.5	2.76	7.2	30.12
	Atten-schwiller	silt loam	20	25	14.9	17.1	1.65	7.6	13.53

Following input of propamocarb-N-oxide degradation data (KCA 7.1.2.1.2/03) into KinGUI2 SFO kinetics were initially applied to all datasets according to the flowcharts.

II. Results and Discussion

Trigger endpoint determination:
According to the decision criteria, the bi-phasic models FOMC and DFOP showed improvement over SFO kinetics for three out of four soils. SFO kinetics was determined to be the best-fit for soil Laacher Hof AXXa while FOMC (M0 fixed) was the best fit for soil Speyer 2.2. Finally, the use of DFOP with M0 fixed each resulted in a best fit for soils Fraunhofer 06A and Attenschwiler.
The resulting non-normalised values for the DT_{50} and the DT_{90} derived were summarised in the table below**.**

Trigger evaluation: Non-normalised DT_{50}-values for propamocarb-*N*-oxide in aerobic soil under laboratory conditions (evaluation of metabolite separately dosed)

Soil	Kinetic model	DT_{50} (days)	DT_{90} (days)	formation fraction	Chi^2 (%)	t-test/ confidence interval	VA[a)]
Speyer 2.2, loamy sand, 20°C	FOMC*	2.37	9.14	n.a.	3.1	-	++
Laacher Hof AXXa sandy loam, 20°C	SFO	1.57	5.23	n.a.	5.8	$k < 0.001$	++
Fraunhofer 06A, silty clay, 20°C	DFOP*	0.06	0.46	n.a.	1.4	$k_1 < 0.001$ $k_2 < 0.001$ $g < 0.001$	++
Attenschwiller, silt loam, 20°C	DFOP*	0.30	2.86	n.a.	6.2	$k_1 < 0.001$ $k_2 = 0.001$ $g < 0.001$	++

Study: KCA7.1.2.1.2/03; n.a. = not applicable; * M0 fixed
[a)] VA = Visual Assessment (++ = very good, + = good, O = acceptable, - = not acceptable)

Modelling endpoint determination:
The FOCUS Kinetics modelling endpoint flowchart [FOCUS, 2006, 2011] was used to evaluate the datasets. The SFO kinetic model was considered visually and statistically acceptable for the two soils Speyer 2.2 and Laacher Hof AXXa to derive modelling endpoints as summarized in Table 11.1.4.3-97. For soils Fraunhofer 06A and Attenschwiller the application of bi-phasic kinetic model FOMC resulted in an improvement to serve as best fit to measured data.
For the use in environmental modelling the degradation half-lives were normalised to reference conditions regarding soil moisture (100% field capacity) and temperature (20°C). The parameters used in the laboratory tests and the respective correction factors calculated were summarised in the table below. The resulting normalised half-lives were summarised in other table below.

Modelling evaluation: non-normalised DT_{50}-values for propamocarb-*N*-oxide, as modelling endpoints, in aerobic soil under laboratory conditions (evaluation of metabolite separately dosed)

Soil	Kinetic model	DT_{50} (days)	DT_{90} (days)	formation fraction	Chi^2 (%)	t-test/ confidence interval	VA[a)]
Speyer 2.2, loamy sand, 20°C	SFO	2.55	8.46	n.a.	3.5	k < 0.001	++
Laacher Hof AXXa sandy loam, 20°C	SFO	1.57	5.23	n.a.	5.8	k < 0.001	++
Fraunhofer 06A, silty clay, 20°C	FOMC	0.16	0.53	n.a.	4.4	-	+
Attenschwiller, silt loam, 20°C	FOMC	0.74*	2.47	n.a.	8.2	-	++

Study: KCA7.1.2.1.2/03; n.a. = not applicable; * back-calculated from DT_{90} by assuming pseudo first order (DT90/3.32)
a) VA = Visual Assessment (++ = very good, + = good, O = acceptable, - = not acceptable)

Correction factors for soil temperature and moisture content

Soil	Tempe-rature (°C)	Correction factor Temperature	Incubation moisture (%w/w)	pF2 moisture (%w/w)	Correction factor Moisture	Total correction factor
Speyer 2.2, loamy sand (Study 1)	20	1.00	16	14.79	1.00	1.000
Laacher Hof AXXa sandy loam (Study 1)	20	1.00	21	25.17	0.881	0.881
Fraunhofer 06A, silty clay (Study 1)	20	1.00	26	39.93	0.741	0.741
Attenschwiller, silt loam (Study 1)	20	1.00	25	32.15	0.827	0.827

Study 1: KCA7.1.2.1.2/03

Modelling evaluation and normalised (20°C and pF2) DT_{50} values for propamocarb-*N*-oxide, as modelling endpoints, in aerobic soil under laboratory conditions

Soil	Kinetic model	Trigger DT_{50} (days)	Trigger DT_{90} (days)	Non-normalised DT_{50} estimate for modelling (days)	DT_{50} [20°C and pF2] (days)
Speyer 2.2, loamy sand (Study 1)	SFO*	2.37	9.14	2.55	2.55
Laacher Hof AXXa sandy loam (Study 1)	SFO	1.57	5.23	1.57	1.38
Fraunhofer 06A, silty clay (Study 1)	FOMC**	0.06	0.46	0.16***	0.12
Attenschwiller, silt loam (Study 1)	FOMC**	0.30	2.86	0.74***	0.62
Geometric mean					0.71

Study 1: KCA7.1.2.1.2/03; * FOMC and M0 fixed for trigger evaluation; ** DFOP and M0 fixed for trigger evaluation
*** The DT50 values are back calculated values due to the use of FOMC model (DT90/3.32): Fraunhofer: DT90 = 0.53 d → DT50 = 0.160 d → DT50 norm. = 0.118 d; Attenschwiller: DT90 = 2.47 d → DT50 = 0.744 d → DT50 norm. = 0.615 d

III. Conclusions

For trigger endpoints the evaluation of aerobic soil degradation data according to actual FOCUS kinetic guidance resulted in non-normalised half-lives of metabolite propamocarb-*N*-oxide to range from 0.06 days to 2.37 days and values of the DT_{90} to range from 0.46 days to 9.14 days.
Degradation was found to be adequately described by SFO as kinetic model for one soil while bi-phasic kinetic models showed best fits with experimental data for three soils.

For use as modelling input parameter in environmental risk assessments the evaluation of the total sets of data available resulted in a normalized geometric mean half-life of 0.71 days.
The approach for fitting with experimental data resulted in the use of the SFO kinetic model for two soils and bi-phasic kinetic models for another two soils to derive non-normalised values for the DT_{50} then normalised for moisture (pF2) and temperature (20°C).

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Assessment of the potential pH dependency of the rate of degradation in soil of the active substance and its metabolites.

There is no significant correlation between the pH value and the degradation rates. Therefore, the degradation of propamocarb-hydrochloride and its metabolites is not pH-dependent (assessment already presented above). A summary of the referred assessment was already presented above.

C.1.2) Anaerobic degradation in soil

The rate of degradation was calculated within the respective studies on route of degradation in anaerobic soils under laboratory conditions in: (KCA 7.1.1.2/01 and KCA 7.1.1.2/02):

- one water-logged soil at 25°C following application of 1-*N*-propyl-^{14}C-labeled active substance (KCA 7.1.1.2 /01);
- one water-logged soil at 20°C following application of 2-*N*-propyl-^{14}C-labeled active substance at two test concentrations (KCA 7.1.1.2 /02).

The evaluation of the data revealed that propamocarb-hydrochloride was degraded slowly and dependent on test concentration under the anaerobic conditions, in particular when being compared to the behaviour under aerobic degradation.
No metabolites being structurally unique for anaerobic conditions were formed at levels requiring further assessment following actual data requirements according to Commission Regulation (EU) Nº 283/2013, amending Regulation (EC) Nº 1107/2009.
It can be concluded from the structure, with no structural elements or functional groups being susceptible for ready anaerobic transformation like nitro groups.

Report:	KCA 7.1.1.2/01; Bruehl, R.; 1979; M-157717-01-1
Title:	Degradation of SN 66 752 in a loamy sand under anaerobic conditions
Report No.:	R+S 31/79-PA 66752.71/6 ; A85478
Document No.:	M-157717-01-1
Guideline(s):	None
Guideline deviation(s):	None
GLP/GEP:	**No**

Comment: key elements in design and conduct reported. Study regarded as scientifically valid. Study according to actual guidelines would not contribute to a better understanding of degradation under anaerobic conditions.

Executive Summary

In laboratory investigations propamocarb hydrochloride slowly degraded under anaerobic conditions, with only slight CO_2 evolution from the test system (maximum of 7.7 %). It might be expected that these results were a consequence of the lack of development of anaerobic bacteria in the flooded soil. Over the incubation period three unidentified metabolites were observed although none amounted to more than 2.0 % of the applied radioactivity.

I. Material and Methods

A. Materials

1. Test Material: propamocarb hydrochloride (SN 66 752)
Specific activity: 9.57 MBq/mg

2. Soil:

Characteristics of the test soils:

Parameter		**Value**
Texture		Loamy Sand
Coarse Sand	(0.2-2.0 mm) (%)	54.1
Fine Sand	(0.02-0.2 mm) (%)	32.6
Silt	(0.002 – 0.02 mm) (%)	8.3
Clay	(< 0.002 mm) (%)	5.0
Total		100.0
pH		6.6
Organic carbon (%)		2.4
Cation exchange capacity (mval/100 g soil)		11.2
Maximum water holding capacity (g H_2O/100g soil)		36.0

B. Study design

1. Experimental conditions: 50 g samples (dry weight) of German standard soil 2.2 (“Neuhofen”, loamy sand) were thoroughly mixed with 10 mg radiolabelled propamocarb hydrochloride (SN 66 752) to give a concentration of 200 mg/kg, corresponding to a field application rate of 150kg a.s/ha, based on 5 cm soil depth and bulk density of 1.5g/cm^3. The samples were transferred to biometer flasks and mixed with 50 mL of water, which had been purged with nitrogen gas for 6 hours. A 0.1 M KOH solution was used as a means of trapping evolved $^{14}CO_2$ from the system. The whole system was purged for an additional 30 minutes with nitrogen gas. Thereafter the flasks were sealed airtight with paraffin and stored in a climatic chamber in the dark at 25 °C.

2. Sampling: Flasks were analyzed after 7, 14, 30, 60, 90, and 180 days.

3. Analytical procedures: Water phases of the samples were separated by centrifuge and extracted with 50 mL of chloroform after addition of 1.7g NaCl and hydrochloride. The solution was further extracted with chloroform after basification. The soil samples were extracted with methanol (300 mL), acetone (50 mL), and toluene (50 mL). Soil samples were further extracted with 5 M NaCl (150 mL). Both soil extracts and the water phase were concentrated for TLC analysis, and measured for ^{14}C-content. In order to determine fulvic acid and humic acid fractions the soil was extracted with 0.5 M NaOH for 24 h using

common methods[8]. The extracted soil was combusted for determination of ^{14}C-residues.

Using the data from the study propamocarb hydrochloride degradation for the total system was described assuming first-order degradation of the active substance, described by linear regression. DT_{50} and DT_{90} were calculated using regression parameters.

II. Results and Discussion

A. Data:

As full anaerobic conditions were maintained during this investigation, it is likely that a viable anaerobic bacteria population can be assumed owing to the provenance of the soil and the aerobic storage conditions of the soil prior to experimentation.

Distribution and material balance of applied radioactivity, expressed as percent of initially applied substance

Day	$^{14}CO_2$	H_2O phase	Extractions		Residues bound to fulvic and humic acids			Combustion	Total balance
			Organic solvents	NaCl	∑	FA	HA		
7	0.3	24.8	45.1	20.9	4.0	3.6	0.6	1.4	96.5
14	1.8	22.9	43.6	18.7	6.0	5.6	0.9	2.1	95.1
30	4.7	22.6	43.9	17.9	4.9	4.5	0.9	1.8	95.8
60	6.0	20.4	30.8	20.5	4.7	4.2	0.9	2.1	84.5
90	7.7	19.1	35.5	22.9	2.5	2.0	0.6	1.8	89.5
180	5.7	17.2	30.3	23.7	4.2	3.8	1.9	3.2	84.3

Characterisation of propamocarb hydrochloride metabolism in a loamy sand under anaerobic conditions (expressed as per cent of initially applied substance)

Day	$^{14}CO_2$	NER	propamocarb hydrochloride [1)]	Origin	I	II	III	Total
7	0.3	5.4	89.9	0.1	<0.1	-	0.7	96.5
14	1.8	8.1	84.1	<0.1	-	1.0	-	95.1
30	4.7	6.7	82.4	0.2	0.4	1.0	0.4	95.8
60	6.0	6.8	70.5	0.1	-	0.8	0.1	84.3
90	7.7	4.3	74.5	0.2	0.4	0.7	1.7	89.5
180	5.7	7.4	67.2	<0.1	2.0	0.8	1.0	84.3

B. Mass balance: Material balance and distribution are presented in table above. The overall mean recovery of radioactivity during the study was 91.0%, although radioactive recoveries declined during the course of the study period from 96.5% on Day 7 to 84.3% on Day 180.

[8] EPA (1975): Pesticide Program Part II (123), 40, June 25, 1975

C. Bound and extractable residues: Bound residues remained between 4.3% and 8.1% of the applied radioactivity during the study. Only small amounts of radioactivity were bound to humic acid (0.6 - 1.9 %) and fulvic acids (2 - 5.6 %)

D. Volatile radioactivity: Only small amounts of $^{14}CO_2$ evolved during the metabolism of propamocarb hydrochloride, with a maximum of 7.7% being reached on Day 90. Such small amount of carbon dioxide provides evidence that anaerobic conditions were maintained through the study period.

E. Transformation of test substance: Chromatographic results of degradation products and metabolites from water samples and soil extracts are provided in table above.

Overall in the anaerobic test system, propamocarb hydrochloride represented the majority of radioactivity, declining in the range 89.9 to 67.2% of applied radioactivity from test initiation to Day 180. Very small amounts of metabolites were detected (≤ 2.0%), but could not be identified. At no time during the study did the metabolites increase in a recognisable pattern. Therefore it can be assumed that the metabolites degraded faster than propamocarb hydrochloride.

F. Degradation kinetics: Under anaerobic conditions propamocarb hydrochloride was degraded slowly, with 67.2% of the applied radioactivity attributed to propamocarb hydrochloride by day 180. Using linear regression the following equation was determined for propamocarb hydrochloride degradation (t in days):

$$y = 85.5x \cdot e^{-1.51\times10^{-3}\,t}$$

The r^2 value was determined to be 0.76 and the DT_{50} was calculated to be 459.0 days. The DT_{90} value was calculated to be 1524.9 days.

III. Conclusion

The persistence of propamocarb hydrochloride under anaerobic soil conditions is considerably higher compared to aerobic conditions. The degradation of propamocarb hydrochloride under anaerobic conditions is characterised by an estimated DT_{50} of 459.0 days (1.25 years). Metabolites were formed in low concentrations, none amounted to more than 2 % AR. Identification of the metabolites was not possible.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Report:	KCA 7.1.1.2/02; Schnoeder, F.; 2002; M-310969-01-1
Title:	(14C)-Propamocarb hydrochloride: Anaerobic route and rate of soil degradation
Report No.:	1758-1669-009
Document No.:	M-310969-01-1
Guideline(s):	EC Directive 95/3 6/EC, Active Substances, Section 7.1.1.1.2 (July 1995); SETAC Procedures for assessing the Environmental Fate and Ecotoxicity of Pesticides, Section 1.2 (March 1995), EPA, Subdivision N, Section 162-3 (October 1982) and The requirement for safety evaluation of agricultural chemicals published in 59 NohSan No. 4200, Japanese Ministry of Agriculture Forestry and Fisheries (28 January 1985)
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

Comment: key elements in design and conduct reported. Study regarded as scientifically valid. Study according to actual guidelines would not contribute to a better understanding of degradation under anaerobic conditions.

Executive summary :

The soil degradation of propamocarb hydrochloride under anaerobic conditions was investigated in a laboratory study at 20°C ± 2°C using a sandy loam. Soil samples were kept incubated in the dark.

Propamocarb hydrochloride, applied at a rate of 250 mg/kg and 10 mg/kg, degrades relatively slowly under anaerobic experimental conditions, in comparison to aerobic investigations. Observed CO_2 levels were negligible (< 2.0 % after 365 days) throughout the study indicating no significant mineralisation of the carbon in the labelled position was observed under anaerobic conditions. Over 30% of the applied radioactivity remained in the soil as NER by the end of the study. The most prominent metabolite formed was a polar component, which was observed in soil at a maximum value of 6.61% of the applied radioactivity at Day 365. The metabolite had a retention time of ~2.5 minutes, but could not be identified after further investigation. A further six unidentified transient degradation products were also formed over the duration of the experiment. These degradation components were only detected occasionally and were observed with usually ≤ 3.0% of applied radioactivity. No metabolites were observed accounting for greater than 10% of the applied radioactivity.

I. Material and Methods

A. Materials

1. Test Material: Common name: propamocarb-hydrochloride
Chemical name: Propyl 3-(dimethylamino)propylcarbamate hydrochloride
Radiolabelled purity: 98.2 %
Lot # 3389-191
Specific activity 8.645 MBq/mg (52.5 mCi/mmol)
Non-radiolabelled purity: 69.1 % w/w (formulation 750.5 g/L)
Lot #31491

2. Soil:

Physico-chemical characteristics of the test soil

Characteristic	Value
	Soil B6
Textural class (UK)	Sandy loam
Sampling location	Woolverstone, UK
Sand (%)	52
Silt (%)	37
Clay (%)	11
Organic carbon (%)	2.5
Organic matter (%)	4.3
CEC (mEq/100g)	14.6
pH in H_2O	7.1
WHC at pF 0.0 (%)	62.8
WHC at pF 2.5 (%)	21.2
Biomass (µg C/g) Day 0	451.35
Biomass (µg C/g) Day 120 [1)]	380.77 [1)]
Biomass (µg C/g) Day 365	230.97 [1)]

CEC = Cation Exchange Capacity; WHC = Water Holding Capacity
[1)] Values measured in report 1669-009

B. Study design

1. Experimental conditions: The test system consisted of incubation units equipped with a series of eight traps for catching organic volatiles and liberated [^{14}C]-carbon dioxide. The first trap was empty, the second contained 2M sodium hydroxide solution, the third was empty, the fourth contained ethanediol, the next two decane and the final two 2M sodium hydroxide solution. Soil samples (50 g dry weight equivalent) were weighed into individual open containers. The units were flooded with deionised water to a depth of 3 cm above the soil surface. The water level was maintained throughout the study. The test soil was maintained under experimental incubation conditions for >30 days prior to application of propamocarb hydrochloride. Soil samples were treated at an application rate of 250 mg/kg (Group A) and 10 mg/kg (Group B), corresponding to a rate equivalent to 187.5 and 7.5 kg a.s/ha, respectively. The test substance was applied dropwise to the surface of 22 soil samples in each dose group. The incubation chamber was purged continuously with nitrogen gas in order to maintain anaerobic conditions.

2. Sampling: Sampling of the soil test systems from group A was undertaken at intervals of 0 h (immediately after application), 1, 3, 7, 14, 30, 60, 91, 121, 182, 269, and 365 days. Group B sampling was undertaken at 0 h (immediately after application), 1, 3, 7, 14, 30, 60, 91, 99, and 121 days. At each sampling point duplicate sub-samples were removed for analysis. At each sampling date the units were flushed with nitrogen in order to transfer all organic volatiles into the trapping system.

3. Analytical procedures: The water phase was separated from the soil through a filter. The filter was washed with acetone and the combined with the water phase. Aliquots of the aqueous phase (250 µl) were counted by LSC for radioactivity determination.

Each soil incubate was transferred to a centrifuge beaker and extracted four times with 150 mL acetonitrile/deionised water/hydrochloride (70:30:1 v/v/v). These three extracts were combined (extract 1) prior to determination of radioactivity by LSC. If more than 3% of applied radioactivity was determined after the fourth extraction procedure the soil was further extracted with 150 mL methanol/saturated NaCl (100:25 v/v). After any extraction procedure the soil was extracted with 150 mL of acetone and allowed to air dry. After extraction and drying both the soil and filters were combusted and radioactivity was counted by LSC.

A catalytic converter system connected to two additional traps filled with 2M sodium hydroxide solution were included at the end of the routine trapping system. The converter system was to catalytically convert e.g. ^{14}C-methane into $^{14}CO_2$ at a temperature of ca 600°C which was then collected in the following traps. After two and four weeks aliquots of the sodium hydroxide solution traps were counted by LSC for determination of the radioactivity for incubation group A.

Water phases and soil extracts taken from the incubation units were analysed for test substance and degradation products by High Performance Liquid Chromatography (HPLC).

II. Results and Discussion

A. Data:

Results on the microbial biomass in the test soil are presented in Table 11.1.4.4-04. From an initial value of 451.35 µg C/g the biomass of the test soil decreased to 84.9% and 47.2% of the initial biomass determination at Day 121 and 365, respectively. The reduction in biomass especially over the 365-day period is indicative of long-term, closed system experimental testing and the results of propamocarb hydrochloride degradation require careful interpretation after day 121.

Distribution of radioactivity and material balance for the test incubation (expressed as percent of applied radioactivity)

Timepoint (d)	Volatiles (CO_2 only)	Water phase	Soil extract	Soil residue	Mass balance
Group A - 250 mg/kg					
0	N/A	95.30	1.17+	1.40	97.87
1	0.00	72.54	21.78 [1)]	1.52	95.85
3	0.00	63.36	30.70	2.06	96.12
7	0.00	54.97	38.57	3.04	96.58
14	0.02	45.79	46.11	5.18	97.10
30	0.04	38.48	46.22 [1)]	7.08	91.81
60	0.17	35.05	52.57 [1)]	8.35	96.14
91	0.30	31.43	49.40 [1)]	12.54	93.67
121	0.35	27.20	50.80 [1)]	17.41	95.76
182	0.73	19.21	49.34	20.97	90.25
269	1.33	12.32	40.55	33.49	87.69
365 [2)]	1.98	9.08	32.33	30.34	73.73
Group B – 10 mg/kg					
0	N/A	98.44	1.26+	2.86	102.55
1	0.00	68.83	31.11	1.39	101.33
3	0.01	61.30	37.78	2.95	102.05
7	0.02	49.67	46.77	4.91	101.37
14	0.07	33.52	56.32	11.25	101.17
30	0.09	17.76	59.51 [1)]	18.19	95.55
60	0.15	15.55	55.71	19.31	90.72
91	1.33	9.31	35.77 [1)]	29.23	75.63
99	1.94	8.05	29.90 [1)]	22.51	62.41
121	3.53	4.62	23.04	40.64	71.83

Notes: - Values represent the mean of duplicate analyses
+ Acetone extract only since < 5% in soil
[1)] Value for soil extract represented concentrated extract plus third extract plus acetone extract owing to too low recoveries in the original extract.
[2)] Values not considered in evaluation of day 365 but replicated B only.
N/A = Not Analysed

Chromatographic results obtained from water and soil under anaerobic conditions (as percent of applied radioactivity)

Time point (d)	P RT=10 min	Unk 1 RT=2.5 min	Unk 2 RT=3 min	Unk 3 RT=6 min	Unk 4 RT=9 min	Unk 5 RT=12 min	Unk 6 RT=14 min	Unk 7 RT=29 min	UR
Group A - 250 mg/kg									
0									
Mean water	91.48	1.58	<LOD	<LOD	0.13	0.31	0.26	<LOD	1.70
Mean soil	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Total system	91.48	1.58	<LOD	<LOD	0.13	0.31	0.26	<LOD	1.70
1									
Mean water	70.63	0.59	<LOD	<LOD	0.19	0.29	<LOD	<LOD	0.94
Mean soil	20.69	0.44	<LOD	<LOD	0.05	<LOD	<LOD	<LOD	0.36
Total system	91.32	1.03	<LOD	<LOD	0.24	0.29	<LOD	<LOD	1.31
3									
Mean water	61.82	0.37	<LOD	0.10	0.09	0.41	0.06	<LOD	0.75
Mean soil	29.01	0.65	<LOD	<LOD	0.10	<LOD	0.06	<LOD	0.52
Total system	90.83	1.02	<LOD	0.10	0.19	0.41	0.12	<LOD	1.27
7									
Mean water	53.56	0.26	<LOD	0.15	0.10	<LOD	0.07	<LOD	0.94
Mean soil	36.87	0.54	<LOD	<LOD	<LOD	<LOD	0.18	<LOD	0.56
Total system	90.43	0.80	<LOD	0.15	0.10	<LOD	0.25	<LOD	1.50
14									
Mean water	44.56	0.07	<LOD	<LOD	0.09	<LOD	0.15	<LOD	0.92
Mean soil	44.64	0.15	<LOD	<LOD	<LOD	<LOD	0.25	<LOD	0.57
Total system	89.21	0.22	<LOD	<LOD	0.09	<LOD	0.39	<LOD	1.49
30									
Mean water	37.77	0.14	<LOD	<LOD	0.08	<LOD	<LOD	<LOD	0.49
Mean soil	43.29	1.14	<LOD	0.07	<LOD	<LOD	0.23	<LOD	0.56
Total system	81.06	1.28	<LOD	0.07	0.08	<LOD	0.23	<LOD	1.05
60									
Mean water	34.07	0.17	<LOD	0.09	0.05	0.12	<LOD	<LOD	0.64
Mean soil	48.25	1.98	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.65
Total system	82.32	2.15	<LOD	0.09	0.05	0.12	<LOD	<LOD	1.29
91									
Water Spare	27.78	<LOD	<LOD	<LOD	<LOD	<LOD	2.82	<LOD	0.83
Soil Spare	45.07	1.89	<LOD	<LOD	0.17	<LOD	0.19	<LOD	0.43
Total system	72.85	1.89	<LOD	<LOD	0.17	<LOD	3.01	<LOD	1.26
121									
Mean water	26.36	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.38
Mean soil	47.55	0.28	<LOD	<LOD	<LOD	<LOD	0.95	<LOD	0.61
Total system	73.91	0.28	<LOD	<LOD	<LOD	<LOD	0.95	<LOD	0.99
182									

Time point (d)	P RT=10 min	Unk 1 RT=2.5 min	Unk 2 RT=3 min	Unk 3 RT=6 min	Unk 4 RT=9 min	Unk 5 RT=12 min	Unk 6 RT=14 min	Unk 7 RT=29 min	UR
Mean water	18.83	0.08	<LOD	<LOD	0.07	0.15	<LOD	<LOD	0.15
Mean soil	43.72	0.99	<LOD	0.22	0.06	0.14	0.05	<LOD	0.18
Total system	62.56	1.07	<LOD	0.22	0.13	0.29	0.05	<LOD	0.33
269									
Mean water	9.44	<LOD	0.07	<LOD	0.07	5.04	<LOD	0.09	0.16
Mean soil	36.74	0.73	<LOD	<LOD	<LOD	<LOD	<LOD	0.07	0.48
Total system	46.18	0.73	0.07	<LOD	0.07	5.04	<LOD	0.16	0.65
365									
Mean water [1)]	8.92	0.04	<LOD	0.07	<LOD	<LOD	<LOD	<LOD	0.04
Mean soil [1)]	25.43	5.15	<LOD	0.34	<LOD	0.21	<LOD	<LOD	0.12
Total system	40.64	6.65	<LOD	0.55	<LOD	0.16	<LOD	<LOD	0.09
Group B – 10 mg/kg									
0									
Water	96.03	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.28
Soil	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Total system	96.03	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.28
1									
Water	65.52	<LOD	<LOD	<LOD	<LOD	<LOQ	<LOD	<LOD	0.43
Soil	30.26	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.49
Total system	95.78	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.92
3									
Water	59.81	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.03
Soil	37.06	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.06
Total system	96.87	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.09
7									
Water	48.86	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.31
Soil	43.56	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.04
Total system	92.42	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.35
14									
Water	31.76	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.38
Soil	54.11	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.56
Total system	85.87	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.94

Time point (d)	P RT=10 min	Unk 1 RT=2.5 min	Unk 2 RT=3 min	Unk 3 RT=6 min	Unk 4 RT=9 min	Unk 5 RT=12 min	Unk 6 RT=14 min	Unk 7 RT=29 min	UR
30									
Water	16.87	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.11
Soil	48.08	<LOQ	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	1.03
Total system	64.95	<LOQ	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	1.14
60									
Water	12.94	<LOD	<LOQ	<LOD	<LOD	<LOD	<LOD	<LOD	0.04
Soil	46.52	3.40	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	-0.08 [2)]
Total system	59.46	3.40	<LOQ	<LOD	<LOD	<LOD	<LOD	<LOD	-0.05 [2)]
91									
Water	7.57	<LOD	<LOD	0.79	<LOD	<LOD	<LOD	<LOD	0.66
Soil	30.01	1.96	<LOQ	<LOD	<LOD	<LOQ	<LOD	<LOD	0.05
Total system	37.58	1.96	<LOQ	0.79	<LOD	<LOQ	<LOD	<LOD	0.71
99									
Water	7.88	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.00
Soil	25.50	1.61	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.49
Total system	33.37	1.61	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.49
121									
Water	4.35	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.03
Soil	19.97	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.32
Total system	24.32	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.36

Note [1)] Replicate A value not considered in evaluation of day 365.
N/A = Not Analysed
< LOD = Limit of Detection
< LOQ = Limit of Quantification
P = propamocarb hydrochloride
UR = sum of radioactivity exceeding the background in the HPLC chromatograms but not integrated
[2)] typing error

B. Mass balance: The distribution and material balance in the water phase, soil, and volatiles are summarised. Overall, the radioactive recovery for the dose groups A and B ranged between 73.73% and 97.87%, and 71.83 % and 102.55% during the test periods, respectively. However, beyond day 269 (group A) and day 30 (group B) the mass balances decreased slightly with time. It is likely, this occurred owing to carbon dioxide escape during the long sampling intervals.

C. Bound and extractable residues: The distribution in the water phase, soil, and volatiles are summarised. In group A the radioactivity in the water phase continuously decreased from 95.30% to 27.20 % of the applied radioactivity after 121 days, this value further decreased to 10.67% after 365 days of incubation. In incubation group B the percentages in the water phase decreased from 98.44% to 4.62% after 121 days. In contrast, the radioactivity distributed to the soil phase in both test groups increased during the incubation period to > 70% of the applied radioactivity. For group A, within the soil fraction the NER portion increased over the study period from 1.40% to 17.41% of the applied radioactivity after 121 days, this further increased to 36.91% after 365 days. In incubation group B NER increased from 2.86% to 40.64% after 121 days. The extractable portion of the soil fraction reached a maximum of 52.57% of the applied radioactivity after 60 days, in group A, and then declined to 38.74% after 365 days. In incubation group B a similar trend was observed with a maximum of 59.51% of applied radioactivity after 30 days in the extractable portion of the soil sample.

D. Volatile radioactivity: Negligible amounts of radioactivity were detected as organic volatiles or $^{14}CO_2$. The low amounts of radioactivity detected in the traps did not exceed 2.0% or 3.5% of the applied radioactivity in groups A and B, respectively. No significant mineralisation of the carbon in the labelled position was observed under anaerobic conditions.

E. Transformation of test substance: For both dose groups the majority of radioactivity in the test system was represented by propamocarb hydrochloride. The percentage amount of propamocarb hydrochloride in the water phase decreased from an initial value of 91.48% to 26.36% after 121 days and continued to decrease to 10.55% after 365 days for incubation group A. For group B 96.03% of applied radioactivity was present as propamocarb hydrochloride, which decreased to 4.35% after 121 days. In parallel, the amount of test item in the soil extract increased to 48.25% of the applied radioactivity at Day 60, subsequently decreasing to 47.55% and 30.09% after 121 and 365 days, respectively, in dose group A. In dose group B a similar trend was observed with an increase to 54.11% of applied radioactivity after 14 days followed by continuous decrease to 19.97% after 121 days.

Unknown metabolites with retention times of ~ 2.5, 3, 6, 9, 12, 14, and 29 minutes were observed in some samples. These smaller radioactive components were observed with usually ≤ 3.0% of the applied radioactivity. However, one compound (Unk5, eluting at 12 minutes) reached 5.04% of the applied radioactivity in one water sample and was then not detected in any other water sample. The most prominent metabolite was a polar component (Unk1) with a retention time of ~2.5 minutes, as also observed in Study M-310828-02-1 (1760-1669-007). Unk1 was observed in the water phase and soil phase at maximum levels of 1.58% and 6.61%, respectively for group A. In group B the maximum amount of Unk1 in soil and total system was observed after 60 days (3.40% of applied radioactivity).

F. Degradation kinetics: The DT_{50} (DT_{90}) of the test item was calculated to be 308 (1024) days in the total system (1st order kinetic, r^2 =0.9815) for incubation group A. The DT_{50} (DT_{90}) of the test item for incubation group B was 66 (218) days in the total system (1st order kinetic, r^2 =0.9838).

III. Conclusion

Propamocarb hydrochloride degrades relatively slowly under anaerobic experimental conditions, in comparison to aerobic investigations. Observed CO_2 levels were negligible (< 2.0% after 365 days) throughout the study. Over 30% of the applied radioactivity remained in the soil as NER by the end of the study. The most prominent metabolite formed was a polar component (with the same retention time as Unk 1 in study M-310828-02-1), which was observed in soil at a maximum value of 6.61% of the applied radioactivity. Identification of the metabolite was not possible in this study (for further characterisation and identification of Unk 1 see study KCA7.1.1.1/10). For different incubation groups the DT_{50} of the test item was in the range of 308 /66 days (total system, 1st order kinetic).

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

The evaluations revealed that the degradation of the active substance propamocarb-hydrochloride was slow under the anaerobic conditions and dependent on test concentration applied.
Values for the DT_{50} of propamocarb-hydrochloride were calculated to 459 days (study KCA 7.1.1.2/ 01) and 308.15 days (study KCA 7.1.1.2/02) at the comparable test concentrations of 200 mg a.s/kg soil and 250 mg a.s/kg soil (incubation group A), respectively. The associated values for the DT_{90} were 1524.9 days (study KCA 7.1.1.2/01) and 1023.69 days (study KCA 7.1.1.2/01) when following the SFO kinetic model for calculation.
For a test concentration of 10 mg a.s/kg soil (incubation group B, study KCA 7.1.1.2/02), values for the DT_{50} and the DT_{90} were estimated to 65.68 days and 218.18 days, respectively.

Anaerobic degradation of metabolites, breakdown and reaction products

Report:	KCA 7.1.2.1.4/01; Bruehl, R.; 1979; M-157717-01-1
Title:	Degradation of SN 66 752 in a loamy sand under anaerobic conditions
Report No.:	R+S 31/79-PA 66752.71/6 ; A85478
Document No.:	M-157717-01-1
Guideline(s):	none
Guideline deviation(s):	none
GLP/GEP:	**no**

Comment: key elements in design and conduct reported. Study regarded as scientifically valid. Study according to actual guidelines would not contribute to a better understanding of degradation under anaerobic conditions. A summary of this study is presented above.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Report:	KCA 7.1.2.1.4/02; Schnoeder, F.; 2002; M-310969-01-1
Title:	(14C)-propamocarb hydrochloride: Anaerobic route and rate of soil degradation
Report No.:	1758-1669-009
Document No.:	M-310969-01-1
Guideline(s):	EC Directive 95/3 6/EC, Active Substances, Section 7.1.1.1.2 (July 1995); SETAC Procedures for assessing the Environmental Fate and Ecotoxicity of Pesticides, Section 1.2 (March 1995), EPA, Subdivision N, Section 162-3 (October 1982) and The requirement for safety evaluation of agricultural chemicals published in 59 NohSan No. 4200, Japanese Ministry of Agriculture Forestry and Fisheries (28 January 1985)
Guideline deviation(s):	not specified
GLP/GEP:	**yes**

Comment: key elements in design and conduct reported. Study regarded as scientifically valid. Study according to actual guidelines would not contribute to a better understanding of degradation under anaerobic conditions. A summary of this study is presented above.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

The evaluations revealed that no metabolites were formed specific for the anaerobic conditions of the test. Moreover, it should be noted that propamocarb-hydrochloride is not intended for use in crops where anaerobic conditions in soil are prevalent.
No further specific information is, therefore, required.

11.1.4.4 Photochemical degradation

A) Soil Photolysis

The route of degradation on irradiated soil surfaces had been investigated under laboratory conditions in:

- one soil at 20°C following application of 1-*N*-propyl-^{14}C-labeled active substance (KCA 7.1.1.3 /01 and its Addendum KCA 7.1.1.3/02)
- one soil at 25°C and a moisture of 75 % of field capacity at 0.33 bar following application of 2-*N*-propyl-^{14}C-labeled active substance (KCA 7.1.1.3/03).

The data requirement was addressed under Point 7.1.1.1.2.2 of the Dossier submitted. The evaluation revealed that propamocarb-hydrochloride was degraded slowly under the conditions of the test, being well in line with the very limited absorption of visible light at wave lengths of more than 290 nm.
For the two studies apart of the formation of non-extractable residues and minor levels of carbon dioxide (< 3% AR for irradiated samples) no metabolites had been formed at levels of more than 10% AR that required further evaluation in the existing environmental risk assessment.
In view of photolytic half-lives of 35.4 days (KCA 7.1.1.3/01 and KCA 7.1.1.3/02) and 199 days (KCA 7.1.1.3/03) reported it was concluded that light had no significant effect on the overall degradation observed. Consequently, photolytical transformation is regarded not to play a significant role in the overall degradation of propamocarb-hydrochloride residues on soil surfaces.
Following actual data requirements of Commission Regulation (EU) No. 283/2013, amending Regulation (EC) No. 1107/2009, the metabolite propamocarb-*N*-oxide (AE F155306, AE B155306, BCS-AU81087)[9] was observed in irradiated soil samples of study KCA 7.1.1.3/01 at levels above the triggers set ('Zone 2', maximum of 8.7% AR after 30.66 days) thus requiring consideration in environmental risk assessment.
Data on rate of degradation of propamocarb-*N*-oxide in aerobic soil and adsorption to soil are addressed under KCA 7.1.2.1.2/02 and KCA 7.1.3.1.2/02, respectively.

Report:	KCA 7.1.1.3/01; Tschampel, M.; 1990; M-157828-01-1
Title:	The photodegradation of propamocarb hydrochloride (Schering Code ZK 66 752) on soil surfaces
Report No.:	APC 87/90 (90/030); A85553
Document No.:	M-157828-01-1
Guideline(s):	US EPA Pesticide Assessment Guidelines, Subdivision N, Section 161-3 (1982)
Guideline deviation(s):	None
GLP/GEP:	No

Report:	KCA 7.1.1.3/02; Tschampel, M.; 1994; M-157830-01-1
Title:	Addendum to report APC 87/90 - The photodegradation of propamocarb hydrochloride (Schering Code ZK 66 752) on soil surfaces
Report No.:	A85554
Document No.:	M-157830-01-1
Guideline(s):	US EPA Pesticide Assessment Guidelines, Subdivision N, Section 161-3 (1982)
Guideline deviation(s):	None
GLP/GEP:	**No**

Executive Summary

The research on the photolytic degradation of propamocarb Hydrochloride was undertaken in two experimental parts. The first experiment investigated photolytic degradation of the test item in a laboratory study at 21°C ± 4°C using a loamy sand soil. The second experiment investigated the identity of photolytic degradation products observed during the first study. Owing to low concentrations of photolysis products in the first experiment the second experiment was conducted with further irradiation of the treated soil surface for an additional 20.7 days followed by storage in darkness for 11 days.

Under experimental conditions the degradation of propamocarb hydrochloride was augmented when applied only to the soil surface in comparison to the dark control. Under irradiated conditions propamocarb Hydrochloride was more readily degraded (54.6% of the applied radioactivity after 30.66 days) relative to the dark control (97.6% of applied radioactivity after 30.66 days). In both irradiated

[9] For structure see Figure 8.1.1.1-03.

and non-irradiated experimental units an increase in NER was observed along with a concomitant decrease in radioactivity extractable from the soil samples, although these trends were more pronounced in the dark control samples. Propamocarb hydrochloride was the major constituent observed in both irradiated and non-irradiated soil samples during the incubation period. Three metabolites were observed. In additional experiments the major photodegradation product (occurring at 8.7% of applied radioactivity) was identified as N,N-dimethyl-N-(3-propoxycarbonylaminopropyl) amine N-oxide. Exposure to sunlight of the test compound at the soil surface appears to increase degradation of propamocarb hydrochloride relative to the dark control samples.
Propamocarb hydrochloride was readily degraded under irradiated conditions on a loamy sand soil. Experimental first-order regression analysis indicated DT_{50} (DT_{90}) values of 35.4 (117.5) days, respectively, although the upper and lower limits of the 95% confidence intervals expanded the range to 20.6 and 123.8 days, respectively.

I. Material and Methods

A. Materials

1. Test Material: Common name: propamocarb hydrochloride
Chemical name: propyl 3-(dimethylamino) propylcarbamate hydrochloride
Radiolabelled purity: 97.6%
Lot # 1795-1
Specific activity 5.43 MBq/mg
Non-radiolabelled purity: 97.7% w/w
Lot # not documented.

2. Soil:

Characteristics of test soils

Characteristic		Value
Textural class (BBA)		**Loamy sand**
Fine Sand	(0.063 – 0.200 mm) (%)	24.7
Middle Sand	(0.200 – 0.600 mm) (%)	51.8
Coarse Sand	(0.600 – 2.0 mm) (%)	1.6
Fine Silt	(0.002 – 0.006 mm) (%)	1.9
Middle Silt	(0.006 – 0.020 mm) (%)	4.1
Coarse Silt	(0.020 – 0.063 mm) (%)	9.5
Clay	(< 0.002 mm) (%)	6.4
Organic carbon (%)		2.45
Organic matter (%)		4.22
CEC (mEq/100g)		13.0
pH in $CaCl_2$		7.1

CEC = Cation Exchange Capacity
Organic matter (%) = OC (%) × 1.724

B. Study design

1. Experimental conditions: Soil covered plates (n=36) of the main experiment were air dried and then equilibrated by irradiation in the irradiation chamber for several days prior to the main experiment.

Typical values of soil water content were determined to be 1.0 % at this time. The resulting soil surface concentration of PHC was 97µg/cm^2 (equivalent to 9.7 kg a.s/ha). Soil samples, in the main experiment, were irradiated with filtered light (λ > 290nm) using a xenon-arc, simulating natural light. Irradiation was carried out for 30.66 days with a photoperiod of 16 hours light and 8 hours dark. The light intensity (in the 290-400 nm wavelength range) was in the same order of magnitude as moderate northern latitudes during the summer months. Dark control experiments were also established in parallel with the main experiment. In both the irradiated and non-irradiated experimental units air was drawn through the photochamber and excited sequentially through 2M sulphuric acid, ethylene glycol, and ethanolamine trapping solutions.

2. Sampling: Sampling of the soil test systems was undertaken at intervals of 0.67, 1.67, 4.67, 8.67, 19.66 and 30.66 days. At each sampling point duplicate sub-samples were removed for analysis.

3. Analytical procedures: Soil samples were extracted with a mixture of methanol, water, and ammonia solution (800:192:8 v/v/v) and then centrifuged twice. Soil residues were dried and combusted. Both soil extract and soil residue radioactivity was determined by LSC. Extracts were analysed by HPLC. In the additional irradiation study the experimental investigation was conducted as described above, but with continuous irradiation of the soil plates for 20.7 days followed by storage in darkness for 11 days. This corresponds to the total incubation time in the main experiment. After the incubation period soil plates were extracted and analysed as described above. After additional irradiation of the soil plates the extract (HPLC eluent) from the irradiated soil plates was investigated by comparative HPLC-MS and GC-MS analyses.

C. Determination of degradation kinetics: Using the data from each study, propamocarb hydrochloride degradation was described assuming first-order degradation of the active substance, described by linear regression. DT_{50} value for propamocarb hydrochloride was estimated from the degradation rate k using the following equation:

$$DT_{50} = \frac{\ln 2}{k}$$

II. Results and Discussion

A. Data:

Results of recovery experiments from test soil plates. Values are expressed in per cent of total radioactivity applied

Radioactivity of extracts (%)	Radioactivity of soil residues (%)	Sum of radioactivity recovered (%)
96.6	1.1	97.7
92.4	1.8	94.2
94.2	1.2	95.4
95.9	1.5	97.4
87.1	1.0	88.1
mean = 93.2 ± 3.8	mean = 1.3 ± 0.3	mean = 94.6 ± 3.9

Material balance for the irradiation of propamocarb Hydrochloride on soil surfaces. Values are expressed in per cent of total radioactivity applied (averages of three segments except for [1]):

Time (days)	I/NI	Extract (%)	Soil residues (%)	Volatile products (%)	Sum (%)	Sum corrected by total recovery [1] (%)
0.67	I	96.1	2.6	<0.1	98.7	104.3
	NI	94.0	1.6	-	95.6	101.1
1.67	I	91.4	6.9	0.1	98.4	104.0
	NI	90.8	2.5	-	93.3	98.6
4.67	I	73.7	8.7	0.3	82.7	87.4
	NI	92.3	3.4	-	95.7	101.2
8.67 [1]	I	86.4	11.1	0.4	97.9	103.5
	NI	92.8	3.9	-	96.7	102.2
19.66	I	65.4	17.0	1.1	83.5	88.3
	NI	92.0	5.5	-	97.5	103.1
30.66	I	62.7	21.0	1.9	85.6	90.5
	NI	88.3	6.6	-	94.9	100.3

Note: I/NI = Irradiated/Non-Irradiated
[1] Total recovery = 94.6%

Radioactivity characterisation of soil extracts from irradiated and non-irradiated soil:

Time (days)	Total extract (%)	HPLC Chromatogram				
		Zone 1 (%)	Zone 2 (%)	Zone 3 (%)	P Hydrochloride (%)	Σ HPLC
Irradiated						
0	93.2	0.7	1.6	1.8	91.6	95.7
0.67	96.1	1.3	3.2	2.0	88.7	95.2
1.67	91.4	1.5	4.9	2.2	83.6	92.2
4.67	73.7	2.3	5.7	2.1	63.9	74.0
8.67 [1]	86.4	3.3	5.6	2.8	76.8	88.5
19.66	65.4	3.7	7.5	2.8	51.9	65.9
30.66	62.7	3.8	8.7	2.7	50.1	65.3
Non-irradiated						
0	93.2	0.7	1.6	1.8	91.6	95.7
0.67	94.0	0.8	1.5	1.9	92.7	96.9
1.67	90.8	0.9	1.5	1.7	92.0	96.1
4.67	92.3	1.0	1.8	1.8	92.8	97.4
8.67 [1]	92.8	0.9	1.7	1.9	96.5	101.0
19.66	92.0	1.0	1.8	1.8	92.2	96.8
30.66	88.3	1.0	1.7	1.6	89.4	93.7

B. Mass balance: Radioactive mass balance of irradiated soil samples and the dark control are summarised in tables above. The results after recovery from soil plates indicate that applied radioactivity is recovered in good yields from the soil segments, having a mean total recovery of 94.6%. The results of the material balance indicate the mean total recovery of radioactivity from the irradiated and non-irradiated was 91.1% and 95.6%, respectively. However, overall radioactivity from the irradiated samples decreased from 98.7% to 85.6% by Day 30.66 possibly owing to incomplete trapping of volatile products.

C. Bound and extractable residues: Radioactive distribution of irradiated soil samples and the dark control are summarised in table above. The recovery of radioactivity from soil extracts decreased during the course of the incubation for both the irradiated (96.1% to 62.7%) and non-irradiated (94.0% to 88.3%) samples. In parallel the soil residues increased during the course of the incubation for irradiated (2.6% to 21.0%) and non-irradiated (1.6% to 6.6%) samples.

D. Volatile radioactivity: Volatiles were ≤ 1.9 % at all sampling intervals.

E. Transformation of test substance: The results of quantitative evaluation of chromatograms used to characterise photo-degradates are summarised in table above. Propamocarb hydrochloride represented the majority of radioactivity recorded from the soil extracts. However, the amount of propamocarb hydrochloride decreased from 91.6% to 50.1% (54.6% of initial amount) after irradiation, and to 89.4% (97.6% of initial amount in the dark controls after 30.66 days). This ready degradation of propamocarb hydrochloride contrasts with the findings in Study 1669/8-D2149 in which propamocarb hydrochloride degradation is more limited than the dark control. It is expected that the different clay content evident between the two test soils will have an influence on the relative rates of propamocarb hydrochloride degradation. Three metabolites are observed at maximum values of 3.8%, 8.7%, and 2.7% in zones 1, 2, and 3, respectively. These degradation products were eluted at shorter retention times than propamocarb hydrochloride.

In the additional experiments identification of the main photolysis product – in zone 2, amounting to 8.7% of applied radioactivity – was investigated. The main product of photodegradation was identified as N,N-dimethyl-N-(3-propoxycarbonylaminopropyl) amine N-oxide by comparative chromatography and HPLC-MS analyses. Also, based on GC-MS analyses, further photolysis products could be identified as propyl N-(3-methylaminopropyl) carbamate and 2-hydroxypropyl N-(3-dimethylaminopropyl) carbamate.

F. Degradation kinetics: The half-life results of the rate propamocarb hydrochloride photolysis are provided in the table below. The DT_{50} of irradiated propamocarb hydrochloride on the surface of a loamy sand soil was estimated to be 35.4 days. Upper and lower bands of the 95 % confidence intervals provide DT_{50} limits of 20.6 and 123.8 days, respectively. However, the confidence intervals may be over-estimated owing to the deviation of the result obtained at sampling time t = 4.67 days. Overall, the rate of propamocarb hydrochloride decline in the loamy sand was greater in the irradiated soil samples than the dark control. After 30 days the percentage of radioactivity characterised as propamocarb hydrochloride was determined to be 50.1% and 89.4% in the irradiated and non-irradiated test systems, respectively.

DT_{50} and DT_{90} values determined for propamocarb Hydrochloride under irradiated experimental conditions

	Values
Irradiated	
DT_{50} (days)	35.4 (20.6-123.8) [1)]
DT_{90} (days)	117.5
K	0.0196
r2	0.819

Note [1)] Limits of the 95 % confidence intervals

III. Conclusion

Propamocarb hydrochloride was readily degraded under irradiated conditions on a loamy sand soil.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Report:	KCA 7.1.1.3/03; Yeomans, P.; 2001; M-310966-01-1
Title:	(14 C)-Propamocarb hydrochloride: Photodegradation on a soil surface
Report No.:	1669/8-D2149
Document No.:	M-310966-01-1
Guideline(s):	SETAC-Europe, Procedures for Assessing the Environmental Fate and Ecotoxicity of Pesticides, Part 1, Section 2 (1995); US EPA Pesticide Assessment Guidelines, Subdivision N, Section 161-3 (1982) (see page 12).
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

Executive Summary

The route of photolytic degradation of propamocarb hydrochloride was investigated in a laboratory study at 25 C±1 C using a clay loam soil held at 75% ± 10% of MWHC.

Under irradiated conditions the degradation of propamocarb hydrochloride was limited when applied to the soil surface, even slower relative to the dark control. Limited degradation of propamocarb hydrochloride may be a result of reduced local soil moisture content at the soil surface due to drying effects of the light source. In both irradiated and non-irradiated experimental units an increase in NER was observed along with a concomitant decrease in radioactivity extractable from the soil samples. propamocarb hydrochloride was the major constituent observed in both irradiated and non-irradiated soil samples during the incubation period. No significant production of photo-degradation metabolites occurred. Exposure to sunlight is not expected to increase the degradation of propamocarb hydrochloride or lead to the formation of unique photo-degradates.

I. Material and Methods

A. Materials

1. Test Material: Common name: propamocarb hydrochloride
Chemical name: propyl 3-(dimethylamino)propylcarbamate hydrochloride
Radiolabelled purity: 98.2%, lot # 3389-191 specific radioactivity 8.64 MBq/mg
Non-radiolabelled purity: 69.1% w/w (formulation 722 g/L), lot #31491.

2. Soil:

Characteristics of the test soils:

Characteristic		Value
Textural class (UK)		Clay loam
Sand	(%)	23
Silt	(%)	57
Clay	(%)	20
Organic carbon	(%)	4.2
Organic matter	(%)	7.2
CEC	(mEq/100g)	21.4
pH in H_2O		6.8
WHC at pF 0.0	(%)	86.8
WHC at pF 2.5	(%)	31.8
Biomass	(µg C/g) Day 0	700.69

CEC = Cation Exchange Capacity; WHC = Water Holding Capacity

B. Study design

1. Experimental conditions: The test system consisted of incubation units equipped with a series of five solid phase trap system for catching organic volatiles and liberated [^{14}C]-carbon dioxide. The first trap was empty, the second and third contained ethandiole and 2% liquid paraffine in xylene. The final

two traps contained 2M sodium hydroxide solutions. Soil samples (15 g dry weight equivalent) were weighed into individual glass vials equipped with quartz glass lids, and inlet/outlet ports for the trapping of volatiles. The units had humidified air drawn over the surface of both the irradiated and non-irradiated (dark) soil samples. Moisture contents of the soils were adjusted daily. Irradiated samples were exposed to simulated sunlight using a photoperiod of 12h light and 12h dark. The light was filtered to remove wavelengths below 290 nm in order to limit exposure to the ultra violet and visible spectrums similar to natural sunlight. Soil samples were treated at a test concentration of 0.2 mg a.s./g of soil (based on the dry weight equivalent. The test substance was applied dropwise to the surface of the soil samples.

2. Sampling: Sampling of the soil test systems was undertaken at intervals of 1, 5, 14, and 31 days (equivalent to 1, 5, 14, and 33 days of Florida summer sunlight). At each sampling point duplicate sub-samples were removed for analysis from both the irradiated and non-irradiated units.

3. Analytical procedures: Each soil incubate was transferred to a centrifuge beaker and extracted four times with 150 mL acetonitrile/deionised water/Hydrochloride (70:30:1 v/v/v). These four extracts were combined prior to determination of radioactivity by LSC. The extracts were concentrated by rotary evaporation and reconstituted in acetonitrile:water (1:1 v/v) prior to chromatographic analysis. Extracted soil samples were air-dried and ground prior to combustion in oxygen to determine the levels of bound residue by LSC. Radioactivity in the trapping solutions was quantified by LSC when units were removed for analysis.

Soil extracts taken from the incubation units were analysed for test substance and degradation products by High Performance Liquid Chromatography (HPLC) and Thin Layer Chromatography (TLC) (Methanol: Ammonia (25%) 98:2 v/v).

4. Determination of degradation kinetics: Using the data from each study propamocarb hydrochloride degradation was described assuming first-order degradation of the active substance, described by the following regression equation:

$$y = a \cdot e^{-k1 \cdot t}$$

DT_{50} and DT_{90} values for propamocarb hydrochloride were estimated from the degradation rate k using the following equations:

$$DT_{50} = \frac{\ln 2}{k} \qquad DT_{90} = \frac{\ln 10}{k}$$

II. Results and Discussion

A. Data:

Recovery and distribution of radioactivity from soil samples under irradiated and dark conditions following application of ^{14}C-propamocarb hydrochloride:

Timepoint	Unit	Soil extract	NER	Unit wash	Volatile			Total
					Etidol	Paraxy	2M NaOH	
Irradiated samples								
0	L1	92.4	4.1	0.0	NA	NA	NA	96.5
	L2	94.8	4.5	0.0	NA	NA	NA	99.3
	Mean	93.6	4.3	0.0	NA	NA	NA	97.9
1	L3	91.4	5.7	0.0	0.0	0.0	0.0	97.1
	L4	93.3	6.0	0.0	0.0	0.0	0.0	99.3
	Mean	92.4	5.9	0.0	0.0	0.0	0.0	98.2
5	L5	92.4	5.2	0.0	0.0	0.0	0.1	97.7
	L6	94.3	5.3	0.0	0.0	0.0	0.1	99.7
	Mean	93.4	5.3	0.0	0.0	0.0	0.1	98.7
14	L7	91.6	6.8	0.0	0.0	0.0	0.5	98.9
	L8	91.2	6.6	0.0	0.0	0.0	0.4	98.2

Timepoint	Unit	Soil extract	NER	Unit wash	Volatile			Total
					Etidol	Paraxy	2M NaOH	
	Mean	91.4	6.7	0.0	0.0	0.0	0.5	98.6
31	L9	86.1	9.5	0.0	0.0	0.0	2.7	98.3
	L10	82.1	9.1	0.0	0.0	0.0	2.0	93.2
	Mean	84.1	9.3	0.0	0.0	0.0	2.4	95.8
Dark Control								
0	L1	92.4	4.1	0.0	NA	NA	NA	96.5
	L2	94.8	4.5	0.0	NA	NA	NA	99.3
	Mean	93.6	4.3	0.0	NA	NA	NA	97.9
1	D3	93.6	6.1	0.0	0.0	0.0	0.1	99.8
	D4	95.0	6.6	0.0	0.0	0.0	0.1	101.7
	Mean	94.3	6.4	0.0	0.0	0.0	0.1	100.8
5	D5	93.1	4.8	0.0	0.0	0.0	0.4	98.3
	D6	93.4	5.1	0.0	0.0	0.0	0.4	98.9
	Mean	93.3	5.0	0.0	0.0	0.0	0.4	98.6
14	D7	91.5	7.4	0.0	0.0	0.0	1.3	100.2
	D8	89.3	6.9	0.0	0.0	0.0	1.8	98.0
	Mean	90.4	7.2	0.0	0.0	0.0	1.6	99.1
31	D9	73.2	15.6	0.0	0.0	0.0	8.8	97.6
	D10	78.1	13.0	0.0	0.0	0.0	5.3	96.4
	Mean	75.7	14.3	0.0	0.0	0.0	7.1	97.0

NA Not Analysed; NER Non-Extractable Residues

Radioactivity present as parent compound and degradation products in soil extracts of samples maintained under irradiated and dark conditions following application of ^{14}C-propamocarb hydrochloride (% AR):

Timepoint	Unit	propamocarb	Unknowns	Unresolved	Total
Irradiated samples					
0	L1	90.8	0.7	0.9	92.4
	L2	94.3	0.1	0.4	94.8
	Mean	92.6	0.4	0.7	93.6
1	L3	90.8	0.0	0.6	91.4
	L4	92.5	0.0	0.8	93.3
	Mean	91.7	0.0	0.7	92.4
5	L5	90.8	0.4	1.1	92.4
	L6	94.2	0.0	0.1	94.3
	Mean	92.5	0.2	0.6	93.4
14	L7	90.7	0.8	0.2	91.6
	L8	88.6	1.2	1.4	91.0
	Mean	89.7	1.0	0.8	91.3
31	L9	84.4	0.0	1.7	86.1
	L10	80.3	1.6	0.2	82.1
	Mean	82.4	0.8	1.0	84.1
Dark Control					
0	L1	90.8	0.7	0.9	92.4
	L2	94.3	0.1	0.4	94.8
	Mean	92.6	0.4	0.7	93.6
1	D3	92.4	0.3	0.9	93.6
	D4	94.9	0.0	0.1	95.0
	Mean	93.7	0.2	0.5	94.3
5	D5	91.7	0.8	0.5	93.1
	D6	90.6	2.7	0.2	93.4
	Mean	91.2	1.8	0.4	93.3
14	D7	90.7	0.0	0.8	91.5
	D8	88.9	0.3	0.1	89.3
	Mean	89.8	0.2	0.5	90.4
31	D9	72.1	1.0	0.1	73.2
	D10	77.2	0.0	0.9	78.1
	Mean	74.7	0.5	0.5	75.7

B. Mass balance: Radioactive mass balance and distribution of irradiated soil samples and the dark control are summarised in table above. The overall mass balance of applied radioactivity was in the range of 96% to 101% for both the irradiated and dark control samples.

C. Bound and extractable residues: The applied radioactivity extracted from the soil decreased over the 31 day incubation period from 94% initially to 84% and 76% for irradiated and dark control samples, respectively. A concomitant increase in NER was observed, with an increase from 4% of applied radioactivity initially to 9% and 14% for irradiated and dark control samples respectively. Soil NER was not characterised. For irradiated and dark control samples up to 2% and 7% of applied radioactivity was trapped in the sodium hydroxide traps.

D. Transformation of test substance: Chromatographic results of metabolites from soil extracts are provided in table above. For the irradiated and dark control units the test item, propamocarb hydrochloride, represented the majority of radioactivity in the soil extracts. Degradation of propamocarb hydrochloride was observed to be more extensive in the dark control samples by Day 31 in comparison to the irradiated samples. The percentage amount of propamocarb hydrochloride decreased to 82% and 75% of the applied radioactivity in the irradiated and dark control samples, respectively, after 31 days. No major degradation products were detected at amounts greater than 1% of applied radioactivity.

E. Degradation kinetics: Irradiation of propamocarb hydrochloride did not augment the rate at which propamocarb hydrochloride was degraded on soil surface, instead the rate of degradation was limited resulting in a DT_{50} value of 199.2 days. It is likely that reduced degradation for irradiated test soil is a result of the reduction in the local soil moisture at the soil surface. In contrast, the rate at which propamocarb hydrochloride degraded was increased in the dark control relative to the irradiated test soil, with a DT_{50} value of 103.1 days (table below).

DT_{50} and DT_{90} values determined for propamocarb hydrochloride under irradiated and non-irradiated experimental conditions:

	Values
Irradiated	
DT_{50} (days)	199.2
DT_{90} (days)	661.7
k	0.00348
r^2	0.812
Dark Control	
DT_{50} (days)	103.1
DT_{90} (days)	342.6
k	0.00672
r^2	0.864

III. Conclusion

Compared to microbial degradation processes, the photodegradation of propamocarb hydrochloride on soil surfaces is of limited significance. Exposure to sunlight is not expected to increase the degradation of propamocarb hydrochloride or lead to the formation of unique photo-degradates. No significant photo-degradates are to be expected.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

B) Aquatic systems - Direct photochemical degradation

The direct photochemical degradation of propamocarb hydrochloride in aquatic systems was investigated in:

• Deionized water at pH 5.5 to 6.0, following application of non-labeled propamocarb-hydrochloride and irradiation at 20°C (KCA 7.2.1.2/01; M-157849-01-1);

• Sterile deionized water at pH 4 to 5, following application of non-labeled propamocarb-hydrochloride and irradiation at 24°C (KCA 7.2.1.2/02; M-157698-01-1);

• Aqueous buffer solution of the non-labeled propamocarb-hydrochloride at pH 7, by determination of the absorption in the ultraviolet/visible spectrum of light (KCA 7.2.1.2/03; M-310246-01-1).

Two older studies (M-157849-01-1 and M-157698-01-1) have been conducted to investigate direct phototransformation of propamocarb-HCl.

Report:	KCA 7.2.1.2/01; Klehr, M.; 1978; M-157849-01-1
Title:	Photolysis of propamocarb. HCl (SN 66 752) in aqueous solution
Report No.:	APC 06/78; A85564
Document No.:	M-157849-01-1
Guideline(s):	US EPA, Federal Register, 40, 26883, 25th June, 1975 (page 5)
Guideline deviation(s):	--
GLP/GEP:	no

Report:	KCA 7.2.1.2/02; Klehr, M.; 1980; M-157698-01-1
Title:	Photolysis experiments with propamocarb HCL (SN 66 752) in heat sterilised aqueous solution
Report No.:	A85466
Document No.:	M-157698-01-1
Guideline(s):	not specified
Guideline deviation(s):	not specified
GLP/GEP:	**no**

Executive Summary

In Study M-157849-01-1, the degradation of propamocarb hydrochloride, under irradiation for 92 hours at a wavelength (λ) > 290 nm and at a light intensity of 2,250 J m^{-2} sec^{-1} in aqueous solution at a pH of between 5.5 and 6.0 and an initial concentration of 500 mg/L, was not greater than in a corresponding solution without irradiation. No photodegradates of propamocarb were detected. Therefore, photodegradation was not considered a relevant pathway for propamocarb hydrochloride in the aquatic environment.

In the study M-157698-01-1, the photolytic degradation of propamocarb hydrochloride was investigated in a heat sterilised buffer solution at a pH of between 4 and 5. No significant difference was recorded in the concentration of propamocarb hydrochloride after approximately 22 days of irradiation. Therefore, photodegradation was not a relevant degradation pathway for propamocarb in the aquatic environment.

I. Material and Methods

APC 06/78: For photolysis approx. 500 mg each of not labelled propamocarb hydrochloride were dissolved in 1 L of deionized water (500 ppm). The pH-values of these solutions were pH = 5.5 - 6.0; 350 mL of the solutions were exposed to irradiation at 20°C for 92 hours in a falling film reactor.

Propamocarb/W8: Aqueous solutions of not labelled SN 66 752 (250 ml with 460 mg/L) were exposed to artificial sunlight in a photochemical reactor. The solution temperature was maintained at

approximately 24°C during the experiments. The initial pH value of the aqueous propamocarb hydrochloride solutions was pH 4-5.

II. Results and Discussion

Overall, in Study APC 06/78 no difference in degradation was found between the irradiated samples and the dark controls about 20°C and 92 hours. A slight decrease in the concentration of propamocarb hydrochloride was noted in both the photochemical and dark solutions. However, this was attributed to possible microbial degradation in solution.

For Study propamocarb/W8 the results of the first photolysis experiment and the results of the corresponding dark reaction are shown in the table below. All values are given as concentrations (mg/L) of the free base (propamocarb) and not of the hydrochloride salt (propamocarb hydrochloride). A second photolysis experiment was carried out in order to verify the results of the first photolysis experiment and the corresponding dark reaction. During this reaction, the concentrations of propamocarb were determined only at the beginning and at the end of the experiment. These results are shown in the table below. There was no significant difference in the concentration of propamocarb hydrochloride after approximately 22 days (522.6 hours) of irradiation with artificial sunlight.

First photolysis experiment (a), concentrations of propamocarb (P0-P7) at the times 0 h to 522.6 h; Dark reaction (b), corresponding to the first photolysis experiment, concentrations of propamocarb (D0-D5) at the times 0 h to 522.6 h; and second photolysis experiment (P0-P2) and the corresponding dark reaction (D0-D1) (c):

(a)	P0	P1	P2	P3	P4	P5	P6	P7
Time (hr.)	0	44.3	94.9	188.5	258.6	332.6	427.3	522.6
1st sample (mg/L)	408.66	396.1	398.79	394.7	402.8	399.43	397.06	390.6
2nd sample (mg/L)	396.20	394.2	403.0	-	401.4	402.8	398.86	398.6
Average (mg/L)	402.4	395.15	400.89	394.7	402.1	401.11	397.96	394.6

(b)	D0	D1	D2	D3	D4	D5
Time (hr.)	0	94.9	188.5	258.6	332.6	522.6
1st sample (mg/L)	391.8	395.4	390.73	403.93	409.8	394.13
2nd sample (mg/L)	-	398.13	399.86	399.93	404.13	395.46
Average (mg/L)	391.8	396.76	395.29	401.93	406.96	394.8

(c)	P0	P1	P2	D0	D1
Time (hr.)	0	24	475.5	24	475.5
1st sample (mg/L)	392.43	396.93	391.22	390.9	393.53
2nd sample (mg/L)	389.33	393.26	391.67	384.53	389.73
Average (mg/L)	390.9	395.1	391.4	387.7	391.63

- no data available

III. Conclusion

No photodegradates of propamocarb were detected. Therefore, photodegradation is not considered a relevant degradation pathway for propamocarb hydrochloride in the aquatic environment.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

Report:	KCA 7.2.1.2/03; Mullee, D. M.; Bartlett, A. J.; 1995; M-310246-01-1
Title:	Propamocarb hydrochloride: Determination of photochemical degradation
Report No.:	722/014
Document No.:	M-310246-01-1
Guideline(s):	The Phototransformation of Chemicals in Water, ECETOC - Technical Report No. 12, Brussels 1984
Guideline deviation(s):	not specified
GLP/GEP:	**No**

Executive Summary

Propamocarb hydrochloride is not expected to photodegrade as absorption was noted in the λmax < 250 nm range. As energy is the prime requisite for a photochemical reaction, irradiation of Propamocarb hydrochloride in the spectrum of λ > 290 nm is not expected to induce any photochemical transformation. The maximum molecular extinction coefficient and λmax were determined for NaOH at 261.0 dm3 mol-1 cm^{-1} and 217 nm, respectively.

I. Material and Methods

A. Materials

1. Test Material: Non-labelled Propamocarb hydrochloride
99.64 % purity
Lot # 123457

2. Test solution:

Summary of the pH 7 buffer solution composition

pH	7
Composition	0.04M disodium hydrogen orthophosphate 0.03M potassium dihydrogen orthophosphate

B. Study design

1. Experimental conditions: The UV/Visible spectra were detailed by determination of the molecular extinction coefficient at 20.5°C ± 0.5°C in a buffer solution at pH 7, 0.1M hydrochloride, and 0.1M NaOH. The specification of the pH 7 buffer solution is provided in table above. All the test solutions were scanned in quartz cells of 1 cm path length.

2. Analytical procedures: The molecular extinction coefficient (ϵ) was calculated using the following equation:

$$\varepsilon = \frac{A}{C \cdot L}$$

A is absorbance, L is cell path length (cm), and C is the concentration (mol dm^{-3}).

II. Results and Discussion

The molecular extinction coefficients at the λmax are provided in the table below for non-labelled Propamocarb hydrochloride. The maximum molecular extinction coefficient and λ max were determined for NaOH at 261.0 dm^3 mol^{-1} cm^{-1} and 217 nm, respectively. Propamocarb hydrochloride is unlikely to photodegradate owing to the low optical density of the test material at wavelengths greater than 290 nm.

Summary of molecular extinction coefficients at the λ max for propamocarb hydrochloride:

Solution matrix	Solution concentration (g/L)	Absorbance	λmax (nm)	ε (dm^3 mol^{-1} cm^{-1})
pH 7 buffer solution	1.17	1.1090	203	214
0.1M Hydrochloride (pH <1)	1.20	1.2463	203	234
0.1M NaOH (pH >13)	1.14	1.3236	217	261

III. Conclusion

Propamocarb hydrochloride is not expected to photodegrade as absorption was noted in the λ max < 250 nm range. As energy is the prime requisite for a photochemical reaction, irradiation of Propamocarb hydrochloride in the spectrum of λ > 290 nm is not expected to induce any photochemical transformation. The maximum molecular extinction coefficient and λ max were determined for NaOH at 261.0 dm^3 mol^{-1} cm^{-1} and 217 nm, respectively.

RMS´s opinion:

Reliability of the study: score 1 of the scoring system of Klimisch *et al*.(1997).

The evaluation of direct photolytic degradation revealed that propamocarb-hydrochloride was neither subject to photolytic transformation (KCA 7.2.1.2/01 and KCA 7.2.1.2/02) nor had the potential for direct photolytic transformation (KCA 7.2.1.2/03). The latter was derived from determination of the ultraviolet/visible spectrum showing the absence of absorption necessary in the relevant range of light, i.e. from 290 to 800 nm, being the prerequisite for energy transfer to cause photolytic transformation.
Conclusively, direct photolytic transformation processes do not contribute to the elimination of propamocarb-hydrochloride from the aquatic environment.
No pathway was, therefore, derived for the direct photolysis of propamocarb-hydrochloride under conditions of photo-transformation in sterile aqueous buffer solution.
Based on the information derived from experimental photolysis data available and associated pre-tests, no quantum yield Φ and, consequently, no environmental half-lives for photo-degradation in water were estimated for propamocarb-hydrochloride.

Indirect photolytic degradation

Information on the behavior of propamocarb-hydrochloride under conditions of indirect photolytic transformation is available, based on tests performed outside the EU (Japan) to fulfill data requirements. The data are regarded as supplemental information as detailed in the following.

Report:	KCA 7.2.1.3/01; Roohi, A.; 2004; M-237606-01-1
Title:	(14C)-propamocarb Hydrochloride: Aqueous photolysis in natural water
Report No.:	C046039
Document No.:	M-237606-01-1
Guideline(s):	JMAF: 13 Seisan No. 3986, October 10, 2001, 2-6-2, amended June 26, 2001, Nousan 8147
Guideline deviation(s):	--
GLP/GEP:	**yes**

Executive Summary

The photolysis of 1-*N*-propyl-^{14}C-labeled propamocarb-hydrochloride was investigated in sterile natural water at pH 8.2 at a test concentration of 1.07 mg a.s./L. Samples were continuously irradiated at 25 ± 2 °C with artificial sunlight (< 290 nm cut-off filter) for four experimental days (96 experimental hours) in maximum equivalent to 30.4 environmental days when considering the light intensity (April to June) at Tokyo, Japan.

The mean recovered radioactivity ranged from 98.8 to 100.3% of AR for irradiated samples and from 97.6 to 99.5% for dark controls. Values of ^{14}C-propamocarb-hydrochloride decreased from 99.0% of AR at time zero to 91.6% after 4 days of irradiation.

Irradiation resulted in formation of a number of minor photo-transformation products occurring at 4.7% after 3 days and 4 days in maximum with none of the components exceeding 5% of AR in the course of the study. In dark controls, no significant degradation of the ^{14}C-test substance was observed.

The experimental DT_{50} of propamocarb-hydrochloride under conditions of the test was determined according to simple first order (SFO) kinetics to be 40.9 days for irradiated samples while no value of the DT_{50} was determined for dark controls. The half-life of irradiated samples was equivalent to 310.8 days for light conditions at Tokyo, Japan. With light conditions comparable, the same environmental half-life can be estimated for Athens, Greece.

Therefore, indirect photolysis is not expected to contribute to the overall elimination of propamocarb-hydrochloride from the aquatic environment.

I. Material and Methods

A. Materials

1. Test Material: [1-*N*-propyl-^{14}C]propamocarb-hydrochloride

Specific radioactivity: 8.44 MBq/mg
Radiochemical purity: 98.0% (HPLC)
Sample ID: BECH 1607

2. Test water

The natural water used for the test was freshly collected from the Reservoir Pond, Boarded Barns Farm, Ongar, Essex, UK. Water samples were characterized as summarized in the table below.

Physico-chemical characteristics of test water:

Water	Reservoir Pond
pH	8.2
Dissolved oxygen at collection (%)	86
Dissolved oxygen after sterilization and re-aeration (%)	96
Electrical conductivity (µS/cm)	477
Total hardness (CaCO3-equiv.; mg/L)	213
Suspended solids (% w/w)	0.017

Dissolved organic carbon (mg/L)	23.8
Dissolved organic matter (mg/L)	41.0
Total phosphorus (mg/L)	< 0.05
Total nitrogen (mg/L)	5.6
Nitrate (mg/L)	< 1.0
Residue on evaporation (% w/w)	0.005

Before the start of irradiation, the natural water was sterilized by passing it through a sterile filter.

B. Study design

1. Experimental conditions: The test was performed with 1-*N*-propyl-^{14}C-propamocarb-hydrochloride at an initial concentration of 1.07 mg a.s./L. The static test system consisted of quartz glass vessels attached to traps for volatile components each containing 18 mL of the sterile test water. The test solutions contained less than 1% of the co-solvent acetonitrile. The samples were continuously irradiated in a ®Suntest system at 25 ± 2°C with simulated sunlight (xenon burner, range of wave length spectrum 290 to 800 nm, i.e. spectral distribution similar to that of natural sunlight) providing a light intensity of 527 W/m^2 (one Suntest irradiation day being equivalent to 7.6 days of sunlight at Tokyo, Japan, 35°N) with cut-off of UV radiation < 290nm by the use of filters (Suprax). In parallel, samples were incubated under static conditions at the same temperature in the dark thus serving as dark controls. Based on intensity measurements a continuous light exposure of four days in maximum (96 experimental hours) was equivalent to 30.4 environmental days when being compared to light conditions at Tokyo, Japan, from April to June.
Duplicate samples were removed for analysis after 0, 0.17, 1, 2, 3, 3.2 and 4 days of irradiation. A single sample was taken after 28 hours of irradiation.
Duplicate samples of dark controls were removed for analysis after 0, 2, 3 and 4 days of incubation.
Sterility was checked for irradiated samples and dark controls at all sampling intervals.
Since recoveries were > 98% AR for all samples, no determination of volatile radioactivity was performed.

2. Analytical procedures: Samples were analysed directly with no additional steps for extraction, clean-up, or sample concentration using LSC for determination of total radioactivity. Reversed-phase HPLC with ^{14}C-flow-through detection techniques was used as chromatographic method for the separation and quantitation of transformation products. HPLC analysis was performed within 24 hours after work-up. Representative samples were additionally investigated by HPLC-MS-MS for confirmation of test item identity.
Based on the lowest integrable peak within ^{14}C-flow-through detection, the LOD was estimated to be less than or equal to 0.01% of AR.

3. Kinetic evaluation: The kinetic evaluation of propamocarb-hydrochloride degradation data was performed with the software Excel by using the SFO model[10] for fitting. Values for half-lives and DT_{90} were calculated for irradiated samples and dark controls. The quality of fit was expressed in terms of the correlation co-efficient.

III. Results and Discussion

The total irradiation time of four days (96 experimental hours) in maximum corresponded to 30.4 environmental days under light conditions of Tokyo, Japan from April to June to reflect a worst-case approach.
Sterility of samples was confirmed throughout the whole testing period. The temperature was maintained at 25 ±2 ºC for irradiated samples and dark controls during the test.

The material balances and distribution of radioactivity are summarized for irradiated samples and dark controls. The material balances ranged from 98.8 to 100.3% AR for irradiated samples and from 97.6 to

[10] SFO = Single First Order

99.5% for dark controls. Volatile components including ^{14}C-carbon dioxide were not determined considering recoveries of > 97% AR in the test solutions. Formation of volatiles was thus expected to be insignificant.
In irradiated samples, propamocarb-hydrochloride showed a decrease from 99.0% AR at time zero to 91.6% after four days. Degradation was negligible in dark controls as demonstrated by values of 99.0% AR at time zero to 97.5% after four days of incubation.
Irradiation resulted in a pattern consisting of minor transformation products all significantly below 5% AR in maximum for an individual peak at any sampling interval during the study (Table CA 8.2.1.3-02). In dark controls, no notable degradation of propamocarb-hydrochloride was observed.
No major and distinct transformation products were, therefore, observed that require further assessment in environmental exposure assessments, as summarized in the table below

Phototransformation of [1-N-propyl-^{14}C]propamocarb-hydrochloride in sterile natural water:

Component		Sampling interval (days)					
	Irradiated	0.0	0.17	1	1.17	2	3
	Dark control	0.0	-	-	-	2	3
Propamocarb-hydrochloride (Test substance)	Irradiated	99.0 ± 0.5	98.1 ± 0.4	95.8 ± 0.8	96.1	93.6 ± 0.6	93.7 ± 2.9
	Dark control	99.0 ± 0.5	-	-	-	96.7 ± 1.8	96.3 ± 1.4
Unknown rrt 0.25	Irradiated	0.2 ± 0.1	0.3 ± 0.0	0.4 ± 0.0	0.5	0.8 ± 0.1	0.6 ± 0.2
	Dark control	0.2 ± 0.1	-	-	-	0.2 ± 0.0	0.2 ± 0.0
Unknown rrt 1.53	Irradiated	0.0 ± 0.0	0.0 ± 0.0	1.3 ± 0.0	2.3	4.2 ± 0.2	4.7 ± 1.5
	Dark control	0.0 ± 0.0	-	-	-	0.0 ± 0.0	0.0 ± 0.0
Total other unidentified radioactivity (each < 2%)	Irradiated	0.2 ± 0.0	0.7 ± 0.5	1.2 ± 0.2	0.8	1.0 ± 0.2	1.3 ± 0.4
	Dark control	0.2 ± 0.0	-	-	-	1.1 ± 0.6	1.0 ± 0.4
Total recovered	Irradiated	99.5 ± 0.6	99.1 ± 0.2	98.8 ± 0.6	99.7	99.5 ± 0.4	100.3 ± 1.6
	Dark control	99.5 ± 0.6	-	-	-	98.0 ± 1.2	97.6 ± 1.8
Volatile radioactivity including ^{14}C-Carbon dioxide	Irradiated	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Dark control	n.d.	-	-	-	n.d.	n.d.
Radioactivity adsorbed to test vessels	Irradiated	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Dark control	n.d.	-	-	-	n.d.	n.d.
Total recovery	Irradiated	99.5 ± 0.6	99.1 ± 0.2	98.8 ± 0.6	99.7	99.5 ± 0.4	100.3 ± 1.6
	Dark control	99.5 ± 0.6	-	-	-	98.0 ± 1.2	97.6 ± 1.8

Component		**Sampling interval** (days)	
	Irradiated	3.2	4
	Dark control	-	4
Propamocarb-hydrochloride (Test substance)	Irradiated	94.1 ± 1.1	91.6 ± 2.7
	Dark control	-	97.5 ± 0.3

Component		Sampling interval (days)					
	Irradiated	0.0	0.17	1	1.17	2	3
	Dark control	0.0	-	-	-	2	3
Unknown rrt 0.25	Irradiated	0.8 ± 0.1	0.7 ± 0.2				
	Dark control	-	0.3 ± 0.1				
Unknown rrt 1.53	Irradiated	3.7 ± 1.2	4.7 ± 1.6				
	Dark control	-	0.0 ± 0.0				
Total other unidentified radioactivity (each <5%)	Irradiated	1.0 ± 0.1	2.0 ± 0.4				
	Dark control	-	0.5 ± 0.1				
Total recovered	Irradiated	99.6 ± 0.2	99.1 ± 0.5				
	Dark control	-	98.4 ± 0.0				
Volatile radioactivity including ^{14}C-Carbon dioxide	Irradiated	n.d.	n.d.				
	Dark control	n.d.	n.d.				
Radioactivity adsorbed to test vessels	Irradiated	n.d.	n.d.				
	Dark control	n.d.	n.d.				
Total recovery	Irradiated	99.6 ± 0.2	99.1 ± 0.5				
	Dark control	-	98.4 ± 0.4				

Unless specified otherwise by standard deviation, single sample analysis; n.d. = not determined
** Numerous unknowns each to account for <5% of AR for a single component, see also total unidentified
All values expressed as percentage of total applied radioactivity

Products of indirect photochemical degradation of ^{14}C-propamocarb-hydrochloride in sterile natural water:

Label	Label position	Component	Maximum fraction (% AR)	Maximum occurrence after days *
1	1-*N*-propyl	none	-	-

* Total duration was four days (96 experimental hours)

The experimental DT_{50} value for propamocarb-hydrochloride in irradiated samples was calculated by applying a simple first order kinetic model. No experimental DT_{50} value was calculated for dark controls considering the stability of the compound under the conditions of the test.
The experimental half-life was determined to 40.9 days for irradiated samples. This experimental DT_{50} had not been corrected for biological degradation due to the insignificant degradation observed in dark controls. When transferring this result to outdoor conditions considering the (lower) light intensities of natural sunlight in Tokyo, Japan, the value for the half-life was 310.8 days. The light intensity is comparable to southern European conditions, i.e. the light intensity at Athens, Greece thus resulting in the same environmental half-life.

IV. Conclusions

The indirect photolytic transformation of propamocarb-hydrochloride in sterile natural water was insignificant to result in a photolytic half-life of 310.8 environmental days when being referenced to natural light conditions of Japan and, thus, comparable to light conditions of Athens in the EU.

Consequently, the application of ^{14}C- propamocarb-hydrochloride to sterile natural water followed by irradiation resulted in no formation of major photo-degradation products to be considered in aquatic risk assessment.
Indirect photolysis processes, therefore, contribute to a negligible extent to the overall elimination of propamocarb-hydrochloride from the aquatic environment.

RMS´s opinion:

Reliability of the study: score 2 of the scoring system of Klimisch *et al*.(1997).

11.2 Environmental transformation of metals or inorganic metals compounds

Not applicable.

11.2.1 Summary of data/information on environmental transformation

Not applicable.

11.3 Environmental fate and other relevant information

Not applicable.

11.4 Bioaccumulation

Table 72: Summary of relevant information on bioaccumulation of propamocarb hydrochloride (PHC)

Method	Results	Remarks	Reference
Guideline(s): - Uptake and loss study under flow-through conditions and static conditions	Bluegills under continuous flow conditions and channel catfish under static conditions accumulated low levels of ^{14}C-PHC equivalents. Concentration of propamocarb ^{14}C Equivalents in Bluegills Exposure / Fillet / Offal 1 / 1.179 / 1.832 28 / 1.070 / 1.885 Concentration of Propamocarb-^{14}C Equivalents in Channel Catfish Exposure / Fillet / Offal 1 / 0.098 / 0.159 28 / 1.157 / 1.081	GLP/GEP: No. Reliability score: (Klimisch et al.,1997): 1.	Anonymous; 1980. *Uptake of propamocarb fungicide by Bluegills and Channel catfish.* (see document M-157741-01-1; KCA 8.2.2.3/01)

<table>
<tr><th>Method</th><th>Results</th><th>Remarks</th><th>Reference</th></tr>
<tr><td>Guideline(s):
-

Uptake and loss study under flow-through conditions and static conditions</td><td>The rapid metabolism and elimination along with low associated tissue residues suggest that PHC will not pose a hazard to bluegills and channel catfish. This conclusion is supported by the fact that PHC possesses low acute toxicity to fishes.

^{14}C-PHC equivalents in selected tissues 24h intraperitoneal injection
<table>
<tr><td>Tissue</td><td>Bluegill</td><td>Channel Catfish</td></tr>
<tr><td>Bile</td><td>12.75</td><td>3.68</td></tr>
<tr><td>Kidney</td><td>2.88</td><td>2.17</td></tr>
<tr><td>Liver</td><td>2.04</td><td>1.04</td></tr>
<tr><td>Pyloric Caeca</td><td>2.00</td><td>-</td></tr>
<tr><td>Intestine</td><td>1.77</td><td>1.45</td></tr>
<tr><td>Heart</td><td>1.22</td><td>0.44</td></tr>
<tr><td>Stomach</td><td>1.19</td><td>0.72</td></tr>
<tr><td>Eye</td><td>1.03</td><td>3.10</td></tr>
<tr><td>Spleen</td><td>1.01</td><td>1.08</td></tr>
<tr><td>Gills</td><td>0.74</td><td>0.54</td></tr>
<tr><td>Gonads</td><td>0.62</td><td>-</td></tr>
<tr><td>Muscle</td><td>0.39</td><td>0.55</td></tr>
<tr><td>Brain</td><td>0.17</td><td>0.21</td></tr>
<tr><td>Fat</td><td>0.11</td><td>0.06</td></tr>
</table></td><td>GLP/GEP: No.

Reliability score: (Klimisch et al.,1997): 1.</td><td>Anonymous; 1981. Metabolic fate and tissue residues of propamocarb in Bluegills and Channel catfish. (see document M-157742-01-1; KCA 8.2.2.3/02)</td></tr>
<tr><td>Guideline(s):
OECD TG 305B (1993), IBAMA 84 (1996)</td><td>Clearance time to eliminate residues in fish:
CT_{50}: 2.9-5.2 days
CT_{90}: 9,8-17.3 days

Bioconcentration factor (BCF): 4.7

Biological half-life: 5.2 days.</td><td>GLP/GEP: Yes.

Reliability score: (Klimisch et al.,1997): 1.

PHC does not bioaccumulate in the Zebrafish.</td><td>Anonymous; 2001. Bioconcentration of Proplant to zebrafish (Danio rerio) ; M-310727-01-1

KCA 8.2.2.3/03</td></tr>
<tr><td>Guideline(s):
Commission Directive 92/69/EEC A.8; OECD 107</td><td>pH 2.0: Log P_{ow} -2.87
pH 7.0: Log P_{ow} -1.21
pH 9.0: Log P_{ow} 0.670</td><td>PHC is not fat soluble.</td><td>Muehlberger, B.; 2001 (please, see document M-203110-01-1)</td></tr>
<tr><td>Guideline(s):
OECD/GD(92)32 Commission Directive 92/69/EEC Method C7</td><td>pH 4.0: Log P_{ow} -0.979
pH 7.0: Log P_{ow} -1.36
pH 10: Log P_{ow} 0.320</td><td>PHC is not fat soluble.</td><td>Walker, A. J.; Mulle, D. M.; Barlett, A. J.; 1995 (please, see document M-309665-01-1)</td></tr>
</table>

11.4.1 Estimated bioaccumulation

Active substance

Although propamocarb hydrochloride would not be expected to bioaccumulate (log Pow < 3), a study has been performed by University of Missouri, USA, with Bluegill sunfish and Channel catfish, to determine quantitatively the bioconcentration factor (BCF) for these species. A second study investigated the metabolism and associated residues in Bluegill sunfish and Channel catfish following intraperitoneal treatment with propamocarb. The results of these studies, which are published in "Chemophere" in 1980 and 1981, provide supporting information and confirmation that bioaccumulation of propamocarb-HCl will not occur in fish. Additionally, in a third study it was detected

that PHC does not appear to bioaccumulate in the Zebrafish (BCF values of 4.7 and a biological half-life of 5.2 days).

In conclusion, the active substance PHC doesn´t have potential to bioaccumulate in fishes.

Metabolites, degradation and reaction products

There are no metabolites that are expected to bioaccumulate, due to the rapid degradation of propamocarb hydrochloride to carbon dioxide. Furthermore, no or low toxicity of the metabolites, degradation or reaction products to fishes, aquatic invertebrates or aquatic plants was observed in the aquatic environment.
In conclusion, it isn´t necessary to perform these bioaccumulation studies.
Below, is presented a summary of each study evaluated.
Also, the Table 75, presented below, gives a summary of relevant information.
A study, referred as M-157741-01-1, was conducted to determine quantitatively the bioconcentration factor (BCF) for the fish species Bluegill sunfish and Channel catfish.

Report:	KCA 8.2.2.3/01;. Anonymous; 1980; M-157741-01-1
Title:	Uptake of propamocarb fungicide by Bluegills and Channel catfish
Report No.:	A85492
Document No.:	M-157741-01-1
Guideline(s):	--
Guideline deviation(s):	--
GLP/GEP:	No

In other study, referred as M-157742-01-1, the metabolism and associated residues in Bluegill sunfish and Channel catfish following intraperitoneal treatment with propamocarb hydrochloride were investigated.

Report:	KCA 8.2.2.3/02; Anonymous; 1981; M-157742-01-1
Title:	Metabolic fate and tissue residues of propamocarb in Bluegills and Channel catfish
Report No.:	A85493
Document No.:	M-157742-01-1
Guideline(s):	--
Guideline deviation(s):	--
GLP/GEP:	**No**

Both studies are published.

A continuous flow uptake and loss study using Bluegill sunfish (Lepomis macrochirus) was conducted over 42 days at 22 °C (± 1 C). 75 fish, weighing approximately 0.5 g each, were held in either a control aquarium, receiving 250 mL/min of clean water, or a dosed aquarium that received 250 mL/min of water containing 1 mg/L of radiolabelled propamocarb hydrochloride (98% pure). Five fish from each aquarium were sampled 1, 3, 7, 10, 14 and 28 days after the start of the experiment. After 28 days the propamocarb hydrochloride dosing was stopped and the fish left to depurate in clean flowing water with five fish being sampled at 1, 3, 7, 10 and 14 days into the depuration period. Fish samples were divided into offal (which consisted of the carcass and viscera) and the fillet (flesh). Each fish was treated as an individual sample with liquid scintillation counting used to determine the total ^{14}C content of the tissue.

For Channel catfish (*Ictalurus punctatus*), a soil/water uptake study was conducted for 28 days with a 14 day depuration period in a clean soil water system. Radiolabelled propamocarb hydrochloride was thoroughly mixed into 5 kg of soil (11% clay, 52% sand and 37% silt) to produce a nominal concentration of 3 mg/kg, which was spread over the bottom of a stainless steel tank and aged aerobically for 14 days. Then 400 L of well water was added to this system followed by 50 catfish (average weight 0.5 g). Analysis of total radioactivity was conducted on water, hydrosoil and three fish after 1, 3, 7, 10, 14, 21 and 28 days exposure. After 28 days 20 fish were transferred to a clean water/soil system and sampled after 1, 3, 7, 10 and 14 days.

Catfish samples were treated in the same manner as the Bluegill sunfish.

For Bluegill sunfish the mean measured water concentration was determined to be 1.11 mg/L of radiolabelled compound throughout the 28 day exposure period. Concentrations of radiolabelled compound in the flesh varied from <0.5 to 1.703 mg/kg (limit of detection 0.5 mg/kg) with no obvious increase in concentration related to exposure time. Offal residue concentrations appeared to be reasonably constant over the whole exposure period and ranged from 1.83 to 3.42 mg compound/kg. Bioconcentration factors (BCF) after 28 days were 1.5 and 3 for the fillet and offal, respectively. The radiolabelled compound depurated rapidly falling below the limits of detection after 7 and 10 days for the fillet and offal, respectively.

For Channel catfish throughout the 28 day period the hydrosoil concentration decreased from 2.601 to 1.278 mg/kg of propamocarb hydrochloride ^{14}C with a corresponding increase of 0.013 to 0.029 mg/L of radiolabelled compound found in the test water. The radiolabelled compound concentrations in fish tissue tended to follow the increase in water concentration. The fillet concentrations ranged from 0.098 mg/kg (on day 1) to 1.157 mg/kg of radiolabelled compound after 28 days. The offal concentrations were similar, increasing from a day 1 value of 0.159 mg/kg to 1.08 mg/kg of radiolabelled product after 28 days. Bioconcentration factors after 28 days were 39.0 and 37.3 for the fillet and offal.

In conclusion, for both Bluegill sunfish and Channel catfish the bioconcentration factors (BCF) after 28 days were below 100. In both species propamocarb residues depurated rapidly with a biological half-life of less than seven days, with tissue levels falling below the limits of detection after 10 days in Bluegills. Bluegills under continuous flow conditions and Channel catfish under static conditions accumulated low levels of propamocarb- ^{14}C equivalents. The rapid metabolism and elimination along with low associated tissue residues suggest that propamocarb will not pose a hazard to bluegills and channel catfish. This conclusion is supported by the fact that propamocarb possesses low acute toxicity to fish.

These findings are supplemented by the results of a third study (M-310727-01-1):

Report:	KCA 8.2.2.3/03; Anonymous; 2001; M-310727-01-1
Title:	Bioconcentration of Proplant to zebrafish (Danio rerio)
Report No.:	RF-0998.210.022.01
Document No.:	M-310727-01-1
Guideline(s):	IBAMA 84 (1996)
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

This third study (M-310727-01-1) investigates the bioconcentration of propamocarb to Zebrafish (*Danio rerio*). 80 fish per test concentration were exposed for 7 days in a semi-static system with renewal of test solution every 48 hours at two test concentrations (low and high, 6.5 and 63.3 mg a.s./L, respectively, with 1 replicate per concentration), one control and one solvent control (40 fish). After exposure to test substance for 7 days, the fish were transferred into untreated dilution water for 7 days. For the purpose of dose verification, radioactivity in the water phase was analysed by LSC every day during the uptake and depuration phases. The fish were sampled each day (on day 0 after 0, 1 and 17 hours) during the uptake phase and on day 0, 1, 2, 3, 4 and 7 during the depuration phase. At each date, 2 fish were collected from control(s) and 4 fish from each tested concentrations and were stored frozen at -20 °C. To elucidate potential effects of the culture conditions on results biological observations (mortality during the acclimation period) as well as physical-chemical measurements (pH, DO (dissolved oxygen), conductivity and temperature were measured for the control, solvent control, low and high concentration treatments) were conducted. Results showed that fish mortality was within acceptable limits (<10%) in the control during the test period. Water quality such as temperature, dissolved oxygen, conductivity and pH were consistent when compared to the controls and found to be acceptable. The average test solution concentration during the uptake phase confirmed by radioanalysis was 6.5 and 63.3 mg a.s./L for the low and high concentrations, respectively. Hence the test is considered to be fully valid.

The uptake rate constant (Ku) was 0.0261 for the low and 0.0319 for the high concentration, while depuration rate constant (Kd) was 0.0055 for the low and 0.0098 for the high concentration. Bioconcentration factor (BCF) was found to be 4.7036 and 3.2553 for the low and highconcentrations,

respectively. Clearance time to eliminate residues in fish was for the low concentration CT_{50} = 5.2 days and CT_{90} = 17.3 day and for the high concentration CT_{50} = 2.9 days and CT_{90} =17.3 days, respectively. Based on these results, propamocarb hydrochloride does not appear to bioaccumulate in the Zebrafish with BCF values of 4.7 and a biological half-life of 5.2 days.

11.4.2 Measured partition coefficient

The partition coefficient n-octanol/water of propamocarb hydrochloride at room temperature (22 °C) has been determined in two independent studies (M-309665-01-1 and M-203110-01-1) on three different pH values (pH 4, 7, 10, in M-309665-01-1 and pH 2, 7, 9, in M-203110-01-1) to check for pH-dependence of the partition coefficient, according to the "flask-shaking" method described in guideline OECD TG 107 and 92/69/EEC, appendix, part A.8. The purity of the test material ranged from to 97.2% (M-203110-01-1) to 99.1% (M-309665-01-1).

The partition coefficient (n-octanol/ water) of the test substance depending on pH-values was:

pH 2.0: Log P_{ow} -2.87
pH 4.0: Log P_{ow} -0.979
pH 7.0: Log P_{ow} -1.21 to Log P_{ow} -1.36
pH 9.0: Log P_{ow} 0.67
pH 10: Log P_{ow} 0.320

The results indicate that propamocarb hydrochloride is not fat soluble.

11.5 Acute aquatic hazard

The studies from which endpoints are derived are part of the Baseline Dossier provided by Bayer CropScience and Arysta LifeScience. These studies are listed in the Table below.
Additionally, two studies on metabolites were performed. Due to the observed absence of acute toxicity of the metabolites N-desmethyl-propamocarb and propamocarb-N-oxide for the aquatic invertebrate *Daphnia magna* and for the green algae *Pseudokirchneriella subcapitata*, in addition to the low toxicity of the parent (PHC), it is unlikely that the fish group is significantly more sensitive to the metabolites than the two other mentioned groups of aquatic organisms. Due to this and also for animal welfare reasons, it was decided not to conduct any additional vertebrate tests with fishes to evaluate the acute toxicity of the metabolites of propamocarb hydrochloride.
Considering the propamocarb hydrochloride results of toxicity to the pelagic aquatic invertebrate *Daphnia magna* and is not expected to strongly adsorb or accumulate in sediments, it is not considered necessary to determine the toxicity to sediment-dwelling invertebrates.
According to CLP Regulation 1272/2008 testing of marine or estuarine organisms is not necessary.

Table 73: Summary of relevant information on acute aquatic toxicity

Method	Species	Test material	Results[1]	Remarks	Reference
Static conditions; US EPA Guideline 72-1; OECD 203; US EPA 72-1	*Onchorhynchus mykiss* (Rainbow trout)	Propamocarb-hydrochloride (PHC)	96h LC_{50} > 99 mg a.s./L	GLP/GEP: No. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Anonymous (1991). *The static acute toxicity of propamocarb-HCl to the rainbow trout, Oncorhyn-chus mykiss.* M-157858-01-1 (KCA 8.2.1/02)

				The 96 h LC50 could not be determined.	
96h Semi static; Directive 92/69/EEC (part C.1; 1992); OECD TG 203 (1992)	*Onchorhynchus mykiss*	PHC	96h LC_{50} > 100 mg a.s./L $_{nom}$	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Anonymous (1996). *96-hour acute limit study in rainbow trout with Proplant (semi-static).* M-310778-01-1 (KCA 8.2.1/03)
Static conditions; US EPA Guideline 72-1	*Lepomis macrochirus* (Bluegill sunfish)	PHC	96h LC_{50} > 92 mg a.s./L $_{nom}$	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997). The 96 h LC50 could not be determined.	Anonymous (1991). *The static acute toxicity of propamocarb-HCl to the bluegill sunfish, Lepomis macrochirus* M-157853-01-1 (KCA 8.2.1/01)
96h Static conditions; EPA OPPTS 850.1075; EPA 712-C; 92/69/EEC (1992) Part C.1; OECD TG 203 (1992)	*Lepomis macrochirus* (Bluegill sunfish)	PHC	96 h LC_{50} = 240 mg a.s./L $_{nom}$	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Anonymous (2001). *96-hour acute toxicity study in bluegill sunfish with Proplant (propamocarb HCL 722 g/l) (static).* M-310734-01-1 (KCA 8.2.1/04)
OECD: 203 (1992)	*Oncorhynchus mykiss*	FLC + PCH SC 687.5 (INFINITO) *	LC_{50} = 6.57 mg prod./L $_{nom}$	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Anonymous (2003). M-225109-01-1 KCP 10.2.1/01
	Cyprinus carpio		LC_{50} = 18 mg prod./L $_{nom}$		Anonymous (2003). M-227280-01-1 KCP 10.2.1/02
96h Static conditions; 92/69/EEC (1992) Part C.1; OECD TG 203 (1992)	*Cyprinus carpio*	PHC SL 722 (PROPLANT)	LC_{50} > 100 mg a.s./L	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch	Anonymous (2000). *96-hour acute toxicity study in carp with Proplant.* M-310773-01-1 KCA 8.2.1/05

				et al. (1997).	
Static conditions; US EPA FIFRA Guideline 72-3	*Cyprinodon variegatus*	PHC SL 722 (PROPLANT)	LC_{50} > 110 mg a.s./L $_{mm}$	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Anonymous (2001). *Proplant (propamocarb HCL 722 g/l SL): Acute toxicity to Sheep-shead minnow (Cyprinodon variegatus) under static conditions.* M-310736-01-1 (KCA 8.2.1/06)
Static conditions; Guideline 72-2	*Daphnia magna*	PHC	48h EC_{50} > 106 mg a.s./L $_{nom}$	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Bruns, E. (2009). *The acute toxicity of propamacarb-HCl to Daphnia magna in a static system*. M-157891-02-1 KCA 8.2.4.1/01
Static conditions; OECD TG 202; US EPA FIFRA 72-2	*Daphnia magna*	PHC and metabolites	48h EC_{50} > 106 mg a.s./L $_{nom}$	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Schupner, J. K.; Stachura, B. J. (1992); M-157891-01-1 and Amendment (2009) Bruns, E.; 2009; M-157891-02-1 (KCA 8.2.4.1/01)
OECD: 202-1 (1984).	*Daphnia magna*	FLC + PCH SC 687.5 (INFINITO) *	EC_{50} = > 100 mg prod./L $_{nom}$	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Gries (2003). M-227283-01-1 KCP 10.2.1/03
Static conditions; 92/69/EEC (part C.2; 1992); OECD TG 202 (1984)	*Daphnia magna*	propamocarb hydrochloride SL 722 (PROPLANT)	48h EC_{50} > 100 mg a.s./L $_{nom}$	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Bogers, M. (1996). *Acute limit study in Daphnia magna with Proplant .* M-310720-01-1 (KCA 8.2.4.1/02)
Static exposure conditions; US EPA OCSPP 850.1010; OECD guideline 202 (2004); EC	*Daphnia magna*	Metabolite propamocarb-N-oxide	EC_{50} > 100 mg/L $_{nom}$	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Kuhl (2015). *Acute toxicity of AE F155306 (BCS-AU81087) to the waterflea Daphnia magna in a static laboratory test system - Limit test.* M-525333-01-1

Council Regulation No 440/2008, Method C.2 (2008); U.S. EPA Pesticide Assessment Guidelines, Subdivision E, § 72-2 (1982); OPPTS Guideline 850.1010 public draft 1996 (modified); JMAFF 12 Nousan No. 8147 (2000)					KCA 8.2.4.1/03
	Daphnia magna	Metabolite N-desmethyl-propamocarb	EC_{50} > 100 mg /L $_{nom}$	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Kuhl (2015). *Acute toxicity of AE B083813 (BCS-AW15480) to the waterflea Daphnia magna in a static laboratory test system - Limit test* . M-525347-01-1 KCA 8.2.4.1/04
Static exposure conditions; Guideline FIFRA 72-3	*Mysidopsis bahia*	PHC	96h LC50 > 105.0 mg /L$_{mm}$	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Schupner (1991). *The static acute toxicity of Propamocarb HCl to the Mysid shrimp, Mysidopsis bahia* M-157843-01-1 KCA 8.2.4.2/01
Static exposure conditions; Guideline FIFRA 72-3	*Americamysis bahia*	Propamocarb-HCl SL 722	96h LC50 = 50.0 mg /L $_{mm}$ NOEC = 15.0 mg /L $_{mm}$	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Putt (2001). *Proplant (propa-mocarb HCL 722 g/l SL): Acute toxicity to Mysids (Americamysis bahia) under static conditions.* M-310709-01-1 KCA 8.2.4.2/02
Flow-through exposure conditions	*Crassostrea virginica* (eastern oyster)	PHC	96h LC50 = 43.9 mg /L $_{mm}$ NOEC = 12.0 mg /L $_{mm}$	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Holmes & Peters (1991). *Propamocarb HCl: A 96-hour shell deposition test with the Eastern oyster (Crassostrea virginica.* M-157857-01-1 KCA 8.2.4.2/03
Flow-through exposure conditions; Guideline FIFRA 72-3; OPPTS 580.1025	*Crassostrea virginica*	Propamocarb-HCl SL 722	96h LC50 = 46.0 mg /L $_{mm}$ NOEC = 7.1mg /L $_{mm}$	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Dionne (2001). *Proplant (propa-mocarb HCL 722 g/l SL): Acute toxicity to Eastern oysters (Crassostrea virginica) under flow-through conditions.* M-310718-01-1 KCA 8.2.4.2/04
72h Fresh Water Algal Growth Inhibition Test; Static	*Pseudokirchne-riella subcapitata*	PHC	72h EbC_{50} > 120 mg a.s./L $_{mm}$ 72h ErC_{50} > 85 mg a.s./L $_{mm}$	GLP/GEP: Yes. Reliable without	Hoberg, J. R. (2001). *Propamocarb hydrochloride - Toxicity to the*

exposure conditions; US EPA OPPTS Draft Guideline 850.5400; OECD TG 201; EC Guideline Annex V – Part C.3				restrictions, code 1 (Klimisch et al. (1997).	*freshwater green alga, Pseudokirch-neriella subcapi-tata.* M-240390-01-1 KCA 8.2.6.1/01
72h Fresh Water Algal Growth Inhibition Test; Static exposure conditions; Directive 92/69/EEC (part C.3; 1992); OECD TG201 (1984); ISO 8692 (1989)	*Selenastrum capricornutum*	PHC	EbC_{50} > 130 mg a.s./L ErC_{50} > 130 mg a.s./L	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Bogers, M. (1996). *Fresh water algal growth inhibition test with Proplant.* M-310692-01-1 KCA 8.2.6.1/02
Static exposure conditions; EU Directive 91/414/EEC; Regulation (EC) No. 1107/2009; U.S. EPA Pesticide Assessment Guidelines, Subdivision J, §122-2, 123-2; OCSPP Guideline 850.4500 (January 2012); OECD Guideline 201: Freshwater Alga and Cyanobacteria, Growth Inhibition Test (July 28, 2011); OCSPP Guideline 850.4500: Algal Toxicity (June 2012)	*Pseudokirchne-riella subcapitata*	Metabolite: propamocarb-N-oxide	E_rC_{50} > 100 mg /L $_{nom}$	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Kuhl (2015). *Pseudokirchneriell a subcapitata growth inhibition test with AE F155306 (BCS-AU81087).* M-525324-01-1 (KCA 8.2.6.1/03)
	Pseudokirchne-riella subcapitata	Metabolite: N-desmethyl-propamocarb	ErC_{50} > 100 mg /L $_{nom}$	-	Kuhl (2015). *Pseudokirchneriell a subcapitata growth inhibition test with AE B083813 (BCS-AW15480).* M-525329-01-1 (KCA 8.2.6.1/04)
Static renewa test system; USEPA (=EPA): 122-2	Aquatic plant *Lemna gibba*	PHC	14 d, ErC_{50} [1] > 18 mg/L $_{nom}$	GLP/GEP: Yes. Reliable without restrictions,	Christ & Ruff (1996). *Propamocarb hydrochloride water-miscible concentrate 68.2*

				code 1 (Klimisch et al. (1997).	*percent w/w (738 g/L) Code: AE B066752 - Toxicity to duckweed (Lemna gibba, G3) in a static renewal system*. M-165250-01-1 KCA 8.2.7/01
Guideline(s): OECD: 201 (1984)	*Navicula pelliculosa*	FLC + PCH SC 687.5 (INFINITO)	$E_bC_{50} >= 0.40$ mg prod./L $_{nom}$ $E_rC_{50} >= 0.63$ mg prod./L $_{nom}$	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Gries (2003). M-227284-01-1 KCP 10.2.1/04
	Pseudokirchneriella subcapitata (syn. *Selenastrum capricornutum*)		$E_bC_{50} > 13.80$ mg prod./L $_{nom}$ $E_rC_{50} > 100$ mg prod./L $_{nom}$		Gries (2003) M-227290-01-1 KCP 10.2.1/05
Semi-static test system; ISO proposal: water quality - duckweed growth inhibition test (30/03/2000); OECD Guideline proposal: Lemna sp. growth inhibition test (15/12/1999)	Aquatic plant *Lemna minor*	Propamocarb-HCl SL 722	7 d, ErC50 > 919 mg L [2]	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Bogers (2001). *A 7-day aquatic plant toxicity test using Lemna minor with Proplant (propa-mocarb HCL 722 g/l).* M-310632-01-1 KCA 8.2.7/02

*** O**nly allowed to determine the toxicity of the formulation (which include two active substances: fluopicolide and propamocarb hydrochloride); didn´t allow to determine the toxicity of each active substance. Therefore, these studies don´t contribute to the (aquatic) acute and chronic classification of propamocarb hydrochloride.

[1] Although the report presents the endpoint based on frond number as EC_{50}, the lack of inhibition caused by the test item allows the assumption that the growth rate endpoint E_rC_{50} is also > 18 mg a.s./L

[2] The effect on growth rate of frond number was regarded the most reliable and sufficiently sensitive parameter in the evaluation of the study by the RMS (Propamocarb HCl - Volume 3: Annex B-9, Ecotoxicology, 2004)

[3] In the EFSA conclusion (2006, 78, 1-80), instead of *Pimephales promelas,* the species *Lepomis macrochirus* is mentioned by error.

Acute toxicity for representative species of aquatic crustaceans

Since propamocarb hydrochloride (PHC) is not applied directly to water, there is no requirement to perform acute toxicity studies with aquatic crustaceans.

However, studies on the acute toxicity of PHC to the Mysid shrimp *Mysidopsis bahia,* have been conducted.

Acute toxicity for representative species of aquatic gastropod molluscs

Since PHC is not applied directly to water, there is no requirement to perform acute toxicity studies with aquatic gastropod molluscs.

However, studies on the acute toxicity of PHC to the Eastern oyster, *Crassostrea virginica,* have been conducted.

No acute toxicity was observed to *Daphnia magna* or the Mysid shrimp *Mysidopsis* spp., but limited toxicity was evident with the Eastern oyster *Crassostrea virginica*, with an EC50 value of 43.9 mg of PHC/L.

11.5.1 Acute (short-term) toxicity to fish

Please consult Table 73 above additionally to the text below.
To investigate acute toxicity of propamocarb hydrochloride (PHC) to fish, a series of studies with rainbow trout (*Onchorhynchus mykiss*), bluegill sunfish (*Lepomis macrochirus*), carp (*Cyprinus carpio*) and sheepshead minnow (*Cyprinodon variegatus*) have been submitted in the context of the last Annex I inclusion. As propamocarb is rapidly degraded by microbial environmental activity to CO_2, there are no major metabolites of concern. Testing was therefore restricted to the technical grade compound.

Report:	KCA 8.2.1/02; Anonymous; 1991; M-157858-01-1
Title:	The static acute toxicity of propamocarb-HCl to the rainbow trout, Oncorhynchus mykiss
Report No.:	509 AV; A85569
Document No.:	M-157858-01-1
Guideline(s):	OECD 203; US EPA 72-1
Guideline deviation(s):	not specified
GLP/GEP:	**No**

Objective:

The objective of this study was to assess the acute toxicity of propamocarb-HCl to the rainbow trout (*Oncorhynchus mykiss*) expressed as 96 h-LC_{50} for mortality, under static conditions.

Material and Methods:
Test Substance: Propamocarb-HCl technical; IUPAC name: Propyl 3-(dimethylamino)propyl-carbamate hydrochloride; Batch: 407720; purity: 719.6 g/L aqueous solution technical grade material.
The acute toxicity of propamocarb-HCl to the Rainbow trout (*Oncorhynchus mykiss*) was assessed in a static system.
Thirty juvenile rainbow trout (42 days old, mean weight 0.604 grams and mean length 3.4 cm) from Aquatic Research Organisms, Hampton, New Hampshire, were exposed to a nominal concentration of 100 mg/L Propamocarb-HCl in soft blended water for 96 hours, and results compared to a control treatment, in which fish were kept in soft blended water (well and DI Blend) only. Both treatment groups were tested in triplicate.
A 2.1 mL aliquot of propamocarb-HCl aqueous solution (ie. Previcur-N) was added to 15 L of dilution water in each of three 19 L tanks to achieve the 100 mg/L nominal test concentration in each tank. The solutions were stirred briefly. A control (dilution water) was also prepared in triplicate.
Samples of the test solutions were analyzed for propamocarb-HCl at test initiation (day 0) and termination (day 4).
The test fish were observed after approximately 24, 48, 72 and 96 h test duration for death and symptoms of abnormal appearance and behavior.

Findings:

Analytical findings:

The mean analyzed concentration over time for the test period was 99 mg/L propamocarb-HCl. There were no mortalities, or signs of abnormal behavior or appearance, in treated or control tanks during the test period, and all fish appeared normal. Therefore, the 96 h LC_{50} of Propamocarb-HCl to Rainbow trout could not be determined, but was greater than 99 mg/L. The mean temperature for the study, calculated as a mean of the minute values, was 11.6° C (SD = 0.12 ° C). The range was 11.4° - 12.7°C. Dissolved oxygen was > 90 % saturated at test initiation and > 87 % saturated at test termination.

Validity criteria :

Validity criteria (according to OECD 203, 2009)	Obtained in this study
Mortality in the controls does not exceed 10% (or one fish if less than 10 are used) at the end of the test	0%
Dissolved oxygen concentration in the control and test vessels is ≥ 60% throughout the test	≥ 87 %
Measured concentration of the test substance is maintained ± 20% of the nominal concentration, or results are based on mean measured concentrations	95% -101%

Conclusion:
In a static acute toxicity test the 96 h LC_{50} of propamocarb hydrochloride (PHC) to Rainbow trout was greater than 99 mg/L; no LC_{50} could be determined. PHC is, therefore, non-toxic to rainbow trout.

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments and for the active substance propamocarb hydrochloride classification purposes. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCA 8.2.1/03; Anonymous; 1996; M-310778-01-1
Title:	96-hour acute limit study in rainbow trout with Proplant (semi-static)
Report No.:	161303
Document No.:	M-310778-01-1
Guideline(s):	Directive 92/69/EEC (part C.1; 1992); OECD Guideline No. 203 (1992)
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

Objective:
The purpose of the study was to evaluate the test substance for its ability to generate acute toxic effects in Rainbow trout (*Oncorhynchus mykiss*) during an exposure period of 96 hours and, if possible, to determine the LC_{50} at all observation times.

Materials and methods:
Test Substance: Propamocarb; IUPAC name: propyl 3-(dimethylamino)propylcarbamate hydrochloride; Batch: T5665; purity: 736.1 ± 2.0 g/L.
Twenty-three Rainbow trouts (*Oncorhynchus mykiss*, Walbaum 1988) from Trout Hatchery Blitterswijk, the Netherlands (mean length: 6.02 ± 0.81 cm, mean weight: 3.93 ± 1.24 g) were exposed to the test substance over a 96 hour exposure period. The test was performed as a limit test at 140 mg Proplant/L = approx. 100 mg Propamocarb hydrochloride/L, and a control at 0 mg test item/L. Each treatment group and control group had 7 fish with a loading of 0.92 g fish/L, i.e. 7 fish per 30 L of medium. (medium: tap water).
A reference test served to control sensitivity of the test: 5 fish per dose group were exposed to 0.00, 0.10, 0.18, 0.32, 0.56 and 1.0 mg pentachlorophenol per L tap water (PCP, Sigma, Batch: 103H-3488).
Test solutions with test item were daily renewed. Photoperiod: 16 hours per day; aeration: continuous; no feeding (stopped 24 hours prior to test start).
Sampling and analysis of test item concentration: at start (t = 0 h), at t = 24 h (1st renewal) 24-h-old and fresh test solution was sampled. Analysis of these samples showed that the propamocarb-HCl concentrations measured corresponded with ca.100 mg/L and remained constant during the 24-hour period of renewal.
Measurements and recordings/observations: mortality/other sublethal effects at 2.5, 24, 48, 72 and 96 hours; dissolved oxygen and pH daily in all vessels, temperature daily in one control vessel.
The test design included daily renewal of the test solutions. Samples for analysis were taken at the start and after 24 hours at the first renewal.

Findings:
<u>Analytical findings:</u>
The test can be rated acceptable since all test conditions remained within the stipulated ranges and the chemical analysis of the test item showed that the actual concentrations had been maintained at >80% of initial/nominal values, as well as no mortalities occurred in the control. Furthermore, the reference test proved the sensitivity of the system by resulting in mortalities of 20 and 100% at 0.56 and 1.0 mg pentachlorophenol per L medium. This result was calculated to a 96h-LC_{50}, pcp of 0.63 mg/L which showed the batch of trout used to be slightly less sensitive than the ones tested before (historical range of 96h-LC_{50}, pcp since 1986: 0.10 to 0.56 mg/L).
<u>Biological findings:</u>
The mortality data of the test with Proplant (propamocarb hydrochloride) are presented in the table below. Other effects (sublethal) were not observed: The fish did not show any visible effects on appearance or swimming behaviour.

Incidence and total mortality of rainbow trout exposed to propamocarb-HCl

Dose group (mg/L)	Initial No. of fish	Cumulative mortality					Total Mortality (%)
		2.5 h	24 h	48 h	72 h	96 h	
0.00	7	0	0	0	0	0	0
140 (100)	7	0	0	0	0	0	0

Validity criteria:

Validity criteria (according to OECD 203, 2009)	Obtained in this study
Mortality in the controls does not exceed 10% (or one fish if less than 10 are used) at the end of the test	0%
Dissolved oxygen concentration in the control and test vessels is ≥ 60% throughout the test	≥ 94%
Measured concentration of the test substance is maintained ± 20% of the nominal concentration, or results are based on mean measured concentrations	≥80 %

Conclusion:
The LC_{50} of propamocarb hydrochloride (Proplant) for rainbow trout in a 96h-exposure test is shown to be >100 mg a.s./L (equivalent to 140 mg Proplant/L).

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments and for the active substance propamocarb hydrochloride classification purposes.
Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCA 8.2.1/01; Anonymous; 1991; M-157853-01-1
Title:	The static acute toxicity of propamocarb-HCl to the bluegill sunfish, *Lepomis macrochirus*
Report No.:	510 AV; A85566
Document No.:	M-157853-01-1
Guideline(s):	OECD 203; US EPA 72-1
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

Objective:
The objective of this study was to investigate if a nominal concentration of 100 mg/L propamocarb HCl is toxic to *Lepomis macrochirus*.

Materials and methods:
Test Substance: Propamocarb HCl technical; IUPAC name: Propyl 3-(dimethylamino)propyl-carbamate hydrochloride; Batch: 407720; purity: 719.6 g/L aqueous solution technical grade material.
The acute toxicity of propamocarb HCl to the Bluegill sunfish (*Lepomis macrochirus* Rafinesque) was assessed in a static system. Fish were purchased from Fattig Fish Hatchery, Brady, NE and were approximately 3 months old at the time of testing. Fish were acclimated to test dilution water for at least 48 hours prior to initiation of testing. Ten juvenile fish/per replicate (average weight = 1.01 -0.32g; average length = 3.3 ± 0.32 cm; loading = 0.22 g/L) were exposed to 0 (water only) and 100 mg/L Propamocarb HCl in soft blended water for 96 hours. Juvenile fish were exposed to a nominal concentration of 100 mg/L propamocarb HCl in soft blended dilution water for 96 hours, and results compared to a control treatment, in which fish were kept in soft blended water only. Both treatment groups were tested in triplicate.
A 6.25 mL aliquot of propamocarb HCl aqueous solution was added to 45 L dilution water in each of 3 68 L tanks to achieve the 100 mg Propamocarb HCl/L nominal test concentration in each tank. Samples

of the test solutions were analysed for Propamocarb HCl at test initiation (day 0) and termination (96 hours).
Test temperature, dissolved oxygen, pH and conductance were measured on day 0, day 2 and day 4 in both the control and treatment group. A 16:8 light:dark photoperiod was maintained throughout the test period. Samples of the test solutions were analysed for PHC at test initiation (day 0) and termination (day 4).
Test was performed as a limit test. Fish were not fed and test solutions were not aerated during study.
Dilution water used in this study was a blend of well water and deionized water. Its hardness was determined on the day of test initiation. The pH of all tanks during the test ranged from 6.6 to 7.2. Samples of all replicates were taken at test initiation and at test termination (after 96 hours). Samples were analysed for PHC by gas chromatography.
Fish were observed for mortality or signs of abnormal behaviour every 24 hours.

Findings:
Analytical findings:
The mean analyzed concentration over time for the test period was 92 mg/L propamocarb hydrochloride.
The mean temperature of the study was 22.2°C ± 0.66°C. Dissolved oxygen was ≥99% saturation at the beginning of the test and ≥78% at test termination.
Determined hardness on day of test initiation was 46 mg/L $CaCO_3$. Conductance during the test was 160 µMhos for the control and 200 µMhos for the treatment.
Biological findings:
There were no mortalities, or signs of abnormal behaviour or appearance, in treated or control tanks during the test period, and all fish appeared normal. Therefore, the 96 hour LC_{50} of propamocarb HCl to Bluegill sunfish could not be determined, but was greater than 92 mg/L.

Validity criteria :

Validity criteria (according to OECD 203, 2009)	Obtained in this study
Mortality in the controls does not exceed 10% (or one fish if less than 10 are used) at the end of the test	0%
Dissolved oxygen concentration in the control and test vessels is ≥ 60% throughout the test	≥ 78%
Measured concentration of the test substance is maintained ± 20% of the nominal concentration, or results are based on mean measured concentrations	91% -95%

Conclusion:
In a static acute toxicity test, the 96 hour LC_{50} of propamocarb hydrochloride to Bluegill sunfish was greater than 92 mg/L. However, the 96 hours LC_{50} could not be determined.

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments and for the active substance propamocarb hydrochloride classification purposes. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCA 8.2.1/04; Anonymous; M-310734-01-1
Title:	96-hour acute toxicity study in bluegill sunfish with Proplant (propamocarb HCL 722 g/l) (static)
Report No.:	329748
Document No.:	M-310734-01-1
Guideline(s):	EPA OPPTS 850.1075; EPA 712-C.96-118 (1996); Directive 92/69/EEC (part C.1; 1992); OECD Guideline No. 203 (1992)
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

Objective:

The aim of this study was to assess the acute toxicity of propamocarb HCl to Bluegill sunfish (*Lepomis macrochirus*), expressed as 96h-LC_{50} for mortality, in a static system.

Material and Methods:
Test material: Propamocarb; IUPAC name: propyl 3-(dimethylamino)propylcarbamate hydrochloride; Batch: 31491; purity: 750.5 g/L.
Bluegill sunfish (*Lepomis macrochirus*) from Osage catfisheries, 1170 Nichols road, Osage Beach, MNO 65065, USA; mean length: 2.7 ± 0.1 cm; mean weight: 0.47 ± 0.05 g; total no. of fish used: 123) were exposed to the test substance for a period of 96 hours.
Test design: due to several reasons (justified in the report), a series of tests had to be performed:

- Range: 0.00, 0.145, 1.45, 14.5 and 145 mg Proplant/L corresponding to 0.00, 0.1, 1.0, 10 and 100 mg Propamocarb HCl/L; a dosage group consisted of 3 to 7 fish.
- Limit-test: 0.00 and 100 mg Propamocarb HCl/L, a dosage group consisted of 7 fish.
-Pre-test at 1000 mg Propamocarb hydrochloride/L to comply with EPA OPPTS Guideline (= maximum specified test conc.) with 2 fish (= loading: 0.4 g fish per L).
- Final LC_{50}-test at 0.00, 145, 261, 464, 812 and 1450 mg Proplant/L dosage corresponding to 0.00, 100, 180, 320, 560 and 1000 mg Propamocarb hydrochloride/L; a concentration group consisted of 7 fish in replicate vessels (i.e., a total of 14 fish) with an average loading of 0.32 g fish/L, i.e. 7 fish per 5 L of medium (medium: tap water).
- Reference test: served to control sensitivity of the test: 5 fish per concentration and blank control) were exposed to 0.00, 0.10, 0.15, 0.22, 0.32 and 0.46 mg pentachlorophenol per L tap water (PCP, Sigma, Batch: 103H-3488).

Test solutions with test item were not renewed (static design). Photoperiod: 16 hours per day; no aeration. Feeding: No feeding (stopped 48 hours prior to test start).
Sampling and analysis of test item concentration: at start (t=0 h), at t=48 h and at termination (t=96h).
Measurements and recordings/observations: mortality/other sublethal effects at 6, 24, 48, 72 and 96 hours; dissolved oxygen and pH daily in all vessels, temperature: daily in all vessels, continuous in one control vessel. Data handling: LC_{50}-values at diverse exposure times were determined statistically.

Findings:
Analytical findings:
The test can be rated acceptable since all test conditions remained within the stipulated ranges and the chemical analysis of the test item showed that the actual concentrations had been maintained at >80% of initial/nominal values.
Physical-chemical values remained in acceptable limits: pH ranged from 8.0 (Day 0) to 8.3 (Day 4), DO from 9.6 (Day 0) to 6.4 mg/L (day 4), temperature varied from 21.5 to 22.1°C.

Biological findings:
No mortality occurred in the control. Furthermore, the reference test proved the sensitivity of the system by resulting in mortalities of 0% and 80% at (or below) 0.32 and 0.46 mg pentachlorophenol per L, respectively. This result was calculated to a 96h-$LC_{50,\ pcp}$ of 0.41 mg/L which showed the batch of bluegill sunfish used to be relatively insensitive (historical range of 96h-$LC_{50,\ pcp}$ since 1988 for carp: 0.10 to 0.46 mg/L). Combined limit/range finding test, as well as the limit test (100 mg/L a.s.) did not result in mortalities while the additional pre-test (to satisfy the US-EPA requirements) did yield 100% mortality.
The mortality data of the combined test with Proplant (propamocarb hydrochloride) are presented in the table below:

Incidence and total mortality of Bluegill sunfish exposed to propamocarb hydrochloride

Concentration a.s. (mg/L)	Initial No. of Fish	Cumulative mortality					Total mortality (%)
		6 h	24 h	48 h	72 h	96 h	
0.00	14	0	0	0	0	0	0
100*	14	0	0	0	0	0	0
180*	14	0	0	0	0	0	0
320*	14	0	0	0	3	14	100
560*	14	0	0	12	14	14	100
1000*	14	0	11	14	14	14	100

* concentration of propamocarb hydrochloride

The sublethal effects and observations recorded included discolouration, snapping at the surface, hypoactive swimming at the 3 highest concentrations with onset of effects between 0 and 6 hours. At concentrations 0.00, 100 and 180 mg/L, no abnormalities were seen in any fish for the total exposure period of 96 hours, while at 320 mg/L complete absence of effects was only recorded for the first 24 hours of exposure.

Validity criteria :

Validity criteria (according to OECD 203, 2009)	Obtained in this study
Mortality in the controls does not exceed 10% (or one fish if less than 10 are used) at the end of the test	0%
Dissolved oxygen concentration in the control and test vessels is ≥ 60% throughout the test	≥ 75%
Measured concentration of the test substance is maintained ± 20% of the nominal concentration, or results are based on mean measured concentrations	> 80%

Conclusion:
Under the conditions of this study, the test item was shown to be slightly toxic to Bluegill sunfish, with a 96 h LC_{50} of 240 mg Propamocarb/L.

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments and for the active substance propamocarb hydrochloride classification purposes. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCA 8.2.1/05; Anonymous; 2000; M-310773-01-1
Title:	96-hour acute toxicity study in carp with Proplant
Report No.:	308622
Document No.:	M-310773-01-1
Guideline(s):	Directive 92/69/EEC (part C.1; 1992); OECD Guideline No. 203 (1992)
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

Objective:
The aim of this study was to assess the acute toxicity of propamocarb HCl to Carp (C*yprinus carpio),* expressed as 96h-LC_{50} for mortality, in a static system.

Material and Methods:
Test material: propamocarb; IUPAC name: propyl (dimethylamino) propylcarbamate hydrochloride; Batch: 31491; purity: 750.5 g/L.
Carp (C*yprinus carpio*, Linnaeus 1758) sourced from Zodiac, proefacc "De Haar Vissen", Wageningen, the Netherlands; mean length: 3.0 ± 0.2 cm, mean weight: 0.87 ± 0.23 g; total no. of fish used: 23 were exposed to the test substance for a period of 96 hours.
The test was performed as combined limit and range-finding test:
- Range: 0.00, 0.133, 1.33, 13.3 and 133 mg Proplant/L corresponding to 0.00, 0.1, 1.0, 10 and 100 mg Propamocarb HCl/L; a dosage group consisted of 3 fish with a loading of 0.52 g fish/Litre, i.e. 3 fish per 5 L of medium. (medium: ISO).
- Limit-test at 133 mg Proplant/L = approx. 100 mg Propamocarb HCl/L, and a control at 0 mg test item/L. A dosage group consisted of 7 fish with a loading of 0.61 g fish/Litre, i.e. 7 fish per 10 L of medium (ISO).
Reference test: served to control sensitivity of the test: 5 fish per dose group (7 in the blank control) were exposed to 0.00, 0.06, 0.10, 0.15, 0.22 and 0.32 mg pentachlorophenol per L tap water (PCP, Sigma, Batch: 103H-3488).

Test solutions with test item were not renewed (static design). Photoperiod: 16 hours per day; aeration: from 24 hours onwards until test termination. Feeding: No feeding (stopped 48 hours prior to test start). Sampling and analysis of test item concentration: at start (t=0 h), at t=24 h and at termination (t=96h). Measurements and recordings/observations: mortality/other sublethal effects at 2.5, 24, 48, 72 and 96 hours; dissolved oxygen and pH daily in all vessels, temperature daily in one control vessel.

Findings:

Analytical findings:
The test can be rated acceptable since all test conditions remained within the stipulated ranges and the chemical analysis of the test item showed that the actual concentrations had been maintained at >80% of initial/nominal values, as well as no mortality occurred in the control.
Physical-chemical values remained in acceptable limits: pH ranged from 7.9 (Day 0) to 8.0 (Day 4) and DO from 9.2 (Day 0) to 9.6 mg/L (day 4). Aeration was introduced, as the oxygen concentration tended to decrease below 6 mg/l. Temperature varied from 20.5 to 21.6°C.
Biological findings:
The reference test proved the sensitivity of the system by resulting in mortalities of 60, 100 and 100% at 0.15, 0.22 and 0.32 mg pentachlorophenol per L medium. This result was calculated to a 96h-$LC_{50, pcp}$ of 0.14 mg/L which showed the batch of carp used to be relatively sensitive (historical range of 96h $LC_{50, pcp}$ since 1988: 0.10 to 0.46 mg/L).
The mortality data of the combined test with Proplant (propamocarb hydrochloride) are presented in the table below. Other effects (sublethal) were not observed.

Incidence and total mortality of Carp exposed to propamocarb hydrochloride

Concentration a.s. (mg/L)	Initial No. of fish	Cumulative mortality					Total mortality (%)
		2.5 h	24 h	48 h	72 h	96 h	
0.00	7	0	0	0	0	0	0
0.133/0.1 *	3	0	0	0	0	0	0
1.33/1.0*	3	0	0	0	0	0	0
13.3/10.0*	3	0	0	0	0	0	0
133/100*	7	0	0	0	0	0	0

* concentration of the formulation Proplant / concentration of propamocarb hydrochloride

Validity criteria :

Validity criteria (according to OECD 203, 2009)	**Obtained in this study**
Mortality in the controls does not exceed 10% (or one fish if less than 10 are used) at the end of the test	0%
Dissolved oxygen concentration in the control and test vessels is ≥ 60% throughout the test	≥ 75%
Measured concentration of the test substance is maintained ± 20% of the nominal concentration, or results are based on mean measured concentrations	86% -92%

Conclusion:
The LC_{50} of propamocarb hydrochloride for carp in a 96h-exposure test is shown to be >100 mg a.s./L (equivalent to > 133 mg Proplant/L).

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments and for the active substance PHC propamocarb hydrochloride classification purposes. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCA 8.2.1/06; Anonymous; 2001; M-310736-01-1
Title:	Proplant (propamocarb HCL 722 g/l SL): Acute toxicity to Sheepshead minnow (*Cyprinodon variegatus*) under static conditions
Report No.:	13763.6104
Document No.:	M-310736-01-1
Guideline(s):	US EPA FIFRA 72-3
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

Objective:
The aim of this study was to assess the acute toxicity of sheepshead minnow (*Cyprinodon variegatus*) under static conditions expressed as 96h-LC_{50} for mortality, in a static system.

Material and Methods:
Test substance: propamocarb; IUPAC name: propyl 3-(dimethylamino)propylcarbamate hydrochloride; Batch: 31491; purity: 750.5 g/L (formulation: Proplant).
Test animal: Sheepshead minnow (*Cyprinodon variegatus*, SLI Lot no. 01A46) sourced at Aquatic BioSystems, Ft. Collins, Colorado; mean length: 2.5 cm (range 1.9-3.6 cm), mean wet weight: 0.48 g (range 0.19-1.1 g); mean of 30 fish.
The test was performed at nominal doses of: 0.00, 7.5, 15, 30, 60 and 120 mg a.s./L corresponding to 0.00, 6.8, 11, 29, 63 and 110 mg propamocarb HCl/L actually measured; a dosage group consisted of 10 fish with a loading of 0.32 g fish/L, i.e. 10 fish per 15 L of test solution (medium: filtered natural sea water).
Test solutions with test item were not renewed (static design); analytical dose verification at 0 and 96 hours (mean conc. stated above). Photoperiod: 16 hours per day; temperature: at 23°C.
Feeding: no feeding (stopped 24 hours prior to test start).
Sampling and analysis of test item concentration: at start (t=0 h), and at termination (t=96h).
Measurements and recordings/observations: mortality/other sublethal effects, physical appearance of test solution: at 0, 24, 48, 72 and 96 hours; dissolved oxygen, salinity and pH daily in all vessels, temperature continuously in one control vessel.

Findings:
Analytical findings:
The test can be rated acceptable since all test conditions remained within the stipulated ranges and the chemical analysis of the test item showed that the actual concentrations had been maintained between 74 to 110% of nominal values, as well as no mortality occurred in the control, nor in all fish in a 48-hour period before test initiation.
Biological findings:
The mean measured concentrations tested, the corresponding cumulative percent mortality and observations made during the definitive exposure are presented in the Table below. Following test termination (96 hours of exposure), no mortality or adverse effects were observed among the fish exposed to each treatment level tested or the control. Other effects (sublethal) were not observed.

Incidence and total mortality of Sheepshead minnow exposed to propamocarb hydrochloride

Dose mean measured (mg/L)	Initial No. of fish	Cumulative mortality					Total mortality (%)
		0 h	24 h	48 h	72 h	96 h	
0.00	10	0	0	0	0	0	0
6.8*	10	0	0	0	0	0	0
11*	10	0	0	0	0	0	0
29*	10	0	0	0	0	0	0
63*	10	0	0	0	0	0	0
110*	10	0	0	0	0	0	0

* concentration of propamocarb hydrochloride

Validity criteria :

Validity criteria (according to OECD 203, 2009)	Obtained in this study

Mortality in the controls does not exceed 10% (or one fish if less than 10 are used) at the end of the test	0%
Dissolved oxygen concentration in the control and test vessels is ≥ 60% throughout the test	≥ 65%
Measured concentration of the test substance is maintained ± 20% of the nominal concentration, or results are based on mean measured concentrations	≥ 74%

Conclusion:
The LC_{50} of propamocarb hydrochloride for sheepshead minnow under the conditions of this study is shown to be > 110 mg/L. The NOEC within this study was determined to be 110 mg propamocarb hydrochloride/L seawater.

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments and for the active substance propamocarb hydrochloride classification purposes Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCP 10.2.1/01; Gries, T.; 2003; M-225109-01-1
Title:	AE B066752 04 SC61 A1: Acute toxicity test with rainbow trout (Oncorhynchus mykiss) under static conditions
Report No.:	C038493
Document No.:	M-225109-01-1
Guideline(s):	OECD: 203, (1992)
Guideline deviation(s):	--
GLP/GEP:	**Yes**

Objective:
The purpose of this study was to determine the acute toxicity (LC_{50}) of AE B066752 04 SC61 A1 on rainbow trout (*Oncorhynchus mykiss*) under static conditions. The LC_{50} is defined as the calculated concentration of the test item in dilution water, which causes mortality of 50% in the exposed test population over a given period of time.

Material and Methods:
Test item: Infinito SC Fungicide (AE B06675204 SC61 A1, FLC + PCH SC 687.5), Batch No.: OP220159, light beige opaque liquid, density 1.129 g/cm^3, containing 64.7 g fluopicolide/L and 634 g propamocarb-HCl).
The toxicity of Infinito SC Fungicide to the rainbow trout, *Oncorhynchus mykiss*, was determined under static conditions over an exposure period of 96 hours. Juvenile trout obtained from Fischzucht Peter Hohler-Gasser, Zeiningen, Switzerland, had a weight ranging from 0.77 to 2.12 g and a length ranging from 4.4 to 6.0 cm.
A total of 60 fish (10 fish per treatment, 5 concentrations + 1 negative control) were exposed to Infinito SC Fungicide nominal test concentrations of 0 (dilution water control), 0.625, 1.25, 2.50, 5.0 and 10 mg/L. Test concentrations were not renewed and analytical verifications were performed at 0 and 96 hours for concentrations of fluopicolide. Observations regarding mortality and any adverse sublethal effects resulting from the exposure to AE B066752 04 SC61 A1 were made daily.
No solvent was used and fish were not fed during the test.
Dates of experimental work: June 13, 2003 to June 17, 2003

Findings:

Analytical findings:
Test conditions during the exposure period were:
Dissolved oxygen: 8.95 – 11.09 mg O_2/L (91 to 113% of air saturation value)

pH: 7.32 – 7.68 pH units
Temperature: 13.9 °C – 14.6 °C
Conductivity: 380-400 µS/cm
Hardness: 152-156 mg $CaCO_3$/L
Fluopicolide was the only active substance analytically measured. Since fluopicolide is the risk driver for aquatic organisms in the formulation, analytical measurements of propamocarb are not considered necessary.
The recoveries of fluopicolide concentrations (compared to nominal values) from the freshly prepared and aged test solutions ranged from 91.8 to 109%, except for the 0.625 mg product/L treatment level where 68.2% recovery was found at hour 0. The 96 hour analysis verified correct dosage (92.2%). There was no fluopicolide residue found in the dilution water or control samples greater that the limit of quantification.

Biological findings:
Given that the toxicity of the product cannot be attributed to any one of the active ingredients but to the product formulation as a whole, LC_{50} values and biological data are based on nominal concentrations.
During the 96 hour observation period, neither mortality nor sublethal effects were observed among trout exposed to the test solutions with 1.25 and 2.50 mg product/L. After 72 and 96 hours of exposure, 10% mortality was observed at the treatment levels of 0.625 and 5.0 mg product/L. After 24, 48, 72 and 96 hours of exposure, 50, 80, 100 and 100% mortality was observed in the test solution with 10 mg Infinito SC Fungicide/L, respectively.

Cumulative mortality:

	Definitive test - Infinito SC Fungicide				
Nominal Concentrations (mg/L)	Cumulative mortality (%)				
	0-6-hour	24-hour	48-hour	72-hour	96-hour
(Control) < LOQ	0	0	0	0	0
0.625	0	0	0	10	10
1.25	0	0	0	0	0
2.50	0	0	0	0	0
5.0	0	0	0	10	10
10.0	0	50	80	100	100

LOQ = Limit of Quantification (0.006 mg fluopicolide/L)

Validity criteria (according to OECD 203, 2009)	Obtained in this study
Mortality in the controls does not exceed 10% (or one fish if less than 10 are used) at the end of the test	0%
Dissolved oxygen concentration in the control and test vessels is ≥ 60% throughout the test	≥ 91 %
Measured concentration of the test substance is maintained ± 20% of the nominal concentration, or results are based on mean measured concentrations	91.8 to 109%*

*except one value (68.2% at 0.625 mg test item/L, hour 0). Analysis of the same test solution after 96 hours of exposure indicates the correct dosage of this test solution (92.2 % recovery).

Conclusion:
Under the conditions of the test and based on nominal concentrations, the acute toxicity of Infinito SC fungicide to the rainbow trout (*Oncorhynchus mykiss*) in a static test system is defined as follows:

96-hour LC_{50} = 6.6 mg/L
NOEC (96 hour) = 2.5 mg/L

RMS' conclusion: This study is regarded as scientifically valid and valid to be used for the toxicity assessments of the formulation but not of the active substance propamocarb hydrochloride. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCP 10.2.1/02; Gries, T.; 2003; M-227280-01-1
Title:	AE B066752 04 SC61 A1: Acute toxicity test with common carp (*Cyprinus carpio*) under static conditions
Report No.:	C039853
Document No.:	M-227280-01-1
Guideline(s):	OECD: 203 (1992)
Guideline deviation(s):	--
GLP/GEP:	Yes

Objective:

The purpose of this study was to determine the acute toxicity (LC_{50}) of AE B066752 04 SC61 A1 on carp (*Cyprinus carpio*) expressed as 96 h-LC_{50} for mortality, under static conditions.

Material and Methods:
Test item: AE B06675204 SC61 A1 (FLC + PCH SC 687.5), Batch No.: OP220159, light beige opaque liquid, density 1.129 g/cm^3, containing 64.7 g Fluopicolide/L and 634 g Propamocarb-HCl.
The toxicity of AE B06675204 SC61 A1 to the common carp, (*Cyprinus carpio*), was determined under static conditions over an exposure period of 96 hours. Juvenile carps obtained from Axel Dieterich Teichbau, Konstanz, Germany, had a weight ranging from 0.23 to 0.71 g and a length ranging from 3.0 to 4.0 cm.
A total of 60 fish (10 fish per treatment, 5 concentrations + 1 negative control) were exposed to AEB066752 04 SC61 A1 nominal test concentrations of 0 (dilution water control), 6.25, 12.5, 25.0, 50.0 and 100 mg/L.
Test concentrations were not renewed and analytical verifications were performed at 0 and 96 hours for concentrations of AE C638206 (code for the a.s. fluopicolide). Observations regarding mortality and any adverse sublethal effects resulting from the exposure to AE B066752 04 SC61 A1 were made daily.
No solvent was used and fish were not fed during the test.
Dates of experimental work: August 18, 2003 to August 22, 2003

Analytical findings:

Test conditions during the exposure period were:

Dissolved oxygen:	6.57 – 8.52 mg O_2/L (79 to 103% of air saturation value)
pH:	7.17 – 7.71 pH units
Temperature:	21.8 – 23.6 °C
Conductivity:	480-500 µS/cm
Hardness:	160-164 mg $CaCO_3$/L

Fluopicolide was the only active substance analytically measured. However, since fluopicolide is the risk driver for aquatic organisms in the formulation (there is no indication of propamocarb being very toxic to aquatic organisms), analytical measurements of propamocarb are not considered necessary to ensure the stability of this active substance as well (a new study is not deemed necessary).
The recoveries of fluopicolide concentrations (compared to nominal values) from the freshly prepared solutions ranged from 94.3 to 101%, indicating correct dosage. The 96 hour analysis indicated stability of active ingredient concentrations at low test levels. The low recoveries at 50 and 100 mg product/L were most likely due to precipitation since precipitated test item was found on the bottom of the test vessel after 48 hours of exposure. There was no fluopicolide residue found in the dilution water or control samples greater that the limit of quantification. Given that the toxicity of the product cannot be

attributed to any one of the active ingredients but to the product formulation as a whole, LC_{50} values and biological data are based on nominal concentrations.

Biological findings:
During the 96 hour observation period, sublethal effects (i.e. partial and complete loss of equilibrium) and/or mortality were observed in the test solutions with 12.5, 25, 50 and 100 mg product/L.

	Definitive test - AE B066752 04 SC61 A1				
Nominal	Cumulative mortality (%)				
Concentrations	0-6-hour	24-hour	48-hour	72-hour	96-hour
(mg/L)					
(Control) < LOQ	0	0	0	0	10
6.25	0	0	0	0	0
12.5	0	0	0	0	0
25	0	10	60	90	100
50	0	20	100	100	100
100	0	10	100	100	100

LOQ = Limit of Quantification (0.0438 mg AEC638206/L)

Validity criteria (according to OECD 203, 2009)	Obtained in this study
Mortality in the controls does not exceed 10% (or one fish if less than 10 are used) at the end of the test	10%
Dissolved oxygen concentration in the control and test vessels is ≥ 60% throughout the test	≥ 79 %
Measured concentration of the test substance is maintained ± 20% of the nominal concentration, or results are based on mean measured concentrations	0 hours: 94.3% -101 96 hours: 68.9 % - 99.8%*

* The lower recoveries at 50 and 100 mg test item/L were most likely due to precipitation since precipitated test item was found on the bottom of the test vessel after 48 hours of exposure. Since all concentrations relevant for the interpretation of the biological data after 96 hours of exposure were within ± 20 % of the mean measured concentration, the biological data were based on nominal concentrations.

Conclusion:
Under the conditions of the test and based on nominal concentrations, the acute toxicity of AE B066752 04 SC61 A1 to the common carp, (*Cyprinus carpio*), in a static test system is defined as follows: 96-hour LC_{50} = 18 mg/Land NOEC (96 hour) = 6.25 mg/L

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments of the formulation but not of the active substance propamocarb hydrochloride. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Acute toxicity of metabolites to fish

For the two metabolites N-desmethyl-Propamocarb and propamocarb-N-oxide acute tests with the aquatic invertebrate *Daphnia magna* and growth inhibition tests with the green algae *Pseudokirchneriella subcapitata* were performed.
For animal welfare reasons and due to the observed absence of toxicity of the metabolites and the low toxicity of the parent for these two groups of aquatic organisms, it was decided not to conduct any vertebrate tests with fishes since is unlikely that this group is significantly more sensitive to the metabolites.

11.5.1.1 Acute (short-term) toxicity to aquatic invertebrates

Please, consult Table 73 above additionally to the text below.
Two studies assessing acute (short-term) toxicity of propamocarb hydrochloride (M-157891-02-1) as well as acute toxicity of the formulated product Proplant (M-310720-01-1) to aquatic invertebrates species *Daphnia magna* have been submitted.
Additionally, two studies were performed to know the toxicity of the two PHC metabolites and it was observed absence of acute toxicity of the metabolites N-desmethyl-propamocarb and propamocarb-N-oxide to *Daphnia magna.*
According to Regulation (EC) No. 1107/2009, testing of marine or estuarine organisms is not necessary. However, some studies had been conducted in the past to cover US EPA requirements. Since these studies had been submitted in 2002 and included by the Competent Authorities in the evaluation for the Annex I inclusion of Propamocarb, the results are presented here.

Report:	KCA 8.2.4.1/01; Bruns, E.; 2009; M-157891-02-1
Title:	The acute toxicity of propamocarb-HCl to *Daphnia magna* in a static system
Report No.:	512AV
Document No.:	M-157891-02-1
Guideline(s):	Guidleine 72-2
Guideline deviation(s):	None
GLP/GEP:	**Yes**

Objective:
The aim of the study was to assess the 48 h-acute toxicity of propamocarb-HCl to the daphnid, *Daphnia magna,* expressed as EC_{50} for immobilization, under static conditions.

Material and Methods:
Test item: propamocarb HCl; propyl 3-(dimethylamino)propylcarbamate hydrochloride; Batch: 407720; purity: 719.6 g/L aqueous solution.
Daphnia magna neonates (< 24 h old) were obtained from an in-house culture at NOR-AM Research Center, Pikeville, NC, the parental stock was purchased from Aquatic Research Organisms, Hampton, NH. Daphnids were exposed to a nominal concentration of 100 mg/L of Propamocarb HCl in hard synthetic fresh water for 48 h in a static system at 20 ± 1°C. A control treatment, water only, was also tested. For each treatment triplicate vessels were prepared, with ten daphnids allocated to each vessel (30 daphnids per treatment). The *Daphnia magna* neonates Chamber dimensions were ~6.3 cm diameter x =9.0 cm high with a test solution depth of =6.2 cm. All test chambers were covered with glass sheets to prevent evaporation and entry of foreign materials. Daphnids were not fed during the study. Test solutions were not aerated during the study.
Samples of the test solutions were analyzed for propamocarb HCl at the start (day 0) and end (day 2) of the study. Test temperature over the duration of the study was 20°C (± 0.1°C). The range was 19.9 to 20.5°C. A 16:8 light:dark photoperiod was provided for the duration of the study. Dissolved oxygen, pH and specific conductance were obtained at test initiation and at test termination.

Findings:

Analytical findings:
The mean measured exposure concentration was 106 mg propamocarb HCl/L. Dissolved oxygen concentration was ≥ 99% saturation at test initiation and ≥ 96% saturation at test termination. The pH was 8.0 in the controls and 7.8 in the 100 mg/L treatment group. Specific conductance ranged from 500 – 600 µMhos. At this concentration there were no mortalities over the duration of the study. Thus, the 48 hour EC_{50} of propamocarb HCl to *Daphnia magna* neonates was greater than 106 mg/L.
Biological findings:
There were no mortalities in the treated or control chambers. There was one daphnid swimming on the surface in one of the treated and in one of the control replicates. All remaining daphnids, treated and controls, appeared normal.

Validity criteria (according to OECD 202, 2004)	Obtained in this study
Immobilization in the control and solvent control does not exceed 10%	0% in control
Dissolved oxygen concentration at the end of the test should be ≥ 3 mg/L in control and test vessels	Dissolved oxygen concentration was ≥ 96% saturation at test termination.

Conclusion:

The 48-hour EC_{50} of propamocarb hydrochloride to *Daphnia magna* neonates was greater than 106 mg/L.

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCP 10.2.1/03; Gries, T.; 2003; M-227283-01-1
Title:	AE B066752 04 SC61 A1: Acute immobilisation test with daphnids (*Daphnia magna*) under static conditions
Report No.:	C039856
Document No.:	M-227283-01-1
Guideline(s):	OECD: 202-1 (1984)
Guideline deviation(s):	--
GLP/GEP:	Yes

Objective:
The purpose of this study was to estimate the acute toxicity (EC50) of the test item to *Daphnia magna* under static test conditions.

Material and Methods:
Test item: INFINITO SC Fungicide (AE B06675204 SC61 A1, FLC + PCH SC 687.5), Batch No.: OP220159, light beige opaque liquid, density 1.129 g/cm^3, containing 64.7 g Fluopicolide/L and 634 g Propamocarb-HCl).
The toxicity of Infinito SC Fungicide to the water flea, *Daphnia magna*, was determined under static conditions over an exposure period of 48 hours. *Daphnia magna* neonates (< 24 h old) were obtained from Springborn Smithers Laboratories (Europe) AG, Horn, Switzerland.
Five daphnids per replicate, 4 replicates per concentration, were exposed to a dilution water control and nominal test concentrations of Infinito SC Fungicide equal to 6.25, 12.5, 25, 50 and 100 mg/L for 48 hours.
The test solutions were sampled and analyzed at the beginning and the end of the test period.
Immobilization and adverse reactions were recorded at 24 and 48 hours after the start of exposure.
Dates of experimental work: June 10, 2003 to June 12, 2003.

Findings:

Analytical findings:
Test conditions during the exposure period were:

Dissolved oxygen:	7.10 – 8.15 mg/L (83 – 95% of the air saturation)
pH:	6.36 – 8.16 pH units
Temperature:	19.4 – 21.2 °C

Fluopicolide was the only active substance analytically measured. Since fluopicolide is the risk driver for aquatic organisms in the formulation, analytical measurements of propamocarb-HCl are not considered necessary.

The recoveries of fluopicolide concentrations (compared to nominal values) from the freshly prepared and aged test solutions ranged from 81.6 to 120%. There was no fluopicolide residue found in the dilution water or control samples greater that the limit of quantification.

Biological findings:
Test conditions during the exposure period were:
Dissolved oxygen: 7.10 – 8.15 mg/L (83 – 95% of the air saturation)
pH: 6.36 – 8.16 pH units
Temperature: 19.4 – 21.2 °C

The recoveries of fluopicolide concentrations (compared to nominal values) from the freshly prepared and aged test solutions ranged from 81.6 to 120%. There was no Fluopicolide residue found in the dilution water or control samples greater that the limit of quantification. Given that the toxicity of the product cannot be attributed to any one of the active ingredients but to the product formulation as a whole, EC_{50} values and biological data are based on nominal concentrations.
At hour 48, no immobilization of the exposed daphnids was observed in the control and in any of the tested concentrations of 6.25, 12.5, 25, 50 and 100 mg product/L.
Lethargic daphnids (4/20) were observed only at the lowest treatment level of 6.25 mg/L. These effects were not dose response related and were not considered as relevant for the definition of the NOEC.

Cumulative immobilization data:

Nominal Concentration (mg/L)	Definitive test			
	Cumulative immobilized Daphnids (initial population = 40 per replicate*)			
	24 hours		48 hours	
	Total	%	Total	%
Control	0	0%	0	**0%**
6.25	0	0%	0	**0%**
12.5	0	0%	0	**0%**
25.0	0	0%	0	**0%**
50	0	0%	0	**0%**
100	0	0%	0	**0%**

Validity criteria (according to OECD 202, 2004)	Obtained in this study
Immobilization in the control and solvent control does not exceed 10%	0% in control
Dissolved oxygen concentration at the end of the test should be ≥ 3 mg/L in control and test vessels	7.10 – 8.15 mg/L

Conclusion:
Under the conditions of the test and based on nominal concentrations, the acute toxicity of Infinito SC Fungicide to daphnids (*Daphnia magna*) in a static test system is defined as follows:

48-hour EC_{50}	> 100 mg/L
NOEC (48 hours)	≥100 mg/L

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity of the formulation but not of the active substance propamocarb hydrochloride. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCP 10.2.1/04; Gries, T.; 2003; M-227284-01-1
Title:	Alga, growth inhibition test with *Navicula pelliculosa* AE B066752 04 SC61 A1
Report No.:	C039857
Document No.:	M-227284-01-1
Guideline(s):	OECD: 201
Guideline deviation(s):	--
GLP/GEP:	Yes

Objective:
The purpose of this study was to estimate the toxicity of the test item on the freshwater diatom *Navicula pelliculosa* (Schlosser, 1994).

Material and Methods:
Test item: INFINITO SC Fungicide (AE B06675204 SC61 A1, FLC + PCH SC 687.5), Batch No.: OP220159, light beige opaque liquid, density 1.129 g/cm^3, containing 64.7 g Fluopicolide/L and 634 g Propamocarb-HCl).
The toxicity of Infinito SC Fungicide on growth of the freshwater diatom, *Navicula pelliculosa*, was determined under static conditions over an exposure period of 72 hours.
Cultures of alga were exposed to a dilution water control and to nominal test concentrations of the test formulated product (3 replicates for the control, 3 replications of each product concentration) equal to 0.1, 0.32, 1.0, 3.2 and 10 mg/L.
Measurements of culture density were made at test initiation (0 hours), at 24 and 48 hours and at test termination (72 hours).
The test solutions were sampled and analyzed at the beginning and the end of the test period.
Dates of experimental work: November 18, 2003 to November 21, 2003.

Analytical findings:
Test conditions during the exposure period were:

pH:	7.44 – 7.50
Temperature:	21.3 – 24.0 °C
Light intensity	7700 – 8200 Lux

Fluopicolide was the only active substance analytically measured. Since fluopicolide is the risk driver for aquatic organisms in the formulation, analytical measurements of propamocarb are not considered necessary.

The analysis of the 0 hour test preparations for fluopicolide showed the measured concentrations to range between 104% and 108% of the nominal test concentrations. Analysis of the test solutions at 72 hours showed the measured concentrations of fluopicolide to range from 96.2% to 107% nominal.
There was no fluopicolide residue found in the dilution water or control samples greater than the limit of quantification.

Biological findings:
Given that the toxicity of the product cannot be attributed to any one of the active ingredients but to the product formulation as a whole, EC_{50} values and biological data are based on nominal concentrations. The mean algal cell densities over the exposure period and the inhibition of growth rate and biomass were as follows:

Mean algal densities:

Nominal Concentrations (mg/L)	Definitive test Mean cell densities (x 10^4cells/mL)		
	24 hours	48 hours	72 hours
0 (control)	2.8	13.3	89.2
0.1	2.2	13.1	87.5
0.32	1.5	10.3	54.5
1.0	1.2	3.0	7.9
3.2	0.8	2.2	0.8
10	0.7	1.1	0.3

Inhibition of growth rate and biomass:

Nominal concentration (mg/L)	Area under curve at 72 h (10^4cells x days/mL)	% inhibition	Growth rate (0 - 72 h)	% inhibition
0 (control)2	58.7	0	1.45	0
0.1	57.0	3.3	1.45	0.5
0.32	36.8*	37.3	1.30	10.9
1.0	5.7*	90.3	0.67*	54.2
3.2	0.9*	98.5	-0.11*	107.3
10	-0.6*	101	-0.37*	125.7

*Statistically significant difference compared to the control

Validity criteria (according to OECD 201, 2006)	Obtained in this study
Biomass increase in the control cultures by a factor of at least 16 within 72 hours. This corresponds to a specific growth rate of 0.92 day^{-1}	Biomass increased in the control cultures by a factor of 89.2 within 72 hours
Coefficient of variation for section by section specific growth rates (days 0-1, 1-2 and 2-3 for 72 hours) in the control cultures must not exceed 35%	32.5
Coefficient of variation of average specific growth rates during the whole test period in replicate control cultures must not exceed 7% in tests with *Pseudokirchneriella subcapitata* (10% for all other species)	2.29%

Conclusion:
Under the conditions of the test and based on nominal concentrations, the toxicity of Infinito SC fungicide to the freshwater diatom (*Navicula pelliculosa*) is defined as follows:

Exposure interval	72 hours
E_bC_{50} (mg/L)	0.40 (NOEC = 0.1)
E_rC_{50} (mg/L)	0.63 (NOEC = 0.32)

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments of the formulation but not of the active substance propamocarb hydrochloride. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al., 1997).

Report:	KCA 8.2.4.1/02; Bogers, M.; 1996; M-310720-01-1
Title:	Acute limit study in *Daphnia magna* with Proplant
Report No.:	161314
Document No.:	M-310720-01-1
Guideline(s):	Directive 92/69/EEC (part C.2; 1992); OECD Guideline No. 202 (1984)
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

Objective:

The purpose of toxicity test was to evaluate the influence of propamocarb HCl on the mobility of *Daphnia magna*.

Materials and methods:

Test Substance: propamocarb; IUPAC name: propyl 3-(dimethylamino)propylcarbamate hydrochloride; Batch: T5665; purity: 736.1 ± 2.0 g/L.

Daphnia magna, Crustacea, Cladocera (Straus, 1820) from an in-house culture (maximum age: 4 weeks) were used during this study. For the test young daphnia with age < 24 hours were selected. The test was a static limit-test over 48 hours of exposure in 100 mL glass vessels with 80 mL test solution.
Daphnia were exposed to test concentrations of 0 and 100 mg Propamocarb HCl/L (test solution: ISO medium prepared in milli-RO water). There were 10 daphnia per vessel with 80 mL in two replicates (= 20 per concentration). A photoperiod of 16 hours per day with no aeration and no feeding was maintained for the duration of the exposure period.
Sampling and analysis of test item concentration was undertaken at test initiation (t=0 h), and at test termination (t=48h) in duplicate.
Mortality (as immobility) was observed in treatment and control groups at 24 and 48 hours. pH and dissolved oxygen (DO) were measured at test initiation and test termination. Temperature was measured daily in one control vessel.

Findings:

Analytical findings:
Analytical dose verification proved the initial concentration to be maintained throughout the exposure period at >80% of nominal. The pH ranged from 8.0 to 7.8 in all replicates from t= 0 h to t= 48 h; DO varied between 8.7 (t= 0 h) and 8.3 mg O_2/L (t= 48 h), the temperature ranged from 21 to 21.2°C.
Concentration of propamocarb in test solutions was determined by gas chromatography.

Biological findings:

In the control, no daphnia became immobilized or trapped at the surface of the water. The biological observations are summarised in the table below.

Time	Concentration propamocarb HCl [mg/L]		
	Nominal	Analysed	Relative to nominal [%]
0	0	n.d.	-
0	95.5	98.9	104
48	0	n.d.	-
48	95.5	108	113

Acute immobilisation of *Daphnia magna* at 24 and 48 hours:

Concentration (mg/L)	Replicate	No. of organisms exposed	No. of immobile organisms at 24h	No. of immobile organisms at 48 h
0	A	10	0	0
	B	10	0	0
100	A	10	0	0
	B	10	0	0

Validity criteria (according to OECD 202, 2004)	Obtained in this study
In the control not more than 10 percent of the daphnids should be immobilised	0%
Dissolved oxygen concentration in the control and test vessels is ≥ 3 mg/L throughout the test	8.3 – 8.7 mg/L

Conclusion:

Under the conditions of the test, the 48h-EC_{50} for immobilisation of daphnia was found to be >100 mg propamocarb hydrochloride/L (equivalent to >140 mg Proplant/L) with a NOEC at 100 mg/L. Results of the study are based on nominal concentrations.

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCA 8.2.4.1/03; Kuhl, K.; 2015; M-525333-01-1
Title:	Acute toxicity of AE F155306 (BCS-AU81087) to the waterflea *Daphnia magna* in a static laboratory test system - Limit test -
Report No.:	E 202 4720-7
Document No.:	M-525333-01-1
Guideline(s):	EU Directive 91/414/EEC; Regulation1107/2009 (Europe); US EPA OCSPP 850.1010; OECD guideline 202,(2004); EC Council Regulation No 440/2008, Method C.2 (2008); U.S. EPA Pesticide Assessment Guidelines, Subdivision E, § 72-2 (1982); OPPTS Guideline 850.1010 public draft 1996 (modified); JMAFF 12 Nousan No. 8147 (2000)
Guideline deviation(s):	None
GLP/GEP:	Yes

Objective:
The study was performed to verify the absence of treatment-related effects on mobility of *Daphnia magna* over 48 hours under static exposure conditions, when exposed to a limit concentration of 100 mg pure metabolite / L.

Material and Methods:
Test item: AE F155306 (BCS-AU81087), batch AE F155306-01-01, (origin batch No.: SES 12811-5-8, purity: 97.6% w/w (TOX10656-00).
Daphnia magna (1st instars < 24 h old, 10 x 5 animals per testing group) were exposed in a static test system for 48 hours to an untreated, pure-water control and a limit-concentration of 100 mg pure metabolite/L, without feeding.
Macroscopic visual counting of mobile of untreated control and treated daphnids at 24 and 48 hours, defined as animals with swimming movements (slight movements of antennae were not interpreted as swimming movement) within approximately 15 seconds after gentle agitation of the test vessel. The content of AE F155306 (BCS-AU81087) in exposure media was measured for verification of the test-concentrations at test initiation (t=0 h), and at test termination (t=48h) in duplicate.
The pH and dissolved oxygen (DO) were measured at test initiation and test termination. Water temperatures within the test system were recorded at start and end of exposure from one vessel of the untreated control group and of the highest treatment group.
Dates of experimental work: March 23 to June 18, 2015

Findings:

Analytical findings:
The accompanying chemical analysis of AE F155306 (BCS-AU81087) resulted in recoveries of 96.4% at the start and 97.5% at the end of the exposure period, demonstrating that the nominal concentration of 100 mg pure metabolite/L has been successfully maintained over the entire test period. Therefore, the results are based on the nominal concentration.
The pH ranged from 6.4 to 7.8 in all replicates from t= 0 h to t= 48 h; DO was 8.9 (t= 0 h and t= 48 h), the temperature ranged from 20.3 to 21.2°C.

Time	Concentration propamocarb HCl [mg/L]		
	Nominal	Analysed	Relative to nominal [%]
0	0	< 0.01	-
0	100	96.4	96.4
48	0	< 0.01	-
48	100	97.5	97.5

Biological findings

Testing group	Exposed daphnids (=100%)	Immobilised daphnids			
		24 h		48 h	
		n	%	n	%
control	50	0	0.0	0	0.0
100 mg pure metabolite / L	50	0	0.0	0	0.0

No immobilities or other effects on behavior occurred in untreated control within 48 hours of exposure.

Validity criteria (according to OECD 202, 2004)	Obtained in this study
In the control not more than 10 percent of the daphnids should be immobilised	0%
Dissolved oxygen concentration in the control and test vessels is ≥ 3 mg/L throughout the test	8.9 mg/L

Conclusions:

As the tested limit-concentration of 100 mg pure metabolite/L caused no treatment-related effects, the EC_{50} for immobilisation of *Daphnia magna* during 48 hours of static exposure to AE F155306 (BCS-AU81087) is greater than 100 mg pure metabolite/L.
Observations on sublethal effects revealed no abnormal behaviour of the exposed daphnids over the entire exposure period of 48 hours. Results of the study are based on nominal concentrations.

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCA 8.2.4.1/04; Kuhl, K.; 2015; M-525347-01-1
Title:	Acute toxicity of AE B083813 (BCS-AW15480) to the waterflea *Daphnia magna* in a static laboratory test system - Limit test -
Report No.:	E 202 4721-8
Document No.:	M-525347-01-1
Guideline(s):	EU Directive 91/414/EEC; Regulation1107/2009 (Europe); US EPA OCSPP 850.1010; OECD guideline 202,(2004); EC Council Regulation No 440/2008, Method C.2 (2008); U.S. EPA Pesticide Assessment Guidelines, Subdivision E, § 72-2 (1982); OPPTS Guideline 850.1010 public draft 1996 (modified); JMAFF 12 Nousan No. 8147 (2000)
Guideline deviation(s):	None
GLP/GEP:	Yes

Objective:
The study was performed, to verify the absence of treatment-related effects on mobility of *Daphnia magna* over 48 hours under static exposure conditions, when exposed to a limit concentration of 100 mg pure metabolite/L.

Material and Methods:
Test item: AE B083813 (BCS-AW15480), batch BCS-AW15480-01-01, (origin batch No.: SES 12807-4-7, purity: 92.4% w/w (TOX10655-00).
Daphnia magna (1st instars < 24 h old, 10 x 5 animals per testing group) were exposed in a static test system for 48 hours to an untreated, pure-water control and a limit-concentration of 100 mg pure metabolite/L, without feeding.
Macroscopic visual counting of mobile of untreated control and treated daphnids at 24 and 48 hours, defined as animals with swimming movements (slight movements of antennae were not interpreted as swimming movement) within approximately 15 seconds after gentle agitation of the test vessel. The content of AE B083813 (BCS-AW15480) in exposure media was measured for verification of the test-concentrations at test initiation (t=0 h), and at test termination (t=48h) in duplicate.
The pH and dissolved oxygen (DO) were measured at test initiation and test termination. Water temperatures within the test system were recorded at start and end of exposure from one vessel of the untreated control group and of the highest treatment group.
Dates of experimental work: March 23 to June 18, 2015

Findings:

Analytical findings:
The accompanying chemical analysis of AE B083813 (BCS-AW15480) resulted in recoveries of 98.8% at the start and 101% at the end of the exposure period, demonstrating that the nominal concentration of 100 mg pure metabolite/L has been, successfully, maintained over the entire test period. Therefore, the results are based on the nominal concentration.
The pH ranged from 7.6 to 7.8 in all replicates from t= 0 h to t= 48 h; DO was 8.9 (t= 0 h and t= 48 h), the temperature ranged from 20.3 to 21.2°C.

Time	Concentration propamocarb HCl [mg/L]		
	Nominal	Analysed	Relative to nominal [%]
0	0	< 0.01	-
0	100	98.8	98.8
48	0	< 0.01	-
48	100	101	101

Biological findings

Testing group	Exposed daphnids (=100%)	Immobilised daphnids			
		24 h		48 h	
		n	%	n	%
control	50	0	0.0	0	0.0
100 mg pure metabolite / L	50	0	0.0	0	0.0

No immobilities or other effects on behaviour occurred in untreated control within 48 hours of exposure.

Validity criteria:

Validity criteria (according to OECD 202, 2004)	Obtained in this study
In the control not more than 10 percent of the daphnids should be immobilised	0%
Dissolved oxygen concentration in the control and test vessels is ≥ 3 mg/L throughout the test	8.9 mg/L

Conclusion:
As the tested limit-concentration of 100 mg pure metabolite/L caused no treatment-related effects, the EC_{50} for immobilisation of *Daphnia magna* during 48 hours of static exposure to AE B083813 (BCS-AW15480) is greater than 100 mg pure metabolite/L.
Observations on sublethal effects revealed no abnormal behaviour of the exposed daphnids over the entire exposure period of 48 hours. Results of the study are based on nominal concentrations.

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

The acute toxicity of propamocarb hydrochloride to the Mysid shrimp (*Mysidopsis bahia*) was assessed in the studies M-157843-01-1 and M-310709-01-1 and on shell deposition of the Eastern Oyster (*Crassostrea virginica*) was assessed in the studies M-157857-01-1 and M-310718-01-1.

Report:	KCA 8.2.4.2/01; Schupner, J. K.; 1991; M-157843-01-1
Title:	The static acute toxicity of Propamocarb HCl to the Mysid shrimp, *Mysidopsis bahia*
Report No.:	A85561
Document No.:	M-157843-01-1
Guideline(s):	Guideline 72-3
Guideline deviation(s):	--
GLP/GEP:	**yes**

Objective:
The purpose of this test was to assess the 96 h acute toxicity of propamocarb-HCl (concentration of 100 mg/L) for *Mysidopsis bahia* in a static system.

Material and Methods:

The acute toxicity of propamocarb hydrochloride (PHC) to the Mysid shrimp (*Mysidopsis bahia*) was assessed in a static system.
Juvenile Mysid shrimp were purchased from Aquatic BioSystems, Inc., Fort Collins, Colorado. Mysids were 3 days old at test initiation.
Mysids were randomly assigned to randomly positioned test chambers (beaker: 15.5 cm height x 10.2 cm diameter x 10 cm solution n depth) in a rectangular glass fish tank (19 L), in which they were exposed in synthetic sea water at 22.0°C (range: 20.5 to 23.2° C) to a nominal concentration of 100 mg/L Propamocarb hydrochloride for 96 hours. Organism loading during the study was 10 mysids/800 ml. The mysids were fed daily with 2 drops *Artemia* larvae twice a day and observed for adverse effects (death, morphological or behavioral abnormalities). Samples of the test solutions were analyzed for PHC at test initiation (day 0) and termination (day 4).

Findings:

Analytical findings:
Nominal concentrations of PHC were achieved with the mean measured concentration over the duration of the study being 105 mg/L. The control samples did not contain any detectable levels of PHC.

Nominal and measured exposure concentrations (expressed as PHC):

Nominal concentration (mg/L) Treatment-replicate	Measured concentrations (mg/L) 0 hour	Measured concentrations (mg/L) 96 hours	Study Mean measured concentration (mg/L)
Control - 1	0	0	0
Control - 2	0	0	0
Control - 3	0	0	0
100 - 1	104.9	103.0	104.0
100 - 2	104.2	106.2	105.2
100 - 3	101.8	107.8	104.8

Biological findings:

There were no mortalities and no signs of abnormal behavior during the test period and all mysids appeared normal. Thus, the 96-hour LC_{50} of PHC to Mysid shrimp was greater than the mean measured concentration 105 mg/L.

Conclusion:
The 96-hour LC_{50} of PHC to Mysid shrimp was greater than 105 mg/L.
Since there was no mortality or abnormal behavior and appearance evident during this study, propamocarb-HCl may be considered non-toxic under the conditions of this test.

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCA 8.2.4.2/02; Putt, A. E.; 2001; M-310709-01-1
Title:	Proplant (propamocarb HCL 722 g/l SL): Acute toxicity to Mysids (*Americamysis bahia*) under static conditions
Report No.:	13763.6101
Document No.:	M-310709-01-1
Guideline(s):	FIFRA 72-3
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

Objective:

The purpose of this study was to estimate the acute toxicity (LC_{50}) of Proplant (propamocarb HCl 722 g/L SL) to mysids (*Americamysis bahia*) under static conditions.

Material and Methods:
The acute toxicity of propamocarb hydrochloride (Batch No.: 1582001, CAS No.: 25606-41-1), to the mysid *Americamysis bahia* was investigated in a static system over a 96 hours exposure period. Mysids were originally obtained from Aquatic BioSystems, Inc., Fort Collins and were fed live brine shrimp nauplii (*Artemia salina* nauplii) twice daily prior and during the test. Dilution water used during this study was prepared by filtering natural seawater collected from the Cape Cod Canal, Massachusetts. The salinity of the natural seawater was adjusted to 20±3 ‰ with laboratory well water prior to use, where Mysids were exposed at 25±1°C with a regulated photoperiod of 16 hours of light and 8 hours of darkness to test concentrations of 0, 7.5, 15, 30, 60 and 120 mg propamocarb hydrochloride/L (corresponding to mean measured concentrations of 7.7, 15, 29, 58 and 120 mg/L).
The test was conducted in 1-L glass beakers which contained 900 mL of test solution (10 mysids per replicated vessel, 20 per treatment and level and control).
Sampling and analysis of test item concentration were done in duplicate at start (t=0 h) and at test termination (t=96h) and biological observations were recorded at 0, 24, 48, 72 and 96 hours. The determination of the median lethal concentrations (LC_{50}) was done by statistical analysis.

Findings:

Analytical findings:

The phys.-chem. parameters of the test remained in acceptable limits: temperature between 24 and 25°C, pH from 7.8 to 7.9, DO ranged between 6.5 and 7.9 mg O_2/L, and salinity from 20 to 21‰. The analytical dose verification (using a previously validated method) proved the concentrations to range between 92.5 to 106% of nominal.

Concentrations of Propamocarb HCl 722 g/L SL measured in exposure solutions during the 96-hour static exposure to mysids (*Americamysis bahia):*

Nominal concentration (mg a.i./L)	Measured Concentration (mg a.i./L)			
	0 Hour	96 Hours	Mean[a]	Percent of Nominal
Control	<0.23	<0.25	NAb	NA
7.5	8.3	7.1	7.7	100
15	16	14	15	99
30	32	26	29	96
60	61	55	58	97

120	120	120	120	100

[a] Mean measured concentrations were calculated using the actual analytical (unrounded) results and not the rounded values presented in this table; b NA = not applicable

Biological findings:
No mortality or adverse effects were observed among mysids exposed to 7.7 and 15 mg a.s./L or in the control. Following 48 hours of exposure, 100% mortality was observed among mysids exposed to the highest treatment level tested, 120 mg a.i./L. At test termination (96 hours of exposure), 5 and 65% mortality were observed among mysids exposed to the 29 and 58 mg a.i./L treatment levels, respectively. The LC_{50} value for 96 hours exposure of mysids was calculated by probit analysis.
Mean measured concentrations tested, corresponding cumulative percent mortality, number of mortalities, and observations made during the 96-hour static exposure of mysids (*Americamysis bahia*) to Propamocarb HCI 722 g/L SL:

	Cumulative Mortality (%)											
	24 Hour			48 Hour			72 Hour			96 Hour		
Nominal conc. (mg a.i./L)	A	B	Mean	A	B	Mean	A	B	Mean	A	B	Mean
Control	0	0	0	0	0	0	0	0	0	0	0	0
7.7	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	10	0	5	10	0	5
58	0	0	0	50	40	45	60	70	65	60	70	65
120	0	0	0	100	100	100	100	100	100	100	100	100

The LC_{50} values, corresponding 95% confidence intervals and NOEC established during the 96-hour exposure of mysids (*Americamysis bahia*) to Propamocarb HCI 722 g/L SL:

		95 % Confidence Intervals	
	LC_{50} (mg a.i /L)	Lower (mg a.i /L)	Upper (mg a.i /L)
24 Hour[a]	>120	NA[b]	NA[b]
48 Hour[c]	61	29	120
72 Hour[d]	50	42	60
96 Hour[d]	50	42	60
NOEC through 96 hours = 15 mg a.i./L			

[a] Empirically estimated to be greater than the highest concentration tested.
[b] NA = Not applicable. Confidence intervals could not be calculated.
[c] LC_{50} value was estimated using non-linear interpolation. Corresponding 95% confidence intervals were calculated using binomial probability.
[d] LC_{50} value and 95% confidence intervals were calculated using probit analysis.

Conclusion:
The LC_{50} value for mysids exposed to Propamocarb hydrochloride was determined as 50 mg a.i./L with a confidence interval of 95%. The NOEC established under the conditions of this study was 15 mg a.s./L.

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCA 8.2.4.2/03; Holmes, C. M.; Peters, G. T.; 1991; M-157857-01-1
Title:	Propamocarb HCl: A 96-hour shell deposition test with the Eastern oyster (*Crassostrea virginica*)
Report No.:	A85568
Document No.:	M-157857-01-1
Guideline(s):	--
Guideline deviation(s):	--
GLP/GEP:	**Yes**

Objective:
The objective of this study was to determine the effects of the test substance, propamocarb-HCl, on shell deposition of the eastern oyster, *Crassostrea virginica*, under flow-through test conditions.

Material and Methods:
The effects of propamocarb-HCl on shell deposition of the Eastern Oyster (*Crassostrea virginica*) were determined under flow-through conditions over a 96 hour exposure period. The study was conducted at 22 ± 1 °C, the salinity of the test water was 23 ‰, and pH ranged between 7.9 – 8.2; the flow of unfiltered saltwater into each test chamber was 1 L water/oyster/hour. A photoperiod of 16 hours of light and 8 hours of darkness was provided. Oysters were exposed to six nominal test concentrations of propamocarb-HCl in unfiltered seawater; 1, 2.2, 6.4,16, 40, 100 mg/L(corresponding to mean measured test concentrations 1.1, 2.2, 6.6, 12, 38 and 104 mg propamocarbHCl/L) and a negative control (unfiltered seawater) for a period of 96 hours. Test chambers were filled with 12.6 L of test solution, containing 20 organisms per test concentration. Oysters (38 to 49 mm) long were obtained from World´s End Aquaculture, Maryland. Immediately prior to test initiation 3-5 mm of the shell periphery were removed from each oyster using motorized grinder. Algal cells (*Isochrysis*, *Tetraselmis* and *Thalassiosira*) were provided to supplement naturally-occurring algae and maximize oyster growth rates under test conditions.
Samples of the test concentrations were taken and analyzed for propamocarb-HCl at test initiation (day 0) and termination (day 4). Measurement of shell deposition was recorded after 96 h.

Findings:
Analytical findings:
Mean measured concentrations of propamocarb-HCl over the duration of the study were: 1.1, 2.2, 6.6, 12, 38 and 104 mg propamocarb-HCl /L.
Biological findings:
The 96 hour EC_{50} for shell deposition was 43.9 mg/L. Based on visual interpretation of the growth data, the no-observed-effect concentration (NOEC) was 12 mg/L.

96- Hour Shell Deposition:

Mean Measured Concentration	Shell deposition (mm) Mean ± SD*	Shell deposition expressed as a percentage of control growth
Negative control	3.69 ± 1.38	100
1.1 mg	4.54 ± 1.63	123
2.2 mg	3.64 ± 1.31	98.6
6.6 mg	4.14 ± 1.39	112
12 mg	3.44 ± 1.14	93.2
38 mg	2.2 ± 0.85	59.6
104 mg	0.16 ± 0.31	4.33

EC_{50} Values:

Time	EC_{50} (mg/L)	Lower 95 % Confidence Limits	Upper 95 % Confidence Limits	Statistical Methods
96 Hours	43.9 mg Propamocarb-HCl/L	38 mg Propamocarb-HCl/L	104 mg Propamocarb-HCl/L	Binomial

Conclusion:

The 96 hour EC_{50} for oyster shell growth was 43.9 mg propamocarb-HCl /L and the NOEC was 12 mg/L.

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCA 8.2.4.2/04; Dionne, E.; 2001; M-310718-01-1
Title:	Proplant (propamocarb HCL 722 g/l SL): Acute toxicity to Eastern oysters (*Crassostrea virginica*) under flow-through conditions
Report No.:	13763.6102
Document No.:	M-310718-01-1
Guideline(s):	FIFRA 72-3; OPPTS 580.1025
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

Objective:

The purpose of this study was to estimate the acute toxicity of the test substance, propamocarb-HCl, to Eastern oysters, *Crassostrea virginica*, under flow-through conditions.

Material and Methods:
The effect of Propamocarb hydrochloride (batch No.: 1582001, CAS No.: 25606-41-1) on Eastern oyster *Crassostrea virginica* was investigated under flow-through conditions with 96 hours of exposure in natural seawater.
The oysters were obtained from Circle C Oysters, Maryland, with a mean valve height of 37 mm. Prior to testing, 3 to 5 mm of the new peripheral shell growth of each oyster were removed by grinding the shell to a blunt edge using a fine-grit grinding wheel.
Twenty oysters were exposed to test concentrations of 0, 6.3, 13, 25, 50 and 100 mg propamocarb-HCl /L (corresponding to mean measured concentrations of 7.1, 14, 26, 53 and 110 mg/L) and to a negative control). All Treatment levels and control were maintained in duplicates (40 oysters per treatment level and the controls). During the exposure, the oysters received supplemental feedings of algae (*Isochrysis galbana*, Parke T-ISO), three times daily to maintain an average concentration of approximately 10^7 cells/mL in the test solutions during the four-day exposure. A photoperiod of 16 hours light and 8 hours darkness and 20 ±2 C were maintained throughout the test. Natural unfiltered seawater (Cape Cod Canal, Massachusetts) was used as dilution and control water, which had a salinity of 31 ‰ and a pH of 8.0. Test vessels consisted of glass aquaria (49.5 x 25.5 x 29 cm) and were equipped with an overflow side drain (height at 14 cm) which maintained a test solution volume of approximately 18 L. Sampling and analysis of test item concentration were done at start (t=0 h) and at test termination (t=96h) in duplicate. The determination of significant shell deposit differences (to controls), NOEC and EC_{50}, was done by statistical analysis.

Findings:

Analytical findings:

The phys.-chem. parameters of the test remained in acceptable limits: temperature between 21 and 22°C, pH from 7.9 to 8.1, DO ranged between 6.3 and 7.3 mg O_2/L, and salinity stayed at 31‰. The analytical dose verification (using a previously validated method) proved the concentrations to range between 85.3 to 115% of nominal.

Nominal Concentration (mg a.i./L)	Measured Concentration (mg a.i./L)			Percent of Nominal
	0 Hour	96 Hour	Mean[a]	

Control	<0.24	<0.24	NA[b]	NA
6.3	6.8	7.5	7.1	113
13	13	15	14	110
25	26	27	26	106
50	49	56	53	105
100	100	110	110	107

[a] Mean measured concentrations were calculated using the actual analytical (unrounded) results and not the rounded (two significant figures) values presented in this table; [b] NA = not applicable

Biological findings:

No mortality occurred; the average growth of control oysters was determined as 2.3 mm shell deposit. The reduction in growth in oysters exposed to 14, 26, 53 and 110 mg propamocarb hydrochloride/L was shown to be statistically significant compared to the control.
Effects of Propamocarb HCl 722 g/L SL on the shell deposition of Eastern oysters after 96 hours:

Mean Measured Concentration (mg a.i./L)	Mean Shell Deposition[a], mm (SD[b])	Mean Percent Reduction[c]
Control	2.3	NA[d]
7.1	1.8	20
14	1.5	35[e]
26	1.9	16[e]
53	0.7	68[e]
110	0.3	89[e]

[a] Mean shell deposition represents the measurements of 40 oysters per treatment; [b] SD = Standard deviation;
[c] Unrounded replicate mean shell growth was compared to the control to determine treatment effects.
[d] NA = Not applicable; [e] Significantly reduced compared to the control based on Williams' test.

Conclusion:

The obtained reduction in shell deposit was shown to be dose-dependent. The 96-hour EC_{50} was calculated by linear regression to be 46 mg propamocarb hydrochloride /L, the NOEC was 7.1 mg/L.

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

11.5.2 Acute (short-term) toxicity to algae or other aquatic plants

Please consult Table 73 above additionally to the text below.
Acute (short-term) toxicity of propamocarb hydrochloride (PHC) to algae or other aquatic plants has been investigated in two independent growth inhibitions tests with *Pseudokirchneriella subcapitata* formerly *Selenastrum capricornutum* (M-240390-01-1, M-310692-01-1).
Additionally, two studies were performed to know the toxicity of the two PHC metabolites to algae and it was observed absence of acute toxicity of the metabolites N-desmethyl-propamocarb and propamocarb-N-oxide to the green algae *Pseudokirchneriella subcapitata*.
The most conservative endpoint that is presented in the List of Endpoints was obtained in the *Lemna gibba* study by Christ & Ruff (1996). In this study no toxicity of the test item was observed at the single test concentration.
The *Lemna minor* study by Bogers (2001) was noted to be acceptable and valid. As this study explores the effects on aquatic plants at higher test concentrations than the other study, it is deemed appropriate to present the results.

Report:	KCA 8.2.6.1/01; Hoberg, J. R.; 2001; M-240390-01-1
Title:	Propamocarb hydrochloride - Toxicity to the freshwater green alga, *Pseudokirchneriella subcapitata*
Report No.:	13726.6139; B003349
Document No.:	M-240390-01-1
Guideline(s):	US EPA OPPTS 850.5400; OECD 201; EC Annex V Part C.3
Guideline deviation(s):	not specified
GLP/GEP:	Yes

Objective
The objective of this study was to determine the effect of propamocarb hydrochloride (PHC) on the growth of the freshwater green algae *Pseudokirchneriella subcapitata.*

Materials and methods:
Test Substance: propamocarb-HCl (Previcur N); Batch: AABA00270; Purity: 67.8%(w/w).
The toxicity of Previcur N to fresh water green alga *P. subcapitata* was determined in a growth inhibition test over a 96 h exposure period. Algae were obtained from Carolina Biological Supply Co., Burlington, North Carolina, and were maintained in stock culture at Springborn.
Nominal test concentrations were 0, 3.1, 6.3, 13, 25, 50, 100 mg PHC/L, prepared in AAP test media. The AAP media was prepared with sterile deionised water.
P. subcapitata (1 x 10^4 cells/mL) were added to the test media in triplicate vessels for each test concentration and cultured at 24 °C under constant illumination (3200 – 5400 lux) and agitation (100 revs/min). Six replicate control vessels, containing algal AAP media only, were also inoculated and maintained under the same conditions. All test vessels were fitted with steel caps which permit gas exchange. Approximately 70 min after the test solutions were added to the test flasks, a 0.179 mL inoculum of *P. subcapitata* cells, at a density of approx. 559 x 10^4 cells/mL, was aseptically introduced into each flask. This inoculum provided the required initial (0 hour) cell density of approximately 1.0 x 10^4 cells/mL.
Samples of the cultures were removed daily and cell numbers determined using a haemocytometer and compound microscope. Observations of the health of the algal cells were also made and recorded at each 24 h interval.
The test was conducted in an environmental chamber designed to maintain the test conditions – test temperature of 24 ± 1 °C and continuous light intensity of 300 to 5000 foot-candles. An orbital shaker table provided a shaking rate of 100 ± 10 ppm. Water quality and pH were measured at test initiation and at test termination after 96 hours.
A composite sample of 3 replicate vessels (A, B, and C) was removed from the 100 mg PHC/L. The sample was then diluted with freshly prepared AAP medium to prepare a subculture with a nominal concentration of 3.1 mg propamocarb HCl/L. The performance of this subculture was used to determine if the effects of the test substance on the alga were algistatic, in which case cells would resume growth in the subculture, or algicidal, in which case no growth would occur in the subculture.
The subculture was incubated for 4 days under conditions consistent with those maintained during the definitive exposure. The subculture was discontinued after a substantial increase in cell density (i.e.>10x) was observed. Concentrations of the test substance in the algal medium were determined and all effect concentrations were based on mean measured concentrations. Analysis of the samples was performed by gas chromatographic with mass selective detection procedure.

Findings:

Analytical findings

Nominal concentration (mg a.i./L)	Measured Concentration	
	Mean	Percent of Nominal
Control	NA	NA
3.1	3.2	100
6.3	5.9	93
13	13	97
25	20	80
50	35	70
100	85	85

NA: not applicable

Mean measured concentrations of the test substance in the algal medium were 0, 3.2, 5.9, 13, 20, 35, 85 mg/L and all effect concentrations were based on these measured concentrations.
The pH of the test and control solutions ranged from 7.0 – 7.4 at test initiation, and 8.4- 8.7 at test termination (96 h). Conductivity of the exposure and control solutions ranged from 80 to 120 µMhos/cm. The temperature was maintained at 24°C for the duration of the study period. Light intensity was also maintained between 450 – 500 foot-candles throughout the exposure period. At 96 h cells exposed to all treatment levels tested and the control were observed to be normal.

Cell density after 24, 48, 72 and 96 hours:

Mean measured concentration propamocarb hydrochloride (mg/L)	Cell Density (x10^4 cells/mL)				Percent inhibition
	24h	48h	72h	96h	
Control	5.92	21.42	92.73	308.0	n.a.
3.2	5.08	18.67	96.0	295.0	4
5.9	5.75	21.58	116.8	379.0	-23
13	4.00	23.75	113.3	307.0	0
20	3.92	16.33	91.3	258.0	16
35	3.50	17.42	74.8	212.0	31
85	3.50	15.25	49.8	160.0	48

n.a. = not applicable

Calculated biomass (area under the growth curve) after 24, 48, 72 and 96 hours:

Mean measured concentration propamocarb hydrochloride (mg/L)	Biomass (x10^4 cells x days/mL)				Percent inhibition
	24h	48h	72h	96h	
Control	2.43	12.7	56.0	71.5	n.a.
3.2	2.01	10.88	56.7	69.6	3
5.9	2.34	12.67	68.6	83.6	-17
13	1.48	12.88	68.0	82.3	-15
20	1.44	9.13	53.2	63.8	11
35	1.23	9.46	45.4	56.1	22
85	1.23	8.38	31.8	41.4	42

n.a. = not applicable

Calculated growth rate after 24, 48 and 72 hours:

Mean measured concentration Propamocarb hydrochloride (mg/L)	Growth rate (days^{-1})			Percent inhibition[a]
	0-24h	0-48h	0-72h	
Control	1.80	1.54	1.50	n.a.
3.2	1.59	1.47	1.52	3
5.9	1.76	1.55	1.59	-17
13	1.39	1.59	1.58	-15
20	1.36	1.39	1.51	11
35	1.25	1.44	1.44	22
85	1.21	1.37	1.30	42

[a] Percent inhibition relative to control

The 0 – 72 h E_rC_{50} and E_bC_{50} for propamocarb hydrochloride were determined to be > 85 mg/L and 120 mg/L respectively.

Toxicity of propamocarb hydrochloride to green algae:

Time	E_rC_{50} values propamocarb hydrochloride (mg/L)	E_bC_{50} values propamocarb hydrochloride (mg/L)
72-hours EC_{50}	> 85	120
NOEC	35	13

Validity criteria (according to OECD 201, 2006)	Obtained in this study
Biomass increase in the control cultures by a factor of at least 16 within 72 hours. This corresponds to a specific growth rate of 0.92 day^{-1}	1.0 day^{-1}
Coefficient of variation for section by section specific growth rates (days 0-1, 1-2 and 2-3 for 72 hours) in the control cultures must not exceed 35%	Not reported
Coefficient of variation of average specific growth rates during the whole test period in replicate control cultures must not exceed 7% in tests with *Pseudokirchneriella subcapitata* (10% for all other species)	7.25%

Conclusion:
Propamocarb hydrochloride had low toxicity to *Pseudokirchneriella subcapitata* with a 72hr E_rC_{50} greater than 85 mg/L and a 72hr E_bC_{50} of 120 mg/L.

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCA 8.2.6.1/02; Bogers, M.; 1996; M-310692-01-1
Title:	Fresh water algal growth inhibition test with Proplant
Report No.:	165364
Document No.:	M-310692-01-1
Guideline(s):	Directive 92/69/EEC (part C.3; 1992); OECD Guideline No. 201 (1984); ISO 8692 (1989)
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

Objective:
The purpose of the study was to evaluate the test substance for its ability to inhibit the growth of fresh water algae in a short-term experiment.

Material and Methods:
Test Substance: ISO common name: propamocarb; IUPAC name: propyl 3-(dimethylamino)propyl-carbamate hydrochloride; Batch: T5665; purity: 736.1 ± 2.0 g/L.
Selenastrum capricornutum, (unicellular green alga), strain CCAP 278/4 was exposed to propamocarb hydrochloride over a period of 72 hours under static conditions in 100 mL glass vessels. The initial cell densitywas 1 x 104 cells/mL (medium: ISO (1989, prepared with Milli-Q water)). Illumination was continuously maintained at 6500 to 7000 lux and algal cells were kept in suspension by continuous shaking.
Test concentrations were as follows:
- Range-finding test: 0.09 to 85 mg propamocarb-HCl/L.
- Final test: 0, 12, 22, 38, 68, 120, 220, 380, 680 mg propamocarb-HCl/L (nominal).

There were 3 replicates per test concentration, 6 replicates of blank control and 1 replicate of 680 mg/L without algae.
Sampling for analysis of test item concentration was undertaken at test initiation (t=0h), and at test termination (t=72h) in duplicate.
The following measurements and recordings were taken during the study period:
- pH: at start and termination;
- temperature: daily in a control vessel;
- cell densities: at start (microscopically by counting), at 24, 48 and 72 hours spectroscopically (based on calibration curve).

Findings:

Analytical findings

Log nominal concentration (mg/L)	Log actual concentration (mg/L)
1.079	1.079
1.833	1.833
2.342	2.367
2.833	2.917
1.079	1.064*
1.342	1.339*
1.580	1.587»
1.833	1.852*
2.079	2.109*
2.342	2.384*
2.580	2.632*
2.833	2.897

* Interpolated from the regression line: Y = 1.0452 X -0.0641

Analytical dose verification proved the initial concentration to be maintained throughout the exposure period between 80 and 120% of nominal. The pH ranged from 7.9 to 8.3 in all replicates from t= 0 h to t= 72 h; the temperature ranged from 22 to 23°C.
The biological recordings regarding cell growth together with derived data are summarised in the following table.

Mean cell densities of *Selenastrum capricornutum:*

Concentration of Propamocarb hydrochloride (mg/L) #	Mean cell densities during exposure (x10^4 cells/mL)			
	0 h	24 h	48 h	72 h
0 (control)	1.00	2.08	8.9	33.0
12	1.00	2.50	9.3	33.7
22	1.00	2.82	10.2	34.8
39	1.00	3.01	10.3	35.0
71	1.00	2.88	10.4	35.3
130	1.00	3.08	7.7	24.8
240	1.00	3.01	5.3	9.3
430	1.00	2.88	2.4	2.4

790	1.00	1.70	2.3	1.7

based on actual measured concentrations of Propoamocarb at the end of the 72h period

Inhibition of Cell Growth and reduction of cell growth:

The tables below indicate the calculation of the percentages of inhibition of cell growth and the percentages of growth rate reduction at two time intervals. No inhibition of cell growth was recorded at test concentrations ranging from 12 to 71 mg PHC/L. The negative values for inhibition indicated a stimulation of cell growth. Inhibition of cell growth increased with increasing concentration of PHC from 130 mg PHC/L upwards.

Comparison of the values for total cell growth of the 0 – 72h interval with those of the 24 – 72h interval showed that total cell growth was increasingly inhibited during the last 48 hours of exposure resulting in 100% inhibition at and above nominally 430 mg PHC/L. Statistically significant inhibition of cell growth was found at test concentration of 130 mg PHC/L and higher (Williams' test: P=0.05).

Percentage inhibition of cell growth of *Selenastrum capricornutum:*

Concentration of Propamocarb hydrochloride (mg/L)#	Cell growth 0-72 h		Cell growth 24-72h	
	Area (mean)	Inhibition (%)	Area (mean)	Inhibition (%)
0 (contr.)	599.56	---	534.90	---
12	627.77	-4.7a	538.00	-0.6 a
22	669.52	-11.7 a	560.41	-4.8 a
39	679.56	-13.3 a	558.87	-4.5 a
71	681.88	-13.7 a	568.92	-6.4 a
130	496.37	17.2	371.80	30.5**
240	252.10	58.0	131.41	75.4 **
430	94.42	84.3	-18.55	103.5**
790	56.68	90.5	14.86	97.2 **

based on actual measured concentrations of Propoamocarb at the end of the 72h period; [a] negative inhibition values mean growth stimulation relative to the blank-control; ** significantly different from control

The values for growth rate reduction based on the intervals of 0 – 72h and 24 – 72h showed the same pattern. Growth rate reduction for the 24 – 72h interval increased with increasing concentration of PHC from 71 mg/L upwards resulting in 100% reduction at and above nominally 430 mg PHC/L. Statistically significant reduction in growth rate for the 24 – 72h interval was found at test concentrations of 22 mg PHC/L and higher (Williams test: P=0.05). However, there was no test concentration related response from 12 – 71 mg PHC/L and the percentage reduction remained below 10% except at 39 mg PHC/L. Hence, the statistically significant reduction rates recorded at 12 to 71 mg PHC/L were not considered to be biologically relevant.

Percentage reduction of growth rate of *Selenastrum capricornutum:*

Concentration of Propamocarb hydrochloride (mg/L)#	Growth rate (cells/mL/h)			
	0-72 h mean µ	Reduction (%)	24-72 h mean µ	Reduction (%)
0 (contr.)	0.04836	---	0.05766	---
12	0.04883	-1.0a	0.05429	5.9
22	0.04925	-1.8a	0.05242	9.1*
39	0.04937	-2.1a	0.05117	11.3*
71	0.04951	-2.4a	0.05222	9.4*
130	0.04458	7.8	0.04347	24.6**

Concentration of Propamocarb hydrochloride (mg/L)[#]	Growth rate (cells/mL/h)			
	0-72 h mean µ	Reduction (%)	24-72 h mean µ	Reduction (%)
240	0.03099	35.9	0.02354	59.2**
430	0.01184	75.5	-0.00425	107.4**
790	0.00728	84.9	0.00157	97.3**

[#] based on actual measured concentrations of Propamocarb at the end of the 72h period; [a] = negative inhibition values mean growth stimulation relative to the blank-control; [*] significantly different from control but not considered biologically significant

[**] significantly different from control and considered biologically significant

Validity criteria:

Validity criteria (according to OECD 201, 2006)	Obtained in this study
Biomass increase in the control cultures by a factor of at least 16 within 72 hours. This corresponds to a specific growth rate of 0.92 day^{-1}	Biomass increased in the control cultures by a factor of 33 within 72 hours
Coefficient of variation for section by section specific growth rates (days 0-1, 1-2 and 2-3 for 72 hours) in the control cultures must not exceed 35%	Not reported
Coefficient of variation of average specific growth rates during the whole test period in replicate control cultures must not exceed 7% in tests with *Pseudokirchneriella subcapitata* (10% for all other species)	5.36%

Conclusion:
The test is acceptable and valid: the cell density of the algae *Selenastrum capricornutum* in controls increased by a factor >16 within 3 days; dose verification proved the exposure concentrations to remain above 80% of initial values throughout the 72 hours; all parameters/conditions remained within an acceptable range.
The following ecotoxicological parameters are concluded: The test item affected cell growth significantly at ≥ 130 mg PHC/L.

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCA 8.2.6.1/03; Kuhl, K.; 2015; M-525324-01-1
Title:	*Pseudokirchneriella subcapitata* growth inhibition test with AE F155306 (BCS-AU81087)
Report No.:	E 201 4736-3
Document No.:	M-525324-01-1
Guideline(s):	EU Directive 91/414/EEC; Regulation (EC) No. 1107/2009; U.S. EPA Pesticide Assessment Guidelines, Subdivision J, §122-2, 123-2; OCSPP Guideline 850.4500 (January 2012); OECD Guideline 201: Freshwater Alga and Cyanobacteria, Growth Inhibition Test (July 28, 2011); OCSPP Guideline 850.4500: Algal Toxicity (June 2012)
Guideline deviation(s):	None
GLP/GEP:	Yes

Objectives:
The aim of the study was to determine the influence of the test item Propamocarb-N-oxide on exponentially growing populations of *Pseudokirchneriella subcapitata* expressed as NOEC, LOEC and EC_x for growth rate and further endpoints of algal biomass (cells per volume).

Material and Methods:

Test material: AE F155306 (BCS-AU81087; Propamocarb-N-oxide); analysed purity: 97.6 % w/w was tested, specified by origin batch no.: SES 12811-5-8, identification code: TOX10656-00 and batch code: AE F155306-01-01.
Pseudokirchneriella subcapitata (freshwater microalgae, formerly known as *Selenastrum capricornutum*) were exposed in a chronic multigeneration test for 72 hours with a prolongation to 96 hours in order to cover OECD and OCSPP guidelines under static exposure conditions to nominal concentrations of 6.25, 12.5, 25.0, 50.0 and 100 mg p.m./L in comparison to control. The pH values ranged from 7.9 to 8.8 in the control replicates and the incubation temperature ranged from 22.4 °C to 23.2 °C (measured in an additional incubated glass vessel) over the whole period of testing at a continuous illumination of 4.50 klux (mean value).
Quantitative amounts of AE F155306 (BCS-AU81087) were measured in all treatment groups and in the controls at test start, after 72 hours and test end (96 hours).
Dates of experimental work: May 18 to June 16, 2015

Validity Criteria (OECD 201):	Obtained in this study
Biomass in the control cultures should have increased exponentially by a factor of at least 16 within the 72 hour test period	77.4
Mean coefficient of variation for section-by-section specific growth rates (days 0-1, 1-2 and 2-3) in the control cultures should not exceed 35 %	13.9 %
Coefficient of variation of average specific growth rates during the whole test period between the replicate control cultures should not exceed 7 %	1.2 %

Validity Criteria (OCSPP 850.4500):	Obtained in this study
Biomass in the control cultures should have increased exponentially by a factor of at least 100 within the 96 hour test period	204.3
Coefficient of variation for mean control yield at test termination should be ≤ 15 %	8.8 %
Coefficient of variation for average specific growth rates of controls at test termination should be ≤ 15 %	1.7 %

The study conditions met all validity criteria, requested by the mentioned guidelines.
The analytical findings of AE F155306 (BCS-AU81087) in the treatment levels found on day 0 were 92.2 % to 96.4 % of nominal (average 95.0 %). After 72 hours analytical findings of 96.4 % to 97.8 % of nominal (average 97.4 %) were found and after 96 hours analytical findings of 95.8 % to 100 % of nominal (average 97.5 %) were found. All results are based on nominal test concentrations of the pure metabolite.

Results after 72 hours:

Nominal concentration [mg p.m./L]	Cell number after 72 h (means) per mL	(0-72h)-Average specific growth rates [$days^{-1}$]	Inhibition of average specific growth rate [%]
control	774 000	1.449	0.0
6.25	755 000	1.441	0.6
12.5	786 000	1.454	-0.3
25.0	800 000	1.460	-0.8
50.0	792 000	1.455	-0.4
100	795 000	1.457	-0.6

test initiation with 10,000 cells/mL; - % inhibition: increase in growth relative to the pooled control

Results after 96 hours:

Nominal concentration [mg p.m./L]	Cell number after 96 h (means) per mL	(0-96h)-Average specific growth rates [$days^{-1}$]	Inhibition of average specific growth rate [%]
control	2 182 000	1.346	0.0
6.25	2 188 000	1.347	-0.1
12.5	2 260 000	1.355	-0.7
25.0	2 287 000	1.358	-0.9
50.0	2 183 000	1.346	0.0
100	2 043 000	1.330	1.2

test initiation with 10,000 cells/mL; - % inhibition: increase in growth relative to the pooled control

Summary of the results:

Average growth rate (0 - 72 h)	E_rC_{50}	>100 mg p.m./L
	LOE_rC	>100 mg p.m./L
	NOE_rC	≥100 mg p.m./L
Average growth rate (0 - 96 h)	E_rC_{50}	>100 mg p.m./L
	LOE_rC	>100 mg p.m./L
	NOE_rC	≥100 mg p.m./L

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCA 8.2.6.1/04; Kuhl, K.; 2015; M-525329-01-1
Title:	Pseudokirchneriella subcapitata growth inhibition test with AE B083813 (BCS-AW15480)
Report No.:	E 201 4735-2
Document No.:	M-525329-01-1
Guideline(s):	EU Directive 91/414/EEC; Regulation (EC) No. 1107/2009; U.S. EPA Pesticide Assessment Guidelines, Subdivision J, §122-2, 123-2; OCSPP Guideline 850.4500 (January 2012); OECD Guideline 201: Freshwater Alga and Cyanobacteria, Growth Inhibition Test (July 28, 2011); OCSPP Guideline 850.4500: Algal Toxicity (June 2012)
Guideline deviation(s):	none
GLP/GEP:	yes

Objectives:
The aim of the study was to determine the influence of the test item N-desmethyl-Propamocarb on exponentially growing populations of *Pseudokirchneriella subcapitata* expressed as NOEC, LOEC and EC_x for growth rate and further endpoints of algal biomass (cells per volume).

Material and Methods:
Test material: AE B083813 (BCS-AW15480; N-desmethyl-Propamocarb) analysed purity: 92.4 % w/w was tested, specified by origin batch no.: SES 12807-4-7, identification code: TOX10655-00 and batch code: BCS-AW15480-01-01.
Pseudokirchneriella subcapitata (freshwater microalgae, formerly known as *Selenastrum capricornutum*) were exposed in a chronic multigeneration test for 72 hours with a prolongation to 96 hours in order to cover OECD and OCSPP guidelines under static exposure conditions to nominal concentrations of 0.954, 3.05, 9.77, 31.3 and 100 mg p.m./L in comparison to control. The pH values ranged from 7.9 to 8.8 in the control replicates and the incubation temperature ranged from 22.4 °C to 23.2 °C (measured in an additional incubated glass vessel) over the whole period of testing at a continuous illumination of 4.50 klux (mean value).
Quantitative amounts of AE B083813 (BCS-AW15480) were measured in all treatment groups and in the controls at test start, after 72 hours and test end (96 hours).
Dates of experimental work: May 15 to June 16, 2015

Validity Criteria (OECD 201):	Obtained in this study
Biomass in the control cultures should have increased exponentially by a factor of at least 16 within the 72 hour test period	77.4
Mean coefficient of variation for section-by-section specific growth rates (days 0-1, 1-2 and 2-3) in the control cultures should not exceed 35 %	13.9 %
Coefficient of variation of average specific growth rates during the whole test period between the replicate control cultures should not exceed 7 %	1.2 %

Validity Criteria (OCSPP 850.4500):	Obtained in this study
Biomass in the control cultures should have increased exponentially by a factor of at least 100 within the 96 hour test period	218.2
Coefficient of variation for mean control yield at test termination should be ≤ 15 %	8.8 %
Coefficient of variation for average specific growth rates of controls at test termination should be ≤ 15 %	1.7 %

The study conditions met all validity criteria, requested by the mentioned guidelines.
The analytical findings of AE B083813 (BCS-AW15480) in the treatment levels found on day 0 were 89.8 % to 101 % of nominal (average 97.2 %). After 72 hours analytical findings of 84.9 % to 101 % of nominal (average 92.4 %) were found and after 96 hours analytical findings of 85.2 % to 102 % of nominal (average 93.0 %) were found. All results are based on nominal test concentrations of the pure metabolite.

Results after 72 hours:

Nominal concentration [mg p.m./L]	Cell number after 72 h (means) per mL	(0-72h)-Average specific growth rates [$days^{-1}$]	Inhibition of average specific growth rate [%]
control	774 000	1.449	0.0
0.954	709 000	1.420	2.1
3.05	747 000	1.437	0.8
9.77	746 000	1.437	0.9
31.3	750 000	1.439	0.7
100	117 000	0.819	43.5*

test initiation with 10,000 cells/mL
* significantly (α=0.05, one-sided smaller) reduced, based on Williams multiple sequential t-test procedure

Results after 96 hours:

Nominal concentration [mg p.m./L]	Cell number after 96 h (means) per mL	(0-96h)-Average specific growth rates [$days^{-1}$]	Inhibition of average specific growth rate [%]
control	2 182 000	1.346	0.0
0.954	2 114 000	1.338	0.6
3.05	2 102 000	1.337	0.7
9.77	2 156 000	1.343	0.2
31.3	1 975 000	1.321	1.8*
100	226 000	0.779	42.1*

test initiation with 10,000 cells/mL
* significantly (α = 0.05, one-sided smaller) reduced, based on Williams multiple sequential t-test procedure

Summary of the results:

Average growth rate (0 - 72 h)	E_rC_{50}	>100 mg p.m./L
	LOE_rC	100 mg p.m./L
	NOE_rC	31.3 mg p.m./L
Average growth rate (0 - 96 h)	E_rC_{50}	>100 mg p.m./L
	LOE_rC	31.3 mg p.m./L
	NOE_rC	9.77 mg p.m./L

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCP 10.2.1/05; Gries, T.; 2003; M-227290-01-1
Title:	AE B066752 04 SC61 A1: Alga, growth inhibition test with *Pseudokirchneriella subcapitata* (syn. *Selenastrum capricornutum*)
Report No.:	C039863
Document No.:	M-227290-01-1
Guideline(s):	OECD: 201 (1984)
Guideline deviation(s):	--
GLP/GEP:	Yes

Objective:
The purpose of this study was to estimate the toxicity of the test item on the freshwater green alga *Pseudokirchneriella subcapitata,* previously called *Selenastrum capricornutum* (Schlösser, 1994).

Material and Methods:
Test item: AE B06675204 SC61 A1 (FLC + PCH SC 687.5), Batch No.: OP220159, light beige opaque liquid, density 1.129 g/cm^3, containing 64.7 g Fluopicolide/L and 634 g Propamocarb-HCl.
The toxicity of AEB06675204SC61A1 on growth of the freshwater green alga, *Pseudokirchneriella subcapitata*, (syn .*Selenastrum capricornutum*), was determined under static conditions over an exposure period of 72 hours.
Cultures of alga were exposed to a dilution water control and to nominal test concentrations of the test formulated product (12 replicates for the control, 3 replications of each product concentration) equal to 1.9, 4.3, 9.4, 20.7, 45.5 and 100 mg/L.
Measurements of culture density were made at test initiation (0 hours), at 24 and 48 hours and at test termination (72 hours).
The test solutions were sampled and analyzed at the beginning and the end of the test period.
Dates of experimental work: June 10, 2003 to June 13, 2003.

Findings:

Analytical findings:
Test conditions during the exposure period were:

pH:	7.67 – 7.83 pH units
Temperature:	23.7 – 25.2 °C
Light intensity	7300 – 8700 Lux

Fluopicolide was the only active substance analytically measured. Since fluopicolide is the risk driver for aquatic organisms in the formulation, analytical measurements of propamocarb are not considered necessary.
The analysis of the 0 hour test preparations for fluopicolide showed the measured concentrations to range between 82.3% and 102% of the nominal test concentrations, indicating that the test solutions were correctly dosed. Analysis of the test solutions at 72 hours showed the measured concentrations of

fluopicolide to range from 89.1% to 105% nominal for the treatment levels with 1.9 to 45.5 mg product/L. For the 100 mg product/L treatment level, 62.8% recovery was found.
There was no fluopicolide residue found in the dilution water or control samples greater that the limit of quantification.

Biological findings:
Given that the toxicity of the product cannot be attributed to any one of the active ingredients but to the product formulation as a whole, EC_{50} values and biological data are based on nominal concentrations.
Due to a high variability in the results of the growth of the control vessels, the controls of a second test which had run in parallel to this test and under the same environmental conditions are included.
The mean algal cell densities over the exposure period and the inhibition of growth rate and biomass were as follows:

Mean algal densities:

Nominal concentrations (mg/L)	Definitive test		
	Mean cell densities (x 10^4cells/mL)		
	24 hours	48 hours	72 hours
0 (control)	6.2	25.5	95.6
1.9	3.1	27.4	89.5
4.3	2.6	17.1	74.7
9.4	2.6	9.0	57.0
20.7	0.8	5.6	51.3
45.5	1.3	5.4	27.6
100	0.9	8.1	27.8

Inhibition of growth rate and biomass:

Nominal concentration (mg/L)	Area under curve at 72 h (10^4cells x days/mL)	% inhibition	Growth rate (0 - 72 h)	% inhibition
0 (control)	79.8	0	1.48	0
1.9	75.8	5.0	1.46	1.3
4.3	56.9	28.7	1.40	5.3
9.4	39.3*	50.8	1.32*	11.2
20.7	30.9*	61.3	1.28*	13.6
45.5	18.8*	76.5	1.08*	27.2
100	21.3*	73.3	1.08*	27.0

* Statistically significant difference compared to the control

Validity criteria (according to OECD 201, 2006)	Obtained in this study
Biomass increase in the control cultures by a factor of at least 16 within 72 hours. This corresponds to a specific growth rate of 0.92 day^{-1}	Biomass increased in the control cultures by a factor of 95,7 within 72 hours
Coefficient of variation for section by section specific growth rates (days 0-1, 1-2 and 2-3 for 72 hours) in the control cultures must not exceed 35%	39.7
Coefficient of variation of average specific growth rates during the whole test period in replicate control cultures must not exceed 7% in tests with *Pseudokirchneriella subcapitata* (10% for all other species)	7.52%

Conclusion:

Under the conditions of the test and based on nominal concentrations, the acute toxicity of AE B066752 04 SC61 A1 to the freshwater green alga (*Pseudokirchneriella subcapitata*) is defined as follows:

Exposure interval	72 hours
E_bC_{50} (mg/L)	13.8 (NOEC = 4.3)
E_rC_{50} (mg/L)	>100 (NOEC = 4.3)

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCP 10.2.1/04; Gries, T.; 2003; M-227284-01-1
Title:	Alga, growth inhibition test with Navicula pelliculosa AE B066752 04 SC61 A1
Report No.:	C039857
Document No.:	M-227284-01-1
Guideline(s):	OECD: 201
Guideline deviation(s):	--
GLP/GEP:	**Yes**

Objective:
The purpose of this study was to estimate the toxicity of the test item on the freshwater diatom *Navicula pelliculosa* (Schlosser, 1994).

Material and Methods:
Test item: Infinito SC Fungicide (AE B06675204 SC61 A1, FLC + PCH SC 687.5), Batch No.: OP220159, light beige opaque liquid, density 1.129 g/cm^3, containing 64.7 g Fluopicolide/L and 634 g Propamocarb-HCl).
The toxicity of Infinito SC Fungicide on growth of the freshwater diatom, *Navicula pelliculosa*, was determined under static conditions over an exposure period of 72 hours.
Cultures of alga were exposed to a dilution water control and to nominal test concentrations of the test formulated product (3 replicates for the control, 3 replications of each product concentration) equal to 0.1, 0.32, 1.0, 3.2 and 10 mg/L.
Measurements of culture density were made at test initiation (0 hours), at 24 and 48 hours and at test termination (72 hours).
The test solutions were sampled and analyzed at the beginning and the end of the test period.
Dates of experimental work: November 18, 2003 to November 21, 2003

Analytical findings:
Test conditions during the exposure period were:

pH:	7.44 – 7.50
Temperature:	21.3 – 24.0 °C
Light intensity	7700 – 8200 Lux

Fluopicolide was the only active substance analytically measured. Since fluopicolide is the risk driver for aquatic organisms in the formulation, analytical measurements of propamocarb are not considered necessary.
The analysis of the 0 hour test preparations for fluopicolide showed the measured concentrations to range between 104% and 108% of the nominal test concentrations. Analysis of the test solutions at 72 hours showed the measured concentrations of fluopicolide to range from 96.2% to 107% nominal.
There was no fluopicolide residue found in the dilution water or control samples greater than the limit of quantification.

Biological findings:
Given that the toxicity of the product cannot be attributed to any one of the active ingredients but to the product formulation as a whole, EC_{50} values and biological data are based on nominal concentrations. The mean algal cell densities over the exposure period and the inhibition of growth rate and biomass were as follows:

Mean algal densities

Nominal Concentrations (mg/L)	Definitive test Mean cell densities (x 10^4cells/mL)		
	24 hours	48 hours	72 hours
0 (control)	2.8	13.3	89.2
0.1	2.2	13.1	87.5
0.32	1.5	10.3	54.5
1.0	1.2	3.0	7.9
3.2	0.8	2.2	0.8
10	0.7	1.1	0.3

Inhibition of growth rate and biomass

Nominal concentration (mg/L)	Area under curve at 72 h (10^4cells x days/mL)	% inhibition	Growth rate (0 - 72 h)	% inhibition
0 (control)2	58.7	0	1.45	**0**
0.1	57.0	3.3	1.45	**0.5**
0.32	36.8*	37.3	1.30	**10.9**
1.0	5.7*	90.3	0.67*	**54.2**
3.2	0.9*	98.5	-0.11*	**107.3**
10	-0.6*	101	-0.37*	**125.7**

*Statistically significant difference compared to the control

Validity criteria (according to OECD 201, 2006)	**Obtained in this study**
Biomass increase in the control cultures by a factor of at least 16 within 72 hours. This corresponds to a specific growth rate of 0.92 day^{-1}	Biomass increased in the control cultures by a factor of 89.2 within 72 hours
Coefficient of variation for section by section specific growth rates (days 0-1, 1-2 and 2-3 for 72 hours) in the control cultures must not exceed 35%	32.5
Coefficient of variation of average specific growth rates during the whole test period in replicate control cultures must not exceed 7% in tests with *Pseudokirchneriella subcapitata* (10% for all other species)	2.29%

Conclusion:
Under the conditions of the test and based on nominal concentrations, the toxicity of Infinito SC fungicide to the freshwater diatom (*Navicula pelliculosa*) is defined as follows:

Exposure interval	72 hours
E_bC_{50} (mg/L)	0.40 (NOEC = 0.1)
E_rC_{50} (mg/L)	0.63 (NOEC = 0.32)

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments of the formulation but not of the active substance propamocarb hydrochloride. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Effects on growth of an additional algal species

No additional species were tested since it is not a data requirement for fungicides.

11.5.3 Acute (short-term) toxicity to other aquatic organisms

Please, consult Table 73 above additionally to the text below.

Effects on aquatic macrophytes

The most conservative endpoint that is presented in the List of Endpoints (EFSA Scientific Report 78, 2006) was obtained in the *Lemna gibba* study by Christ & Ruff (1996). In this study no toxicity of the test item was observed at the single test concentration.
The *Lemna minor* study by Bogers (2001) was noted to be acceptable and valid during Annex I inclusion. As this study explores the effects on aquatic plants at higher test concentrations than the other study, it is deemed appropriate to present the results in the context of this Annex I Renewal.

Acute toxicity to aquatic macrophytes exposed to propamocarb hydrochloride:

Test substance	Test species	Endpoint		Reference
Propamocarb-HCl	Aquatic plant *Lemna gibba*	14 d, E_rC_{50}[1]	> 18 mg a.s./L $_{nom}$	KCA 8.2.7/01 Christ & Ruff (1996) M-165250-01-1
Propamocarb-HCl SL 722	Aquatic plant *Lemna minor*	7 d, E_rC_{50}	> 919 mg a.s./L $_{nom}$ [2]	KCA 8.2.7/02 Bogers (2001) M-310632-01-1

[1] Although the report presents the endpoint based on frond number as EC_{50}, the lack of inhibition caused by the test item allows the assumption that the growth rate endpoint E_rC_{50} is also > 18 mg a.s./L
[2] The effect on growth rate of frond number was regarded the most reliable and sufficiently sensitive parameter in the evaluation of the study by the RMS (Propamocarb HCl - Volume 3: Annex B-9, Ecotoxicology, 2004)

Report:	KCA 8.2.7/01; Christ, M. T.; Ruff, D. F.; 1996; M-165250-01-1
Title:	Propamocarb hydrochloride water-miscible concentrate 68.2 percent w/w (738 g/L) Code: AE B066752 - Toxicity to duckweed (Lemna gibba, G3) in a static renewal system
Report No.:	O703/U042; A89710
Document No.:	M-165250-01-1
Guideline(s):	USEPA (=EPA): 122-2
Guideline deviation(s):	not specified
GLP/GEP:	Yes

Objective:
The toxicity of Propamocarb hydrochloride to the aquatic plant *Lemna gibba*, G3, was assessed in a static renewal test system.

Materials and methods:
Test substance: Propamocarb HCl; Batch: 140-79; Purity: 68.2% (w/w).
Cultures were maintained in the Environmental Biological Laboratory since 02, 1995.
The toxicity of Propamocarb hydrochloride to the aquatic plant *Lemna gibba*, G3, was assessed over 14 day period in a static renewal test system. Test chambers were 1200 mL crystallizing dishes containing 900 mL of test solution. Each test chamber contained 5 plants with three fronds per plant.
Six replicate *Lemna gibba* cultures with an initial frond number of 15 fronds per replicate were exposed to Propamocarb HCl in 20X-AAP medium at a concentration of 18 mg/L. There were also six control replicates without test substance. Growth and abnormal appearance of fronds were determined on Days 0, 2, 4, 7, 9 and 14. Test solutions were renewed on Days 3, 7 and 10 of the test. Test solutions were analyzed for Propamocarb hydrochloride at Day 0, 3, 7 and 10 (old and fresh solutions) and on Day 14 (old). The test was conducted in an environmental chamber designed to maintain the test conditions – test temperature of 24.1 - 27.6°C and continuous light intensity of 5100 to 5200 lux. Water quality and pH were measured on Days 3, 7 and 10 and at test termination. Test solutions were analysed by gas chromatography with nitrogen/ phosphorous detection.

Findings:
Analytical findings

The mean measured Propamocarb HCl concentration in the fresh test solutions was 14.7 mg/L (82% nominal) and 12.0 mg/L for old solutions (67% nominal). The pH of the test and control solutions ranged from 7.5 to 8.6 at test initiation. Conductivity of the exposure and control solutions ranged from 1500 to 1600 µMhos/cm. The temperature was maintained at 24°C for the duration of the study period. Light intensity was also maintained between 5100 and 5200 lux throughout the exposure period.
Biological findings:
Mean number of fronds (corrected for initial frond number) in the control and 18 mg/L treated groups on Day 14 was 2805 and 2744, respectively. The mean number of fronds increased from 15 initially to 2805 after Day 14 representing an increase of 187 times. The calculated difference in frond number between the treatment and the control was 2%. No significant decrease (α=0.05) was indicated in mean frond production between the control and the 18 mg/L treated group. No phytotoxic effects were observed. Thus, the 14-day EC_{50} was greater than 18 mg/L Propamocarb hydrochloride.

Nominal	**Mean number of fronds**						
Conc. (mg/L)	**Day 0**	**2**	**4**	**7**	**9**	**14**	**% Reduction**
Control	15	19	60	236	554	2805	
18.0	15	21	63	242	551	2744	2

Validity criteria:

Validity criteria (according to OECD 221, 2006)	**Obtained in this study**
Doubling time of frond number in the control must be less than 2.5 d (60 h), corresponding to a 7-fold increase in seven days (growth rate 0.275/d)	16-fold increase

Conclusions:

Propamocarb hydrochloride was not toxic to *Lemna gibba* at concentrations up to 18 mg/L, thus the 14-Day EC_{50} is > 18 mg/L based on a nominal concentration in respect of frond growth.

RMS' conclusion:

This study is regarded as scientifically valid and valid to be used for the toxicity assessments. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCA 8.2.7/02; Bogers, M.; 2001; M-310632-01-1
Title:	A 7-day aquatic plant toxicity test using Lemna minor with Proplant (propamocarb HCL 722 g/l)
Report No.:	329254
Document No.:	M-310632-01-1
Guideline(s):	ISO proposal: water quality - duckweed growth inhibition test (30/03/2000); OECD Guideline proposal: Lemna sp. growth inhibition test (15/12/1999)
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

Objective:

The purpose of the study is to evaluate the influence of Proplant (Propamocarb HCl 722 G/L) on the growth of aquatic plants (*Lemna minor*).

Materials and methods:

Test Substance: Propamocarb; Batch: 31491; purity: 750.5 g/L (= 691 g/kg).

Lemna minor (duckweed); (source: Delft University of Technology, Delft, the Netherlands) was exposed in a semi-static test system to Propamocarb-HCl for a period of 7-days (168 ± 2 hours) with

renewal of test solutions on Days 2 and 5. Test system and culture information: Medium used in the test was SIS-medium. Stock cultures: axenically grown in 500 ml flasks; restarted every 4 weeks; Pre-cultures: 7 to 9 days prior to test initiation with 2 or 3 plants with maximum 3 fronds each in 100 ml vessels; following validity criteria were met by preculture used for final test:

Total number of fronds increased by a factor of ≥8 in 7 days (>9); av. doubling time of fronds ≤2.5 days (≤2.0 days); no visible lesions, chlorosis, gibbosity or necrosis. There were 4 plants with a total of 10 fronds/vessel. Continuous illumination (white fluorescent) at 82-92 µE m-2 s-1 was maintained for the duration of the study. A temperature range 24.5 to 26°C was maintained throughout the exposure period. Test vessels were gently shaken to facilitate gas exchange.

The following test concentrations were tested:

- Range-finding test: 0.13 to 1330 mg Proplant/L.

- Final test: 0, 91.9, 166, 294, 515, 919 mg Propamocarb HCl/L (nominal); 3 replicates per conc., 6 replicates of control.

Sampling for analysis of test item concentration was undertaken at test initiation (t=0h), at 48 hours (= Day 2, fresh and aged sample) and at 72 hours (= Day 5, aged) of concentrations 0, 91.9, 294 and 919 mg Propamocarb hydrochloride/L.

The following measurements and recordings were also taken during the study:

- pH: at start, at each renewal and at termination in at least one vessel per concentration;
- temperature: daily in a control vessel without plants.

Biological parameters/measurements:

- frond number: at start, Days 2, 5 and 7 (=termination);
- frond appearance: at start, Days 2, 5 and 7 (=termination);
- frond biomass: at termination (Day 7) as wet weight;
- photosynthetic pigments: at termination (extraction and photometrical quantitation).

Data handling: regression and statistical analysis (ANOVA-Dunnett at p=0.05).

The concentration of the test item was performed by high performance liquid chromatography with mass spectrometric detection.

Findings:

Analytical findings

Analytical dose verification proved the initial concentration to be maintained throughout the exposure period between 85 and 100% of nominal. The pH ranged from 6.9 to 7.6 in all replicates from t = 0 h to termination; the temperature ranged from 24.5 to 25°C. The biological findings are summarised in the following tables. Growth was affected in a dose-dependent manner and the fronds in the replicates at highest concentration were visibly smaller.

Time of Sampling [day]	**Concentration**		
	Nominal [mg/L]	**Analysed [mg/L]**	**Relative to nominal [%]**
0	0	0.909	n.a.
	91.9	79.9	87
	294	264	90
	919	866	94
2 (48h-old)	0	0.0180	n.a.
	91.9	83.9	91
	294	269	91
	919	822	89
2 (fresh)	0	0.122	n.a.
	91.9	86.1	94
	294	272	92
	919	782	85

5 (72h-old)	0	0.0192	n.a.
	91.9	89.8	98
	294	287	98
	919	912	99

n.a. not applicable

Biological findings

Results are based on mean measured concentrations.

Impact of propamocarb hydrochloride on growth of *Lemna minor*

Concen-tration a.s. (mg/L)	No. of fronds on Day				Mean growth rate					
	0	2	5	7	µ (0-d)	Reduction (%)	µ (2-d)	Reduction (%)	µ (0-7d)	Reduction (%)
0	10	26	79	157	0.481	---	0.411	---	0.390	---
91.9	10	25	81	157	0.464	3.6	0.417	-1.4	0.392	-0.4
166	10	25	69	124	0.451	6.2	0.385	6.3	0.360	7.7
294	10	23	62	104	0.423	12.1	0.366	11.0	0.334	14.3
515	10	22	52	98	0.383	20.4	0.329	19.9	0.324	16.9
919	10	17	40	63	0.273	43.3	0.278	32.3	0.262	32.9

Impact of propamocarb hydrochloride on biomass of *Lemna minor*

Concentration a.s. (mg/L)	Mean wet weight in mg	SD wet weight in mg	Percentage of wet weight of control
0	459.4	152.5	----
91.9	450.3	22.5	98
166	385.1	45.7	84
294	311.7	60.0	68
515	234.3	61.6	51
919	65.4	28.6	14

Impact of propamocarb hydrochloride on pigment content of *Lemna minor*

Concentration a.s. (mg/L)	Total pigments*	
	µg/ml	Reduction in %
0	6.39	----
91.9	6.37	0
166	5.04	21
294	3.91	39
515	3.40	47
919	0.92	86

* sum of chlorophylls a and b, carotene and xanthophyll

The effect concentrations for different parameters based on the actual loadings of Proplant (Propamocarb HCl 722 G/L)

Effect parameter	NOEC (mg/L)	MATC (mg/L)	LOEC (mg/L)	EC_{10} (mg/L) (95%-confidence interval)	EC_{50} (mg/L) (95%-confidence interval)
Frond growth rate 0-7 d	220 [1]	293	390 [1]	280 (111 – 703)	5940 (1800 – 19500)
Biomass (wet weight)	390 [1]	519	690 [1]	177 (84 – 372)	564 (273 – 1170)
Chlorophyll	690 [1]	921	1230 [1]	166 (76 – 367)	543 (252 – 1170)

[1] Based on the ANOVA – Dunnet t-test, P=0.05

Validity criteria:

Validity criteria (according to OECD 221, 2006)	Obtained in this study
Doubling time of frond number in the control must be less than 2.5 d (60 h), corresponding to a 7-fold increase in seven days (growth rate 0.275/d)	Total frond number increased by a factor of > 8 in 7 days with a doubling time of < 2.5 days (average specific growth rate of > 0.275 d^{-1}

Conclusions:

The test is acceptable and valid: The average specific growth rate in controls was > 0.275 d^{-1}; dose verification proved the exposure concentrations to remain above 80% of initial values throughout the 7 days of exposure; all parameters/conditions remained within an acceptable range. The following ecotoxicological parameters are concluded: The test item affected growth significantly at > 166 mg Propamocarb hydrochloride/L.

RMS' conclusion:

This study is regarded as scientifically valid and valid to be used for the toxicity assessments. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Further testing on aquatic organisms

No further testing on aquatic organism is required.

11.6 Long-term aquatic hazard

Table 74: Summary of relevant information on chronic aquatic toxicity

Method	Species	Test material	Results[1]	Remarks	Reference
Fish 21-day prolonged toxicity studies under flow-through conditions; OECD Guidelines Number 204	*Oncorhynchus mykiss* (Rainbow trout)	propamocarb hydrochloride	NOEC = 69 mg a.s./L $_{nom}$	-	Anonymus; 1990; M-157819-02-1; KCA 8.2.2/01
Fish juvenile growth test 28 days toxicity studies under flow-through conditions; OECD revised Guideline No. 211 (Draft 1997)	*Oncorhynchus mykiss* (Rainbow trout)	propamocarb hydrochloride SL 722 (PROPLANT)	NOEC = 90 mg a.s./L $_{nom}$	-	Anonymus; 1998; M-310732-01-1; KCA 8.2.2/02
Fish early life stage toxicity test under flow-through conditionsUS EPA FIFRA 72-4	*Pimephales promelas* (Fathead Minnow)	propamocarb hydrochloride	NOEC = 6.3 mg a.s./L $_{mm}$	Result is likely to have been influenced by a temporary increase in test concentrations due to a malfunction in the dosing system which resulted in	Anonymus; 1991; M-157854-01-1

Method	Species	Test material	Results[1]	Remarks	Reference
				measured concentrations of up to 146 mg/L on day 14 (very conservative estimate of chronic toxicity)	
Fish early life stage toxicity test under flow-through conditions; OECD No. 210, US EPA OPTTS 850.1400	*Pimephales promelas* (Fathead Minnow)	propamocarb hydrochloride	NOEC = 37.5 mg a.s./L mm	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Anonymus; 2002; M-310729-01-1
Aquatic invertebrates Life-cycle/ reproductive study under semi-static test conditions; FIFRA 72-4(B)	*Daphnia magna* (water flea)	propamocarb hydrochloride	21 d NOEC = 12.3 mg a.s./L	-	Young, B. M.; Ruff, D. F.; 1996; M-165289-01-1
Aquatic invertebrates Life-cycle/ reproductive study under semi-static test conditions; OECD Guideline 202 (1984) & OECD revised Guideline No. 211 (Draft 1997)	*Daphnia magna* (water flea)	propamocarb hydrochloride	21 d NOEC = 30 mg a.s./L	-	Bogers, M.; 1998; M-310697-01-1
Static exposure conditions; Guideline FIFRA 72-3	*Americamysis bahia*	propamocarb HCL 722 g/l SL (PROPLANT)	21 d NOEC = 15 mg a.s./L	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Putt (2001); M-310709-01-1; KCA 8.2.4.2/02
Flow-through exposure conditions; Guideline FIFRA 72-3; OPPTS 580.1025	*Crassostrea virginica (eastern oyster)*	propamocarb HCL 722 g/l SL (PROPLANT)	21 d NOEC = 7.1 mg a.s./L mm	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Dionne (2001); M-310718-01-1; KCA 8.2.4.2/04
Flow-through conditions	*Crassostrea virginica* (eastern oyster)	propamocarb hydrochloride	21 d NOEC = 12 mg a.s./L	GLP/GEP: Yes. Reliable without restrictions, code 1 (Klimisch et al. (1997).	Holmes & Peters (1991); M-157857-01-1; KCA 8.2.4.2/03
Semi-static renewal test systems	*Lemna gibba*	propamocarb hydrochloride	ErC_{50} = 18 mg a.s./L	It is considered	Christ & Ruff (1996)

Method	Species	Test material	Results[1]	Remarks	Reference
				to be superseded by the ErC50 > 919 mg a.s./L which is the one to be taken into account.	M-165250-01-1 KCA 8.2.7/01
Additional studies of long-term and chronic toxicity					
	Pimephales promelas [1]	PHC	NOEC > 6.3 mg a.s./L [2]		Anonymous (1991) . M-157854-01-1 KCA 8.2.2.1/01
	Pimephales promelas	PHC	NOEC = 37.5 mg a.s./L [3]		Anonymous (2002). M-310729-01-1 KCA 8.2.2.1/02
	Daphnia magna	PHC	NOEC = 12.3 mg a.s./L		Young & Ruff (1996). M-165289-01-1 KCA 8.2.5.1/01

[1] In the EFSA conclusion (2006, 78, 1-80), instead of *Pimephales promelas,* the species *Lepomis macrochirus* is mentioned by error.

[2] The result of this study is likely to have been influenced by a temporary increase in test concentrations due to a technical malfunction in the dosing system which resulted in measured concentrations of up to 146 mg/L on day 14. Therefore, the NOEC value of > 6.3 mg propamocarb-HCl/L should be considered as a very conservative and non-realistic endpoint of chronic toxicity.

[3] This realistic endpoint value should be used for refinements or classification purpose.

Considering the propamocarb-HCl results of toxicity to the pelagic aquatic invertebrate *Daphnia magna* and is not expected to strongly adsorb or accumulate in sediments, it is not considered necessary to determine the toxicity to sediment-dwelling invertebrates.

11.6.1 Chronic toxicity to fish

Please, consult the Table 74 above, additionaly to the text below.

Chronic toxicity of propamocarb hydrochloride to fish has been investigated in two prolonged toxicity studies in the Rainbow trout (*Oncorhynchus mykiss*) under flow-through conditions (M-157819-02-1, M-310732-01-1). Additionally two early life stage toxicity tests with the Fathead minnow under flow-through conditions have been conducted (M-157854-01-1, M-310729-01-1).

According to SANCO/3268/2001 (2002) Guidance Document on aquatic ecotoxicology chronic fish testing is required in cases of DT_{50} (water) > 2 d (17.3 day from water-sediment studies) or multi-application uses. ELS is triggered by BCF > 100 and/or LC_{50} < 0.1 mg/L and/or DT_{90} (water-sediment study) > 100 d. FLC is triggered by LC_{50} < 0.1 mg/L and BCF > 1000 (DT_{95} > 14 d) and DT_{90} (water-sediment study) > 100 d or generally in cases of effects on reproduction. Based on these conditions and trigger values, only a chronic fish test according to OECD 204/215 is required for propamocarb.

In the first of the studies with *Oncorhynchus mykiss* (M-157819-02-1) the toxicity of propamocarb hydrochloride applied as Previcur N (68.6% w/w purity) to Rainbow trout was assessed over 21 days

under flow-through conditions at 15 C (±1 C). Ten juvenile fish were exposed to nominal concentrations of 0.10, 0.4, 2.0, 6.0, 25 and 100 mg/L. The fish were fed and monitored daily for mortality and sublethal (morphological and behavioural) responses. Prior to the start of exposure ten fish were randomly selected and the length and wet weight recorded. In addition, the total wet weight of fish allocated to each treatment was recorded at the start of the study (day 0), prior to exposure, and the wet weight and length of all surviving fish were recorded at the end (day 4). The average fish biomass was 0.06 – 0.14 g fish/L of test medium. The concentration of propamocarb hydrochloride in the test solutions was determined for the 0.10, 6.0 and 100 mg/L Previcur N test concentrations at test initiation, day 9 and day 21. Measured concentrations of propamocarb hydrochloride in water ranged between 55.7 and 88.4 % nominal, with a mean measured concentration of the highest treatment level of 82.6 mg/L Previcur N.
There were no treatment-related effects on mortality, fish weight or length at rates up to 100 mg/L. There were also no treatment related sublethal (morphological and behavioural) responses observed up to the highest concentration. The no observed effect concentration (NOEC) and lowest observed effect concentration (LOEC) based on mortality data and clinical signs were therefore nominally ≥ 100 mg/L and > 100 mg/L Previcur N, respectively. This was equivalent to a nominal concentration of > 69 mg/L propamocarb hydrochloride.
In conclusion, propamocarb hydrochloride had low chronic toxicity to Rainbow trout with a nominal NOEC of at least 69 mg/L.
In the second study with Rainbow trout (M-310732-01-1) the toxicity of propamocarb hydrochloride applied as Proplant (65.1% w/w purity) to Rainbow trout was assessed over 28 days under flow-through conditions at 15 C (±1 C). Twelve fish were exposed to nominal concentrations of 4.1, 9, 20, 41 and 90 mg propamocarb hydrochloride/L and a control at 0 mg test item/L. The test item was continuously freshly dosed by means of a flow-through design with a flow rate of 6 L/h. Measurements and recordings/observations shown to be appropriate and validated and included physical-chemical characteristics (dissolved oxygen (DO), pH and temperature), mortality (assessed daily), clinical signs (thrice a week vs. controls fish), size and length (all surviving fish on day 14 and termination). Analytical dose verification: Results obtained prove the concentrations at the sampling points to be, with one exception at start for concentration 4.1 mg/L, within a range of 94-130 % of nominal.
The findings, measurements and recordings prove the validity of the test system. There were no treatment-related effects on mortality, fish weight or length at rates up to 90 mg/L. There were also no treatment related sublethal (morphological and behavioural) responses observed up to the highest concentration. The 28 day NOEC was concluded as being the highest concentration the Rainbow trout were exposed to i.e. 90 mg propamocarb hydrochloride /L equivalent to 139 mg Proplant/L. Threshold levels for both effects and lethal effects were not met (i.e. > 90 mg a.s./L).

An early life stage study to determine the effects of propamocarb hydrochloride on the fathead minnow (*Pimephales promelas*) (M-157854-01-1), was conducted over 33 days (28 days post-hatch) at 25º ± 1°C under flow-through conditions.

Report:	KCA 8.2.2.1/01; Anonymous; 1991; M-157854-01-1
Title:	Propamocarb HCl: An early life stage toxicity test with the fathead minnow (Pimephales promelas)
Report No.:	244A-101; A85567
Document No.:	M-157854-01-1
Guideline(s):	US EPA FIFRA 72-4
Guideline deviation(s):	not specified
GLP/GEP:	Yes

Objective
The objective of this study was to determine the effects of Propamocarb HCl on the hatching success, survivance and growth of fathead minnows, *Pimephales promelas*, during early life stage development.

Materials and methods:
Test Substance: Previcur N; Batch: RL46/90; purity: 719.6 g/L Propamocarb hydrochloride.
An early life stage study to determine the effects of Propamocarb HCl on the Fathead minnow (*Pimephales promelas*; eggs < 24 hours old at test initiation) was conducted over 33 days (28 days post-hatch) at 25 ± 1°C under flow-through conditions.

Fathead minnow embryos were exposed to five nominal test concentrations of Propamocarb HCl; 2.69, 5.49, 10.86, 21.73 and 43.6 mg/L (mean measured concentrations were 3.5, 6.3, 13, 25 and 51 mg a.i./L). Duplicate tanks, each containing two groups of twenty embryos, were used for each test concentration and the water control. At test initiation, groups of newly fertilized embryos were placed in incubation cups and exposed to test water. Two incubation cups, each containing 20 embryos were placed in each of two replicate chambers per treatment. After hatching, larvae were released from the incubation cups into larger test chambers, where exposure to the respective control or treated water continued for 28 days. Hatching success, growth and survival were assessed over the duration of the study. Newly-hatched larvae were fed live brine shrimp nauplii at least twice daily during the first 9 days. On Days 10 through 26 post-hatch, all fish were fed live brine shrimp nauplii 3 times daily on weekdays and 2 times daily on weekends. The fish were not fed for 48 hours prior to test termination to ensure that their digestive tracts were cleared before weights were taken. On the last day of exposure, loading in the controls was 0.05 g fish per L of solution which passed through the test chamber in 24 hours. Instantaneous loading was 0.39 g fish per L of test solution in the test chamber at any given time. Dilution water was freshwater from a 45 meter deep well. The well water was characterized as medium-hard water and samples were taken weekly.
The water solubility of the test substance was indicated to be 867 g/L at 25°C.
A photoperiod of 16:8 light dark ratio was provided for the duration of the test. Hardness, alkalinity and conductivity of the negative control water were measured at the beginning and end of the test and at weekly intervals during the test. pH and dissolved oxygen were also measured daily during the first 7 days of the test and at weekly intervals thereafter. Temperature was measured continuously throughout the test period.

Findings:
A rotameter malfunction in the water delivery system was discovered on Day 15 and resulted in higher than nominal concentrations delivered to all treatment groups as indicated by the Day 14 sample analysis. The problem was corrected on Day 16 samples verified appropriate delivery of the test substance. There was a temporary increase in test concentrations due to a malfunction in the dosing system approximately two weeks after egg-hatch. This resulted in measured concentrations of up to 560 % nominal on Day 14 in all test concentrations. The highest test concentration reaching 146 mg/L (compared to 43.6 mg/L nominal).

Analytical findings:
With exception of the Day 14 concentrations (which were not included in the calculation of the study mean concentrations), the mean measured concentrations of Propamocarb hydrochloride were 3.5, 6.3, 13, 25 and 51 mg/L (i.e., 115 – 130 % nominal). Effect concentrations were reported based on the lower mean measured concentrations (i.e., effects which occurred on Day 14 were due to malfunction in delivery system and are considered not to be treatment related).

Nominal concentrations	Mean measured concentrations	
	Replicate A	Replicate B
Negative control	n.d.	n.d.
2.5	3.5	3.4
5.0	6.5	6
10	13.7	13
20	25.8	25
40	50.3	51.2

Dissolved oxygen concentrations ranged from 7.4 - 8.4 mg/L. Test temperature ranged between 24.4 and 26.1°C. pH ranged from 8.0 to 8.3 and hardness ranged from 136 to 148 mg/L as $CaCO_3$.
There was no significant difference in mean hatching success between the control and treatment groups, with survival values ranging between 91.9 and 94.7 %. In all concentrations up to 25 mg/L there was no significant difference in post-hatch survival between the control and treatment groups, with mortality ranging between 0 and 4.5 %. There was reduced survival at the 51 mg/L test concentration, and although not statistically significant, the observed reduction appeared to be treatment related. However, at the highest concentration, 51 mg/L, mean mortality was 55.8 %, with significant numbers of mortalities occurring on Day 14. These may have been attributable to a malfunction in the flow-through

apparatus on that day which resulted in a short-term elevation of the test concentration to 146 mg/L or more.
Concentrations of ≤ 6.3 mg/L produced no treatment-related effects on length or weight. In the 13 mg/L concentration there was a treatment related reduction in mean dry weight, while at 25 and 51 mg/L there were treatment-related reductions in weight and fish length. Thus, based on the most sensitive endpoint, mean dry weight after 33 days, the NOEC and LOEC were determined to be 6.3 mg/L and 13.0 mg/L Propamocarb HCl, respectively.
However, as for survival, this NOEC should be considered conservative, and is likely to have been influenced by the temporary increase in test concentrations that arose due to a malfunction in the dosing system approximately two weeks after egg-hatch. It is possible that the increase in exposure contributed to the reduced growth (weight and length) of the fish in the lower test concentrations during the last two weeks of the study.

Biological findings:

Toxicity of propamocarb hydrochloride to the early life stage of the Fathead minnow:

Parameter measured	Concentration (mg Propamocarb hydrochloride/L)					
	Control	3.5	6.3	13	25	51
Hatching Success	94.7	93.1	93.2	91.9	93.4	94.2
Survival (mean %)	97.2	95.5	97.0	100.0	95.7	54.2 [a]
Length (mm)	19.5±1.8	19.2±2.6	19.5±1.8	19.0±2.4	18.3±2.0*	16.6±2.8*
Wet weight (mg)	73.0±22.4	71.6±24.0	74.3±20.1	64.0±18.6	62.2±21.4*	52.3±23.1*
Dry weight (mg)	14.6±5.1	14.5±6.0	14.7±4.4	12.5±3.9*	12.0±4.6*	9.9±4.9*

* Statistically different from the controls; [a] see section on survival above

Toxicity of Propamocarb hydrochloride to the early life stage of the Fathead minnow:

Endpoint*	propamocarb hydrochloride
NOEC	6.3 mg/L
LOEC	13.0 mg/L

* Based on mean dry weight

Validity criteria (according to OECD 210, 26 July 2013)	Obtained in this study
Dissolved oxygen concentration in the control and test vessels is ≥ 60% throughout the test	≥78%
Measured concentration of the test substance is maintained ± 20% of the nominal concentration, or results are based on mean measured concentrations	115% - 130%
Water temperature must not differ by more than 1.5°C between test chambers and successive days and should be within 25 ± 2 °C	24.4 – 26.1 °C
Overall hatching success should be ≥ 70% and post hatch success should be ≥ 75%	Hatching success: 94.7 Survival: 97.2

Conclusion:
Propamocarb hydrochloride was of low toxicity to fish early life stages. The worst-case NOEC and LOEC for the most sensitive endpoint measured were determined to be 6.3 mg/L and 13.0 mg/L respectively. However, the NOEC should be considered conservative in the light of the temporary increase in test concentrations that arose due to a malfunction in the dosing system approximately two weeks after egg-hatch. Results are based on mean measured concentrations.

RMS' conclusion:

This study is regarded as scientifically valid and valid to be used for the toxicity assessments. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Other early life stage study to determine the effects of propamocarb hydrochloride on the fathead minnow (*Pimephales promelas*) (M-310729-01-1):

Report:	KCA 8.2.2.1/02; Gries, T.; 2002; M-310729-01-1
Title:	Proplant: Early life-stage toxicity test with fathead minnow (Pimephales promelas) under flow-through conditions
Report No.:	1038.004.122
Document No.:	M-310729-01-1
Guideline(s):	OECD No. 210, US EPA OPTTS 850.1400
Guideline deviation(s):	not specified
GLP/GEP:	**Yes**

Objective:
The aim of this study is to determine lethal and sublethal effects of Propamocarb hydrochloride on early life stages of Fathead Minnow (*Pimephales promelas*).

Material and Methods:
Test Substance: ISO common name: Propamocarb; IUPAC name: propyl 3-(dimethylamino) propylcarbamate hydrochloride; Batch: 41090; purity: 711.7 g/L.
Pimephales promelas (Fathead minnow) were used in this study. Fertilised eggs (≤ 24 hours) (source: Aquatic Research Organisms, Hampton, NH, USA) were used to initiate the study. Test vessels were impartially positioned in a waterbath containing circulating water designed to maintain the test solution temperature at 25 ± 2°C. Illumination was provided by fluorescent lamps located above the test vessels. A 16 hours light and 8 hours dark photoperiod with a 30 minute transition period was maintained throughout the test. The light intensity was maintained between 400 and 800 lux.
Egg and Fry Incubation: Following arrival at the laboratory, eggs were impartially distributed to the egg incubation cups following an initial transfer into petri dishes until each egg cup contained 60 eggs. To start the exposure (day 0), the egg incubation cups, were then suspended in the respective exposure vessels (one cup per replicate vessel). The egg cups were oscillated at 2rpm in the test solution.
Following completion of hatch, 40 randomly selected larvae were transferred into the larva chambers (approx. 1 L glass jars). On Day 10 (post-hatch), the fry was released from the larval chambers into the exposure vessels. Directly after completion of hatch, the fry was fed live brine shrimp at least twice daily on working days and once on weekends. At each feeding, fry was fed excess of live brine shrimp ad libitum such that all fry were afforded equal access to food. Representative samples of the food source were periodically analysed for the presence of contaminants. Fish were not fed during the 24 hours prior to sacrificing them for weight and length measurements on day 28 (post-hatch) (32 days after the start of the exposure).
Eggs and larvae were exposed to various test concentrations and control (0, 2.50, 5.00, 10.0, 20.0 and 40.0 mg Propamocarb HCl/L, nominally, two replicates per concentration) under continuous flow conditions for 32 days (28 days post-hatch). The test item was diluted in modified fish medium to reach test solutions.
Doses in test solutions were verified at test initiation in all replicates, then weekly in alternating replicates, and again in all replicates on Day 32 (= termination of exposure).
Observations and measurements:
Biological observations: mortality and adverse effects daily, counts of eggs daily, counts of larvae (post-hatch) on Days 0, 10 and 28; Phys.-chem. measurements: pH, DO (dissolved oxygen) and temperature on Days 0, 7, 14, 19, 26 and 32 in all vessels/replicates (temperature was measured as single point, in one control vessel continuously); hardness and alkalinity on days 0 and 32 in all replicate vessels, on Days 6 and 14 in one replicate each of control and highest concentration.

Findings:

The measured water temperatures ranged from 24.3 to 25.6°C (mean: 25.1 ± 0.3 °C), the continuously measured temperature ranged from 23.0 to 26.1°C. The dissolved oxygen concentrations ranged from 5.50 to 8.71 mg/L (mean: 7.65 ± 0.76 mg/L) which is equivalent to 69 to 110 % of the air-saturation value (mean 96 ± 9 %). The pH ranged from 7.02 to 7.71 (mean: 7.3 + 0.2).

Analytical findings:
The mean measured concentrations were determined as 2.63 (± 34%), 4.05 (± 40%), 9.25 (± 9.9%), 20.0 (± 8.5%) and 37.5 (± 1.8%) mg Propamocarb hydrochloride/L. Interpretation of biological observations was based on mean measured concentrations.
Hardness and alkalinity measured weekly in the highest test concentration and the control ranged from 152 to 172 mg/L and from 26 to 30 mg/L respectively both expressed as CaCO3.
These water quality conditions were within those stated in the guidelines and were suitable to promote the embryo hatchability, larval survival and larval growth (egg hatchability at 80%, post-hatch success 88%, rel. s. d. of wet weight of control at 35%). During the 28-day post-hatch exposure period, biomass loading did not exceed 0.51 g/L or 0.077 g/L per 24 hours in any replicate test vessel.

Biological findings:
Two days after the exposure the egg mortality at the different treatment levels ranged from 13 to 22% of the exposed eggs. Statistical analysis verified that the differences to the control were not statistically significant. Four days after start of the exposure, hatch was complete in all test solutions and the controls. After completion of the hatch, egg hatchability of the exposed eggs averaged 80% in the control and thus fulfils the quality criterion of > 66% hatching success as given in the relevant guideline. All parameters measured are presented in Table below.

Toxicity of Propamocarb HCl to the early life stage of the Fathead minnow:

Mean Concentration (mg a.s./L)	Hatching success (%)	Post-hatch success (%)	Total length on Day 28 post-hatch (mm)	Wet weight on Day 28 post-hatch (mg/fish)	Dry weight on Day 28 post-hatch (mg/fish)
0	80	88	23.0 (±2.5)	119 (±41)	28.6 (±11)
2.63	75	96	23.1 (±2.3)	120 (±38)	28.3 (±8.8)
4.05	85	89	24.3 (±3.6)	128 (±55)	30.1 (±14)
9.25	82	90	22.7 (±3.7)	105 (±43)	27.2 (±11)
20.0	84	96	23.5 (±3.2)	125 (±47)	28.9 (±12)
37.5	86	81	24.1 (±2.7)	132 (±42)	31.1 (±10)

Directly after hatching no deformed larvae were observed in any of the test solutions or the control. During the study exposure period, single deformed fry was observed. However, no dose response was observed (2 in the control, 1 in 4.05, 2 in 9.25 and 1 in 37.5 mg/L treatment groups) and therefore the deformities were not test substance related. Other signs of sublethal effects such as loss of equilibrium, respiratory function, exophthalmus, feeding activity, reaction to external stimuli and changes in the coloration were not observed in any of the test solutions and the control.

Validity criteria (according to OECD 210, 2013)	Obtained in this study
Water temperature does not differ more than ± 1.5°C between chambers/successive days and is within the recommended range for the test species (25 ± 1.5°C)	24.3 to 25.6 °C(mean 25.1 0.3 °C, single point measurements)
Dissolved oxygen concentration in the control and test vessels is ≥ 60% throughout the test	69 to 110%
Chemical analysis is performed	Yes
Survival of fertilised eggs is at least 70 % and post-hatch success is at least 75 % in controls for *P. promelas*	Egg hatchability in the control group was 80 %, post-hatch was success was 88 %

Conclusion:
Propamocarb hydrochloride had no statistically significant negative effect on any of the endpoints (summarised above) up to 37.5 mg/L during hatch and 28 days post-hatch (= fish early life stage). Hence, the overall NOEC is 37.5 mg Propamocarb hydrochloride/L, and the LOEC is concluded to be > 37.5 mg Propamocarb hydrochloride/L.

RMS' conclusion:

This study is regarded as scientifically valid and valid to be used for the toxicity assessments. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Fish full life cycle test

Since Propamocarb hydrochloride is of low acute and chronic toxicity to fishes, has a low BCF (< 50) and is not persistent in water or sediment (DT_{90} < 100 days), it is not considered necessary to perform a fish full life-cycle study.

11.6.2 Chronic toxicity to aquatic invertebrates

Please, consult the Table 74 above, additionaly to the text below.
Long-term and chronic toxicity of propamocarb hydrochloride to aquatic invertebrates has been investigated in life-cycle/ reproductive studies on the water flea (*Daphnia magna*) under semi-static test conditions (M-165289-01-1, M-310697-01-1).
The chronic toxicity of propamocarb hydrochloride to *Daphnia magna* was assessed in a static renewal test system (M-165289-01-1). *Daphnia magna* neonates (< 24 hours old) were exposed to nominal concentrations of 15.6, 31.3, 62.5, 125 and 250 mg propamocarb hydrochloride/L for a 21 day period. A control treatment containing no test material was also tested. In line with EPA guideline requirements, all treatments consisted of ten individual replicate vessels containing a single daphnid and three replicates containing 5 daphnids per chamber. Daphnids were fed with algae plus a commercial fish food suspension during the study. Survival, growth and behaviour were observed for the duration of the study. Fresh test solutions were prepared every 2 to 3 days. Following organisms observations and water quality measurements on the fresh solutions were performed, all surviving parental daphnids were transferred by glass pipette into clean test chambers containing fresh test solution. At study termination, all surviving daphnids were measured and then dried for 96 hours at which point they were weighed. Samples of the freshly prepared and old test solutions were analysed for propamocarb hydrochloride using gas liquid chromatography (GLC) with nitrogen/phosphorous detection. Test temperature was monitored continuously throughout the study. Dissolved oxygen, pH and specific conductivity were obtained at each renewal period.
The test was rated as acceptable since all test conditions remained within the stipulated ranges. Mean measured concentrations were 12.3, 24.7, 49.4, 102 and 198 mg propamocarb hydrochloride/L. All end points are subsequently reported based on the mean measured concentrations of propamocarb hydrochloride. *Daphnia* survival during the 21 day exposure exhibited a definite dose response. Survival in the control, 12.3, 24.7, 49.4, 102 and 198 mg Propamocarb hydrochloride/L was 88, 88, 96, 96, 12 and 16%, respectively. At concentrations of 102 and 198 mg/L a significant decrease ($P \leq 0.05$) in parent survival was observed when compared to controls. Due to the survival effect at concentrations of 102 and 198 mg/L, subsequent data at these concentrations were excluded from further statistical analysis.
Initial neonate production occurred on average at day 8 for controls and all concentrations except 102 and 198 mg/L. The 102 mg/L concentration averaged first brood at day 10, while the 198 mg/L concentration had no neonate production. No immobile or dead young were observed at any concentration. The total young per surviving adult was significantly different ($P \leq 0.05$) at the 49.4 mg/L concentration compared to the controls.
Daphnia dry weight was significantly different ($P \leq 0.05$) at concentrations of 24.7 and 49.4 mg/L when compared to controls. *Daphnia* length was significantly different ($P \leq 0.05$) at concentrations of 24.7 and 49.4 mg/L compared to controls.
Due to insufficient mortality, the day 7 and 14 EC_{50} values were estimated to be greater than 198 mg/L. The day 21 EC_{50} value was calculated to be 74.6 mg/L.
Daphnid growth was determined by individual weight and length data at the study termination. Daphnids in the control, 12.3, 24.7, 49.4, 102 and 198 mg Propamocarb hydrochloride/L treatments had a mean dry weight of 0.66, 0.60, 0.57, 0.48, 0.07 and 0.04 mg, respectively. *Daphnia* dry weight was

significantly different ($P \leq 0.05$) at concentrations of 24.7 and 49.4 mg/L when compared to controls. Daphnids in the control, 12.3, 24.7, 49.4, 102 and 198 mg propamocarb hydrochloride/L treatments had a mean length of 5.2, 5.1, 5.1, 4.7, 3.8 and 2.0 mm, respectively. *Daphnia* length was significantly different ($P \leq 0.05$) at concentrations of 24.7 and 49.4 mg/L compared to controls.
Based on the most sensitive endpoint in this study (growth), the NOEC was 12.3 mg propamocarb hydrochloride/L and the LOEC was 24.7 mg propamocarb hydrochloride/L. The MATC was calculated as the geometric mean of the LOEC and the NOEC and was determined to be 17.4 mg Propamocarb hydrochloride/L.
In a second study M-310697-01-1, a *Daphnia magna* reproduction test with Proplant have been performed. For the test young *Daphnia magna* neonates with age < 24 hours were selected. The study was conducted as a semi-static test (renewal of test solutions 3x per week) carried out in 10x100 ml glass vessels (with one neonate per vessel and 50 ml M7) per concentration (controls: 20x) for a period of 21 days. Daphnids were fed alga (*Chlorella pyrenoidosa*) 3x per week (corresponding to 0.1 mg C/daphnia and day). Daphnids were exposed individually to 0, 3.0, 6.5, 14, 30 and 65 mg propamocarb hydrochloride/L (the selection was based on the fact that the EC_{10} for fresh water alga was <100 mg Proplant/L and the 48 hours EC_{50} for the daphnids >100 mg propamocarb hydrochloride/L). The test was conducted under controlled environmental conditions and analysis of test item concentration (dose verification) was undertaken. For parental daphnids daily biological recordings/observations included the immobility (including mortality) and presence of eggs in brood pouch. For the F1-generation biological recordings/observations included number of neonates and unhatched eggs and immobility (including mortality). *Daphnia* reproduction was expressed as mean number of living young per parent. The results were statistically analysed. Physical-chemical parameters measured throughout the experiment included pH, dissolved oxygen (DO) and temperature.
The findings, measurements and recordings prove the validity of the test system with dose verification, physical-chemical parameters, mortality in controls and average cumulative numbers of young per female in the controls at 21 days were all within the acceptable ranges. Mortality of parental *Daphnia magna* in chronic exposure to propamocarb hydrochloride was not observed for nominal concentrations ≤ 30 mg propamocarb hydrochloride/L. For a nominal concentration of 65 mg propamocarb hydrochloride/L at day 21 total parental mortality of 50% was observed.
Statistical analysis of reproduction performances (ANOVA-Tukey, p= 0.05) revealed significant inhibition between controls and concentrations 6.5 and 65 mg/L however, this is not dose dependant and therefore is not considered to be a treatment related effect at the 6.5 mg/L level. The appearance of eggs and, subsequently, neonates was delayed by approximately one day at 65 mg/L. Immobilisation (including mortality) was not significant (<10%) at all concentrations.
In conclusion, when compared to the acute toxicity test, the mortality was expressed at lower test concentrations with prolonged exposure. The toxicological parameters determined/derived are:

- 21-day EC_{50} for parental immobility: 65 mg propamocarb hydrochloride/L
- 21-day EC_{50} for reproduction: ≥65 mg propamocarb hydrochloride/L
- LOEC: 65 mg propamocarb hydrochloride/L
- NOEC: 30 mg propamocarb hydrochloride/L

Report:	KCA 8.2.5.1/01; Young, B. M.; Ruff, D. F.; 1996; M-165289-01-1
Title:	Propamocarb hydrochloride water-miscible concentrate 68.2 percent w/w (738 g/L); Code AE B066752: Effects on life-cycle of the water flea (*Daphnia magna*) in a static renewal system.
Report No.:	A89730; O008A/U037
Document No.:	M-165289-01-1
Guideline(s):	USEPA (=EPA): FIFRA 72-4(B)
Guideline deviation(s):	--
GLP/GEP:	Yes

Objective
The chronic toxicity of propamocarb hydrochloride to the water flea, *Daphnia magna*, was assessed in a static renewal test system.

Materials and methods:

Test Substance: (propamocarb HCl); Batch: 140-79; purity: 68,2 % w/w (738 g/L)
The chronic toxicity of propamocarb HCl to *Daphnia magna* Strauss was assessed in a static renewal test system. *Daphnia magna* neonates (< 24 h old) were exposed to nominal concentrations of 15.6, 31.3, 62.5, 125 and 250 mg Propamocarb HCl/L for a 21 day period. A control treatment containing no test material was also tested.
Daphnia magna were obtained from an in-house culture at AgrEvo Research Center, Pikeville, NC. Dilution water was synthetic hard fresh water with a hardness range of 160 to 180 mg/L $CaCO_3$. In addition, selenium (SeO_2) and Vitamin B_{12} were supplemented at a concentration of 1 µg/L. The photoperiod was 16 hours light and 8 hours dark at 400 to 800 lux. Test chambers were 100 mL and 600 mL glass beakers for individual and group daphnids, respectively. Test chambers for individuals and groups contained approximately 80 mL and 400 mL of solution, respectively.
In line with EPA guideline requirements, all treatments consisted of ten individual replicate vessels containing a single daphnid and three replicates containing 5 daphnids per chamber. Daphnids were fed (green algae plus a commercial fish food suspension) during the study. Survival, growth and behaviour were observed for the duration of the study.
Fresh test solutions were prepared each Monday, Wednesday and Friday. Following organism observations and water quality measurements on the fresh solutions were performed, all surviving parental Daphnids were transferred by glass pipette into clean test chambers containing fresh test solution.
Starting on Day 6, all individual daphnids were checked daily for initial neonate production. The time to first brood was recorded for each replicate. Following the onset of neonate production for the individual daphnids, all living, dead or immobile neonates were counted and removed from test chambers each Monday, Wednesday and Friday.
At study termination, all surviving daphnids were measured and then dried for 96 hours at which point they were weighed.
Samples of the freshly prepared and old test solutions were analysed for propamocarb HCl using gas liquid chromatography (GLC) with nitrogen/phosphorous detection. Test temperature was monitored continuously throughout the study. Dissolved oxygen, pH and specific conductivity were obtained at each renewal period.

Findings:
Analytical findings:
Mean measured concentrations were 12.3, 24.7, 49.4, 102 and 198 mg propamocarb HCl/L. All endpoints are subsequently reported based on the mean measured concentrations of propamocarb hydrochloride. Temperature during the study ranged from 19.5 - 19.9°C; pH ranged from 7.1 - 8.1. Dissolved oxygen ranged from 97 - 101% saturation. Specific conductivity ranged from 500 to 600 µMhos. Results are based on mean measured concentrations.

Nominal concentration (mg/L)	Mean measured concentration (mg/L)	Percent nominal
Dilution water	<IDL	<IDL
Control	<IDL	<IDL
15.6	12.3	79%
31.3	24.7	79%
62.5	49.4	79%
125	102	82%
250	198	79%

Daphnia survival during the 21 day exposure exhibited a definite dose-response. Survival in the control, 12.3, 24.7, 49.4, 102 and 198 mg propamocarb HCl/L was 88, 88, 96, 96, 12 and 16% respectively. At concentrations of 102 and 198 mg/L, a significant decrease ($P \leq 0.05$) in parent survival was observed when compared to controls. Due to the survival effect at concentrations of 102 and 198 mg/L, subsequent data at these concentrations were excluded from further statistical analysis.

Biological findings:

Initial neonate production occurred on average at Day 8 for controls and all concentrations except 102 and 198 mg/L. The 102 mg/L concentration averaged first brood at Day 10, while the 198 mg/L concentration had no neonate production. No immobile or dead young were observed at any concentration. The total young per surviving adult was significantly different ($P \leq 0.05$) at the 49.4 mg/L concentration, compared to the controls.
Daphnia dry weight was significantly different ($P \leq 0.05$) at concentrations of 24.7 and 49.4 mg/L when compared to controls. Daphnia length was significantly different ($P \leq 0.05$) at concentrations of 24.7 and 49.4 mg/L compared to controls.
Due to insufficient mortality, the Day 7 and 14 EC_{50} values were estimated to be greater than 198 mg/L. The Day 21 EC_{50} value was calculated to be 74.6 mg/L.

Summary of effects of propamocarb-HCl on *Daphnia magna* over 21-day exposure period:

Nominal (Mean Measured)Concentration mg/L	Survival on Day 21(%)	Mean length (mm)	Dry weight (mg)	Mean Total Young/Adult [a]	Day to firstbrood [b]
Control	88	5.2	0.66	238	8
15.6 (12.3)	88	5.1	0.60	243	8
31.3 (24.7)	96	5.1*	0.57*	237	8
62.5 (49.4)	96	4.7*	0.48*	195*	8
125 (102)	12	3.8	0.07	86 [c]	8
250 (198)	16	2.0	0.04	- [c]	8

[a] Total young per surviving adult following 21 days exposure; [b] Observed daily for the presence of neonates from Day 6 until first brood noted
[c] Not included in statistical analysis since there was a survival effect; *Significant difference ($P \leq 0.05$) from control group by Wilcoxon Rank Sum test

Daphnid growth was determined by individual weight and length data at the study termination. Daphnids in the control, 12.3, 24.7, 49.4, 102 and 198 mg propamocarb HCl/L treatments had a mean dry weight of 0.66, 0.60, 0.57, 0.48, 0.07 and 0.04 mg respectively. Daphnia dry weight was significantly different ($P \leq 0.05$) at concentrations of 24.7 and 49.4 mg/L when compared to controls. Daphnids in the control, 12.3, 24.7, 49.4, 102 and 198 mg propamocarb HCl/L treatments had a mean length of 5.2, 5.1, 5.1, 4.7, 3.8 and 2.0 mm respectively. Daphnia length was significantly different ($P \leq 0.05$) at concentrations of 24.7 and 49.4 mg/L compared to controls.

Chronic toxicity of propamocarb hydrochloride to *Daphnia magna:*

Time	EC_{50} values (mg Propamocarb HCl/L)
Parental Data	
7-day EC_{50}	>198
21-day EC_{50}	74.6 (95% C.I.: 67 – 83.7)
Reproduction Data	
NOEC (based on growth)	12.3
LOEC	24.7

Validity criteria:

Validity criteria (according to OECD 211, 2012)	Obtained in this study
Mortality of the parent animals (females) in the controls does not exceed 20% at the end of the test	12%
Mean number of living offspring produced per parent animal surviving at the end of the test in the controls is ≥ 60	238

Dissolved oxygen concentration and pH were in the recommended range of the OECD guideline 211.

Conclusion:

Based on the most sensitive endpoint in this study (growth), the NOEC was 12.3 mg/L propamocarb hydrochloride and the LOEC was 24.7 mg/L. The MATC was calculated as the geometric mean of the LOEC and the NOEC and was determined to be 17.4 mg propamocarb hydrochloride/L.

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Report:	KCA 8.2.5.1/02; Bogers, M.; 1998; M-310697-01-1
Title:	*Daphnia magna*, reproduction test with Proplant (semi-static)
Report No.:	220771
Document No.:	M-310697-01-1
Guideline(s):	OECD Guideline 202 (1984) and OECD revised Guideline No. 211 (Draft 1997)
Guideline deviation(s):	not specified
GLP/GEP:	Yes

Objective:
The study investigated the effects of propamocarb hydrochloride on mobility and reproductive performance in *Daphnia magna* during 21 days of exposure.

Material and Methods:
Test Substance: propamocarb hydrochloride; Batch: 05370; purity: 651 g/kg.
Daphnia magna, Crustacea, Cladocera (Straus, 1820) from an in-house culture, were used during this study. For the test young *Daphnia magna* neonates with age < 24 hours were selected.
The study was a semi-static test (renewal of test solutions 3x per week) carried out in 10 x 100 mL glass vessels (with one neonate per vessel and 50 mL M7) per concentration (controls: 20x) for a period of 21 days. Daphnids were fed alga (*Chlorella pyrenoidosa*) 3x per week (corresponding to 0.1 mg C/daphnia and day).
Daphnids were exposed individually to 0, 3.0, 6.5, 14, 30 and 65 mg propamocarb-HCl/L (the selection was based on the fact that the EC_{10} for fresh water alga was <100 mg/L Proplant, and the 48h-EC_{50} for the daphnids >100 mg/L propamocarb-HCl).
Test vessels were 8 x Ø 4cm with a volume of 100 mL. A photoperiod of 16 hours per day at approx. 600 lux was maintained for the duration of the study.
Sampling for analysis of test item concentration (dose verification) was undertaken as follows:
- At start (t=0 h): all freshly prepared test solutions
- Day 2: fresh solutions at 3.0 and 65 mg/L a.s. as well as control (48 hours old);
- Days 7 and 14: fresh solutions at 3.0, 65 mg/L a.s. (renewal) and control;
- Days 9 and 16: 48h-old solutions at 3.0, 65 mg/L a.s. (to be renewed) and control;
- Day 19: 72h-old solutions (prepared Day 16) at 3.0, 65 mg/L a.s. and control;

The following biological recordings/observations were undertaken:
Parental daphnids: immobility (incl. mortality) and presence of eggs in brood pouch; frequency: daily
F1-generation: no. of neonates and unhatched eggs, immobility (incl. mortality).
Phys.chem. parameters measured were as follows:
pH: at start and just before and after each renewal in one of the vessel of the control and the highest concentration
dissolved oxygen (DO): at start and just before and after each renewal in all test solutions/vessels
temperature: at each renewal in one of the control vessels.
Daphnia reproduction was expressed as mean number of living young per parent. The results were statistically analysed.

Findings:

Analytical findings:
Analytical dose verification at each dosing stage proved the concentrations to be maintained throughout the exposure period at 97 to 119% of nominal with the exception of the highest concentration after 72 h

of aging (65 mg/L treatment had only 30% recovery – this was considered to be an outlier as concentration after 48 h was 110% of nominal).
pH ranged from 7.6 to 8.2 throughout the exposure period; DO varied between 9.6 (day 0) and 8.4 mg O_2/L (day 21), the temperature ranged from 19.8 to 20.6°C.

Biological findings:

The biological observations are summarised below.

Mortality of parental *Daphnia magna* in chronic exposure to Propamocarb hydrochloride

Nominal Conc. a.s. (mg/L)	Number exposed	Cumulative mortality on Day										Total mortality (%)
		0-8	9	12	13	14-15	16	17-18	19	20	21	
0.0 (control)	20	0	1	1	1	1	1	1	2	2	2	10
3.0	10	0	0	0	1	1	1	1	1	1	1	10
6.5	10	0	0	0	0	0	0	0	0	0	0	0
14	10	0	0	0	0	0	0	0	1	1	1	10
30	10	0	0	0	0	0	0	0	0	0	0	0
65	10	0	0	0	0	0	2	2	4	4	5	50

The reproduction yielded is shown in the following mean numbers of living young with performance expressed as percentage of control results (set to 100%).

Cumulative mean number of living offspring and percentage of yield relative to the controls

Nominal Conc. a.s. (mg/L)	Day 12		Day 14		Day 16		Day 19		Day 21	
	mean	%	mean	%	mean	%	mean	%	mean	%
0.0 (control)	31.6	100	53.9	100	60.2	100	78.3	100	99.8	100
3.0	28.0	89	50.8	94	56.2	93	69.0	88	86.2	86
6.5	28.5	90	41.8	78	46.4	77	59.6	76	74.9	75
14	40.8	129	69.5	129	69.6	116	86.3	110	110.0	110
30	33.5	106	60.8	113	61.0	101	79.3	101	99.2	99
65	32.3	102	50.4	94	64.3	107	65.3	83	76.0	76

Statistical analysis (ANOVA-Tukey, p= 0.05) of above reproduction performances revealed significant inhibition between controls and concentrations 6.5 and 65 mg/L. However, this is not dose dependant and therefore it is not considered to be a treatment related effect at the 6.5 mg/L level. The appearance of eggs and, subsequently, neonates was delayed by approximately one day at 65 mg/L. Immobilisation (incl. mortality) was not significant (<10%) at all concentrations. The findings, measurements and recordings prove the validity of the test system:

- Mortality in controls: < 20%
- Average cumulative numbers of young per female in the controls at 21 days was 99.8 (s.d. 10.4; requirement ≥ 60), dose verification, phys.chem. parameters were all within the acceptable ranges and recoveries.

Validity criteria:

Validity criteria (according to OECD 211, 2012)	Obtained in this study
Mortality of the parent animals (females) in the controls does not exceed 20% at the end of the test	<20%
Mean number of living offspring produced per parent animal surviving at the end of the test in the controls is ≥ 60	99.8

Conclusions:
Propamocarb-HCl did not affect the survival or the reproductive capacity of parental *Daphnia* at concentrations up to and including 46 mg Proplant/L, corresponding to 30 mg a.i./L.

When compared to the acute toxicity test, the mortality was expressed at lower test concentrations with prolonged exposure. The toxicological parameters determined/derived are summarised below:

Chronic toxicity of propamocarb hydrochloride to *Daphnia magna*

Parameter	Propamocarb hydrochloride (mg/L)
21-day EC_{50} for parental immobility	65
21-day EC_{50} for reproduction	≥ 65
LOEC	65
NOEC	30

RMS' conclusion:
This study is regarded as scientifically valid and valid to be used for the toxicity assessments. Reliability: Reliable without restrictions, code 1 (according to Klimisch et al.,1997).

Please, refer to the point 11.5.2 of this CLH Report for a summary of the following studies (since is also presented in the referred point):

- Putt (2001), M-310709-01-1, KCA 8.2.4.2/02;
- Dionne (2001), M-310718-01-1, KCA 8.2.4.2/04;
- Holmes & Peters (1991), M-157857-01-1, KCA 8.2.4.2/03.

Reproductive and development toxicity to an additional aquatic invertebrate species

Chronic studies with aquatic gastropods are not triggered, according to the Guidance Document on Aquatic Ecotoxicology (SANCO/3268/2001), as Propamocarb-HCl is not intended to be sprayed directly to water.

Development and emergence in *Chironomus* species

Chronic studies with other aquatic insects are not triggered, according to the Guidance Document on Aquatic Ecotoxicology (SANCO/3268/2001), as propamocarb-HCl is not intended to be sprayed directly to water. Moreover, chronic testing of aquatic insects is not necessary if it is evident that daphnia is representative of the insects, which is also the case for propamocarb-HCl. This fungicide exhibits only limited toxicity to aquatic invertebrates.

Sediment dwelling organisms

Since Propamocarb-HCl has been shown to have very low toxicity to the pelagic aquatic invertebrate *Daphnia magna* and is not expected to strongly adsorb or accumulate in sediments, it is not considered necessary to determine the toxicity to sediment-dwelling invertebrates.

11.6.3 Chronic toxicity to algae or other aquatic plants

Please, consult the Table 74 above and the point 11.5.2 additionaly to the text below.
Chronic toxicity effects of propamocarb hydrochloride on aquatic plants has been studied in two experiments (M-165250-01-1, M-310632-01-1) in (semi) static renewal test systems.
In the first of these studies (M-165250-01-1) the toxicity of propamocarb hydrochloride to the aquatic plant *Lemna gibba*, G3, was assessed over a 14 day period. *Lemna gibba* cultures with an initial frond number of 15 fronds per replicate were exposed to propamocarb hydrochloride in 20X-AAP medium at a concentration of 18 mg/L. There were also six control replicates without the test substance. Growth and abnormal appearance of fronds were determined on day 0, 2, 4, 7, 9 and 14. Test solutions were

renewed on day 3, 7 and 10 of the test. Test solutions were analysed for propamocarb hydrochloride at day 0, 3, 7 and 10 (old and fresh solutions) and on day 14 (old). The test was conducted in an environmental chamber designed to maintain the test conditions.
The mean measured propamocarb hydrochloride concentration in the fresh test solutions was 14.7 mg/L (82% nominal) and 12.0 mg/L for old solutions (67% nominal). Mean number of fronds (corrected for initial frond number) in the control and 18 mg/L treated groups on day 14 was 2805 and 2744, respectively. The mean number of fronds increased from 15 initially to 2805 after day 14 representing an increase of 187 times. The calculated difference in frond number between the treatment and the control was 2%. No significant decrease (α=0.05) was indicated in mean frond production between the control and the 18 mg/L treated group. No phytotoxic effects were observed.
In conclusion, propamocarb hydrochloride was not toxic to *Lemna gibba* at concentrations up to 18 mg/L, thus the 14 day EC_{50} is > 18 mg/L based on a nominal concentration in respect of frond growth.
In the second of these experiments (M-310632-01-1) a 7-day aquatic plant toxicity test using *Lemna minor* was conducted in a semi-static test system with Propamocarb hydrochloride applied as Proplant (Batch: 31491; purity: 69.1%). Experimental phase included a range-finding test with concentrations from 0.13 to 1330 mg Proplant/L.
Set-up of the final test included the concentrations 0, 91.9, 166, 294, 515, 919 mg propamocarb hydrochloride/L (nominal) and was conducted with 3 replicates per concentration and 6 replicates of control. Sampling for analysis of test item concentration was undertaken at test initiation (t=0 hour), at 48 hours (= day 2, fresh and aged sample) and at 72 hours (= day 5, aged) of concentrations 0, 91.9, 294 and 919 mg propamocarb hydrochloride/L.
The following measurements and recordings were taken during the study: pH, temperature, frond number at start, day 2, 5 and 7, frond appearance at start, days 2, 5 and 7, frond biomass as wet weight at termination at day 7, photosynthetic pigments (extraction and photometrical quantitation) at termination and statistical analysis (ANOVA-Dunnett at p=0.05).
Analytical dose verification proved the initial concentration to be maintained throughout the exposure period between 85 and 100% of nominal. The findings, measurements and recordings prove the validity of the test system with dose verification and physical-chemical parameters were all within the acceptable ranges. Growth was affected in a dose-dependent manner and the fronds in the replicates at highest concentration were visibly smaller. The average specific growth rate in controls was > 0.275 d^{-1}, the dose verification proved the exposure concentrations to remain above 80% of initial values throughout the 7 days of exposure and all parameters/conditions remained within an acceptable range. Therefore the following ecotoxicological parameters are concluded: The test item affected growth significantly at > 166 mg propamocarb hydrochloride/L.

11.6.4 Chronic toxicity to other aquatic organisms

Since propamocarb hydrochloride is not applied directly to water there is no requirement to conduct chronic toxicity studies with other aquatic organisms. The Guidance Document on Aquatic Ecotoxicology (Sanco/3268/2001) recommends chronic testing of aquatic insects only under special circumstances, when there is evidence that Daphnia are not representative of insects. Propamocarb hydrochloride is a fungicide that in general exhibits only limited toxicity to aquatic invertebrates and there is no evidence that insects are more susceptible to it than *Daphnia*. Since Propamocarb hydrochloride is not applied directly to water there is no requirement to conduct chronic toxicity studies with aquatic gastropods. Not performed.

11.7 Comparison with the CLP criteria

According to the criteria of the CLP (Regulation 1272/2008/EC), the intrinsic hazard to aquatic organisms is represented by both the acute and long-term hazard of a substance. The core classification system for substances consists of one acute hazard classification category and four long-term hazard classification categories. The acute and the long-term hazard classification categories are applied independently.

The criteria for classification of a substance in category Acute 1 are defined on the basis of acute aquatic toxicity data only (EC_{50} or LC_{50}). The criteria for classification of a substance into the categories Chronic 1 to Chronic 3 follow a tiered approach where the first step is to see if available information on chronic

toxicity merits long-term hazard classification. If adequate chronic toxicity data are available, the next step is to consider if the substance is rapidly degradable or not. In absence of adequate chronic toxicity data, category Chronic 4, the subsequent step is to combine two types of information, i.e. acute aquatic toxicity data and environmental fate data (degradability and bioaccumulation data).

Endpoint	**Classification criteria CLP (Regulation 1272/2008/EC) for propamocarb hydrochloride**	**Relevant data for propamocarb hydrochloride**
Degradation	Convincing scientific evidence that the PHC can be degraded (biotically and/or abiotically) in the aquatic environment to a level > 70 % within a 28-day period. Tests based on dissolved organic carbon: 70 % (28-day ready biodegradation studies) Tests based on oxygen depletion or carbon dioxide generation: 60 % of theoretical maximum (28-day ready biodegradation studies) BOD5/COD is ≥ 0,5	Rapidly degradable in water, sediment and whole aquatic system. $t_{1/2}$ biodegradation in water/sediment: DT50 = 8.7 days $t_{1/2}$ biodegradation in soil: DT50 = 6.5 days $t_{1/2}$ (hydrolysis): stable $t_{1/2}$ (photolysis): stable **Rapidly degradable.**
Bioaccumulation	log K_{ow} >4 and/or experimentally determined BCF ≥ 500	log K_{ow} < 1 (pH 5, 7 and 9) BCF = 4.7 (*Lepomis macrochirus*; measured) **Not bioaccumulative.**

PHC metabolites are also rapidly degradable, not bioaccumulative and are non-toxic to aquatic organisms.

11.7.1 Acute aquatic hazard

The acute toxicity data (EC_{50} or LC_{50}) for all trophic levels is above 1 mg/L, therefore, the worst case of acute toxicity data (lowest EC_{50} or LC_{50}) suitable for aquatic hazard classification is > 1 mg/L and, consequentely, no classification is warranted.
In the Table below is presented the comparison regarding acute toxicity in aquatic organisms with the CLP classification criteria.

Worst case acute toxicity data suitable for aquatic hazard classification	Classification criteria CLP (Regulation 1272/2008/EC)
Acute aquatic toxicity	**Acute Category**
Propamocarb hydrochloride (PHC) and its metabolites (N-desmethyl-propamocarb and Propamocarb-N-oxide). EC_{50} or $LC_{50\ or}$ $EbC_{50\ or}$ Er C_{50} > 1 mg/L Therefore, no classification is warranted.	Propamocarb hydrochloride (PHC) and its metabolites (N-desmethyl-propamocarb and Propamocarb-N-oxide) EC_{50} or $LC_{50\ or}$ $EbC_{50\ or}$ Er C_{50} > 1 mg/L Therefore, no classification is warranted.

11.7.2 Long-term aquatic hazard (including bioaccumulation potential and degradation)

For the long term aquatic hazard, there are adequate chronic toxicity data available for all three trophic levels. Considering this, the classification will be performed according to the criteria given in Table 4.1.0 (Annex I of CLP Regulation).

All the chronic toxicity data (NOEC) for all trophic levels is above 1 mg/L, therefore no classification is warranted.

Worst case long term toxicity data suitable for aquatic hazard classification	Classification criteria CLP (Regulation 1272/2008/EC)
A) Chronic aquatic toxicity Propamocarb hydrochloride (PHC) and its metabolites (N-desmethyl-propamocarb and Propamocarb-N-oxide) NOEC > 1 mg a.s./L **B) Bioaccumulation potential** of the active substance, metabolites, degradation and reaction products PHC doesn´t have potential to bioaccumulate and there isn´t any metabolite, degradation or reaction product that is expected to bioaccumulate. **C) Degradation** PHC is rapidly degraded in the water, in the sediment and in the whole aquatic system. Due to A), B) and C), no classification is warranted.	**Chronic Category** Propamocarb hydrochloride (PHC) and its metabolites (N-desmethyl-propamocarb and Propamocarb-N-oxide) Due to A), B) and C) (please, see the previous columm), no classification is warranted.

11.8 Conclusion on classification and labelling for environmental hazards

Classification Categories:

- Acute toxicity to the aquatic environment: no classification is warranted;
- Chronic toxicity to the aquatic environment: no classification is warranted.

No classification or labelling is warranted for environmental hazards.

Please, consult the points 11.7.1 and 11.7.2, above.

12 EVALUATION OF ADDITIONAL HAZARDS

Propamocarb hydrochloride is not listed in the Montreal Protocol. The molecule is not a halogenated hydrocarbonate/aromate.

12.1 Hazardous to the ozone layer

Table 75: Summary table of data concerning hazardous properties of the substance for the ozone layer

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
Not applicable	propamocarb hydrochloride	_	Not applicable, as PHC is not a substance that depletes the ozone layer.	_

12.1.1 Short summary and overall relevance of the provided information on ozone layer hazard

Not applicable, as PHC is not a substance that depletes the ozone layer.

12.1.2 Comparison with the CLP criteria

Not applicable.

12.1.3 Conclusion on classification and labelling for hazardous to the ozone layer

Propamocarb hydrochloride is not a substance that depletes the ozone layer. Therefore, no classification or labelling is warranted.

13 ADDITIONAL LABELLING

No additional labelling is applicable.

14 REFERENCES

Author(s)	Year	Title **Source** *(where different from company)* **Company name, Report No., Date, GLP status** *(where relevant)*, **published or not**	Vertebrate study Y/N	Owner
Anonymous	1995	Proplant (Propamocarb hydrochloride 722 g/l SL) - Modified nine-induction Buehler delayed contact hypersensitivity study in the Guinea pig Safepharm Lab. Ltd., Derby, United Kingdom Arysta LifeScience, Report No.: 722/5R, Edition Number: M-310356-01-1 Date: 1995-05-22 GLP/GEP: yes, unpublished	Y	Arysta LifeScience
Anonymous	1995	Proplant (Propamocarb hydrochloride 722 g/l SL) - Acute eye irritation test in the rabbit Safepharm Lab. Ltd., Derby, United Kingdom Arysta LifeScience, Report No.: 722/4R, Edition Number: M-310352-01-1 Date: 1995-05-22 GLP/GEP: yes, unpublished	Y	Arysta LifeScience
Anonymous	1995	Proplant (Propamocarb hydrochloride 722 g/l SL) - Acute dermal irritation test in the rabbit Safepharm Lab. Ltd., Derby, United Kingdom Arysta LifeScience, Report No.: 722/3R, Edition Number: M-310346-01-1 Date: 1995-05-22 GLP/GEP: yes, unpublished	Y	Arysta LifeScience
Anonymous	1995	Proplant (Propamocarb hydrochloride 722 g/l SL) - Acute dermal toxicity (limit test) in the rat Safepharm Lab. Ltd., Derby, United Kingdom Arysta LifeScience, Report No.: 722/2R, Edition Number: M-310341-01-1 Date: 1995-05-22 GLP/GEP: yes, unpublished	Y	Arysta LifeScience
Anonymous	1995	Proplant (Propamocarb hydrochloride 722 g/l SL)- Acute oral toxicity study in the rat - fixed dose method Safepharm Lab. Ltd., Derby, United Kingdom Arysta LifeScience, Report No.: 722/1R, Edition Number: M-310337-01-1 Date: 1995-05-22 GLP/GEP: yes, unpublished	Y	Arysta LifeScience

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Anonymous	1987	Technical propamocarb hydrochloride (Previcur N): Metaphase chromosome analysis of human lymphocytes cultured in vitro Huntingdon Research Centre Ltd., Huntingdon, United Kingdom Bayer CropScience, Report No.: A85430, Edition Number: M-157641-01-1 EPA MRID No.: 41278122 Date: 1987-07-15 GLP/GEP: no, unpublished	N	Bayer
Anonymus	1995	Propamocarb hydrochloride soluble concentrate 722 g/L (Code: CR18131) - Degradation in sediment/water microcosms Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer Report No.: ENVIR/94/36; A85614 Report includes Trial Nos.: 40AV Edition Number: M-157923-01-1 MRID#: 48752603 Date: 1995-04-10 GLP/GEP: Yes, unpublished	Y	Bayer
Baker, G.	1998	POSSIBLE PHYSICO CHEMICAL HAZARDS Propamocarb physico-chemical hazards Code:AE B066752 00 TK72 A1 AgrEvo UK Crop Protection Ltd., Chesterford Park, United Kingdom Bayer CropScience, Report No.: C000128, Edition Number: M-180285-01-1 Date: 1998-07-14 GLP/GEP: no, unpublished	N	Bayer
Anonymous	1985	24-month oral (feeding) study with Previcur N in Beagle dogs - unknown - Bayer CropScience, Report No.: A85426, Edition Number: M-157637-01-1 Date: 1985-06-18 GLP/GEP: no, unpublished	Y	Bayer
Anonymous.	1982	28 days toxicity feeding study (range finding) with repetative administration of Previcur N to Beagle dogs RCC, Research and Consulting Company AG, Itingen, Switzerland Bayer CropScience, Report No.: A85422, Edition Number: M-157633-01-1 Date: 1982-05-27 GLP/GEP: no, unpublished	Y	Bayer

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Anonymous	2001	Proplant (Propamocarb HCl 722 g/l) : Embryotoxicity and teratogenicity study by dietary administration in female wistar rats Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience, Report No.: 295471, Edition Number: M-310689-01-1 Date: 2001-12-13 GLP/GEP: yes, unpublished	Y	Arysta LifeScience
Anonymous	2000	Propamocarb hydrochloride - Absorption, distribution, metabolism and excretion following oral administration to the rat Covance Laboratories Ltd., Harrogate, North Yorkshire, United Kingdom Arysta LifeScience, Report No.: 1669/002, Edition Number: M-310331-01-1 Date: 2000-07-07 GLP/GEP: yes, unpublished	N	Arysta LifeScience
Anonymous.	2000	Propamocarb hydrochloride - Identification of selected metabolites in the rat Covance Laboratories Ltd., Harrogate, North Yorkshire, United Kingdom Arysta LifeScience, Report No.: 1669/004-D1140, Edition Number: M-310335-01-1 Date: 2000-12-07 GLP/GEP: yes, unpublished	Y	Arysta LifeScience
Bittner, P.; Rexer, K.	1999	Determination of the density Propamocarb hydrochloride technical concentrate 780 g/L Code: AE B066752 00 TK72 A112 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C003480, Edition Number: M-186226-01-1 Date: 1999-04-16 GLP/GEP: yes, unpublished	N	Bayer
Bittner, P.; Rexer, K.	1999	Determination of the surface tension Propamocarb hydrochloride technical concentrate 780 g/L Code: AE B066752 00 TK72 A112 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C003482, Edition Number: M-186230-01-1 Date: 1999-04-16 GLP/GEP: yes, unpublished	N	Bayer

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Anonymous	1995	Proplant - Acute inhalation toxicity study four - hour exposure (nose only) in the rat SafePharm Lab. Ltd., Derby, United Kingdom Arysta LifeScience, Report No.: 722/6R, Edition Number: M-310999-01-1 Date: 1995-05-16 GLP/GEP: yes, unpublished	Y	Arysta LifeScience
Anonymous	1998	Rat acute (4-hour) inhalation toxicity Propamocarb HCL liquid concentrate 71.2% w/v Code: AE B066752 00 TK72 A1 (CQ 684) AgrEvo UK Crop Protection Ltd., Chesterford Park, United Kingdom Bayer CropScience, Report No.: A91289, Report includes Trial Nos.: TOX 97112 Edition Number: M-167986-01-1 EPA MRID No.: 44563201 Date: 1998-02-17 GLP/GEP: yes, unpublished	Y	Bayer
Anonymous.	2001	A two year oral (dietary) combined chronic toxicity and oncogenicity study in rats with Proplant Springborn Laboratories, Inc., Spencerville, OH, USA Arysta LifeScience, Report No.: 3437.1, Edition Number: M-310604-01-1 Date: 2001-03-23 GLP/GEP: no, unpublished	Y	Arysta LifeScience
Anonymous	2000	A preliminary dose-ranging three-month oral (gavage) dose toxicity study in CD-1 mice with Proplant Springborn Laboratories, Inc., Spencerville, OH, USA Arysta LifeScience, Report No.: 3437.4, Edition Number: M-310427-01-1 Date: 2000-02-02 GLP/GEP: no, unpublished	Y	Arysta LifeScience
Anonymous	2000	A preliminary 28-day oral (gavage) dose range-finding toxicity study in rats with Proplant Springborn Laboratories, Inc., Spencerville, OH, USA Arysta LifeScience, Report No.: 3437.5, Edition Number: M-310378-01-1 Date: 2000-08-10 GLP/GEP: no, unpublished	Y	Arysta LifeScience

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Anonymous	1997	A 28-day range-finding (dietary) toxicity study in rats with Proplant Springborn Laboratories, Inc., Spencerville, OH, USA Arysta LifeScience, Report No.: 3437.2, Edition Number: M-310359-01-1 Date: 1997-07-21 GLP/GEP: no, unpublished	Y	Arysta LifeScience
Bogers, M.	2001	A 7-day aquatic plant toxicity test using Lemna minor with Proplant (propamocarb HCL 722 g/l) Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience Report No.: 329254 Edition Number: M-310632-01-1 Date: 2001-11-13 GLP/GEP: Yes, unpublished ... also filed: 11 / 27	N	Arysta LifeScience
Bogers, M.	1996	Fresh water algal growth inhibition test with Proplant Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience Report No.: 165364 Edition Number: M-310692-01-1 Date: 1996-09-04 GLP/GEP: Yes, unpublished ... also filed: 11 / 19	Yes	Arysta LifeScience
Anonymus	1996	96-hour acute limit study in rainbow trout with Proplant (semi-static) Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience Report No.: 161303 Edition Number: M-310778-01-1 Date: 1996-08-28 GLP/GEP: Yes, unpublished ... also filed: 11 / 15	Y	Arysta LifeScience
Bogers, M.	1996	Acute limit study in Daphnia magna with Proplant Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience Report No.: 161314 Edition Number: M-310720-01-1 Date: 1996-08-28 GLP/GEP: Yes, unpublished ... also filed: 11 / 16	Y	Arysta LifeScience
Anonymus	1998	Rainbow trout, juvenile growth test 28 days with Proplant (flow-through) Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience Report No.: 220782	Y	Arysta LifeScience

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
		Edition Number: M-310732-01-1 Date: 1998-05-08 GLP/GEP: Yes, unpublished ... also filed: 11 / 21		
Bogers, M.	1998	Daphnia magna, reproduction test with Proplant (semi-static) Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience Report No.: 220771 Edition Number: M-310697-01-1 Date: 1998-05-05 GLP/GEP: Yes, unpublished ... also filed: 11 / 20	Y	Arysta LifeScience
Bruns, E.	2009	Amendment no. 1: The acute toxicity of propamacarb-HCl to Daphnia magna in a static system Bayer Report No.: 512AV Edition Number: M-157891-02-1 Date: 1992-09-25 ... amended: 2009-11-25 GLP/GEP: Yes, unpublished	Y	Bayer
Christ, M. T.; Ruff, D. F.	1996	Propamocarb hydrochloride water-miscible concentrate 68.2 percent w/w (738 g/L) Code: AE B066752 - Toxicity to duckweed (Lemna gibba, G3) in a static renewal system AgrEvo USA Company, USA Bayer Report No.: O703/U042; A89710 Report includes Trial Nos.: 522AV Edition Number: M-165250-01-1 MRID#: 44187802 Date: 1996-12-02 GLP/GEP: Yes, unpublished	Y	Bayer
Anonymous	2001	In vitro mammalian cell mutation test with mouse lymphoma cells Propamocarb hydrochloride liquid concentrate, 780 g/L Code: AE B0066752 00 7K72 A101 Huntingdon Life Sciences Ltd., Huntingdon, United Kingdom Bayer CropScience, Report No.: C008167, Report includes Trial Nos.: TOX20042 Edition Number: M-197256-01-1 Date: 2001-04-27 GLP/GEP: yes, unpublished	N	Bayer

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Anonymous	1999	Guinea pig skin sensitisation study (Magnusson & Kligman Method) Propamocarb Hydrochloride liquid concentrate 71.2% w/w Code:AE B066752 00 TK72 A1 Bayer CropScience, Report No.: C002374, Report includes Trial Nos.: TOX98176 Edition Number: M-184379-01-1 EPA MRID No.: 44761401 Date: 1999-02-04 GLP/GEP: yes, unpublished	Y	Bayer
Anonymous.	2002	Subchronic (13-week) neurotoxicity study with propamocarb HCl in rats - Neurobehavioural observations and automated motor activity assessment TNO Nutrition and Food Research Institute, Zeist, Netherlands Arysta LifeScience, Report No.: 3969, Edition Number: M-310751-01-1 Date: 2002-09-24 GLP/GEP: yes, unpublished	Y	Arysta LifeScience
Anonymous	2002	Acute neurotoxicity study after single oral dosing of rats with propamocarb HCL TNO Nutrition and Food Research Institute, Zeist, Netherlands Arysta LifeScience, Report No.: 3873, Edition Number: M-310748-01-1 Date: 2002-03-28 GLP/GEP: yes, unpublished	Y	Arysta LifeScience
de Vries, R.	1997	Propamocarb hydrochloride: Degradation of propamocarb HCL in aerobic aquatic environment Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience Report No.: 161369 Edition Number: M-310804-01-1 MRID#: 48752604 Date: 1997-04-09 GLP/GEP: Yes, unpublished ... also filed: 11 / 41	Y	Arysta LifeScience

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Desmares-Koopmans, M. J. E.	1999	Propamocarb hydrochloride: Determination of ready biodegradability: Carbon dioxide (CO2) evolution test (modified Sturm test) with Proplant Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience Report No.: 247207 Edition Number: M-310925-01-1 Date: 1999-03-15 GLP/GEP: Yes, unpublished ... also filed: 11 / 51	Y	Arysta LifeScience
Dionne, E.	2001	Proplant (propamocarb HCL 722 g/l SL): Acute toxicity to eastern oysters (Crassostrea virginica) under flow-through conditions Springborn Laboratories, Inc., Wareham, MA, USA Arysta LifeScience Report No.: 13763.6102 Edition Number: M-310718-01-1 Date: 2001-08-16 GLP/GEP: Yes, unpublished ... also filed: 11 / 13	N	Arysta LifeScience
Fowles, J.	2005	Propamocarb (Proplant) - Regulatory toxicology - Position paper Bayer CropScience S.A., Sophia Antipolis, France TF- BCS-Agriphar, Report No.: M-256378-01-1, Edition Number: M-256378-01-1 Date: 2005-08-12 GLP/GEP: n.a., unpublished	Y	TF- Bayer-Agriphar
Francois, J. M.	2001	Determination of the flash point the auto-flammability and the explosion properties of EXP10382A Rhodia Rhoditech;Process Safety Lab. Bayer CropScience, Report No.: C016246, Report includes Trial Nos.: 01-01 Edition Number: M-202029-01-1 Date: 2001-01-26 GLP/GEP: yes, unpublished	N	Bayer
Anonymous	2003	52-week oral dietary toxicity study with Proplant (Propamocarb HCl 722 g/l) in male and female beagle dogs Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience, Report No.: 295403, Edition Number: M-310442-01-1 Date: 2003-01-17 GLP/GEP: yes, unpublished	Y	Arysta LifeScience

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Graves, W. C.; Peters, G. T.	1991	Propamocarb HCl: An early life stage toxicity test with the fathead minnow (Pimephales promelas) Wildlife International, Ltd., Easton, MD, USA Bayer Report No.: 244A-101; A85567 Report includes Trial Nos.: 501 AV Edition Number: M-157854-01-1 MRID#: 42083105 Date: 1991-10-18 GLP/GEP: Yes, unpublished	Y	Bayer
Anonymus	1981	Metabolic fate and tissue residues of propamocarb in bluegills and channel catfish Journal: Chemosphere Volume: 10 Issue: 5 Pages: 469-478 Year: 1981 Report No.: A85493 Edition Number: M-157742-01-1 MRID#: 00071476 GLP/GEP: n.a., published	N	published
Anonymus	1980	Uptake of propamocarb fungicide by bluegills and channel catfish Journal: Chemosphere Volume: 9 Pages: 329;333 Year: 1980 Report No.: A85492 Edition Number: M-157741-01-1 MRID#: 41278114 GLP/GEP: n.a., published	N	published
Anonymus	2002	Proplant: Early life-stage toxicity test with fathead minnow (Pimephales promelas) under flow-through conditions Springborn Laboratories AG, Horn, Switzerland Arysta LifeScience Report No.: 1038.004.122 Edition Number: M-310729-01-1 Date: 2002-02-26 GLP/GEP: Yes, unpublished	Y	Arysta LifeScience
Anonymous	2001	Acute Eye irritation in Rabbits PREVICUR-N (AE B066752 00 SL67 A2 - EXP10382A) CIT Centre Internationale de Toxicologie, Evreux, France Bayer CropScience, Report No.: C013767, Report includes Trial Nos.: 21135TAL Edition Number: M-205226-01-1 Date: 2001-05-02 GLP/GEP: yes, unpublished	Y	Bayer

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Anonymous	2001	Acute dermal irritation in rabbits PREVICUR-N (AE B066752 00 SL67 A2 - EXP10382A) CIT Centre Internationale de Toxicologie, Evreux, France Bayer CropScience, Report No.: C013765, Report includes Trial Nos.: 21134TAL Edition Number: M-205222-01-1 Date: 2001-03-21 GLP/GEP: yes, unpublished	Y	Bayer
Anonymous	1998	Mouse dietary oncogenicity (18 months) study Propamocarb HCL liquid concentrate Code: AE B066752 00 TK72 A101 AgrEvo UK Crop Protection Ltd., Chesterford Park, United Kingdom Bayer CropScience, Report No.: C001201, Report includes Trial Nos.: Tox94146 Edition Number: M-182006-01-1 EPA MRID No.: 44693801 Date: 1998-11-12 GLP/GEP: yes, unpublished	Y	Bayer
Anonymous	1992	Previcur N (propamocarb HCl) - Rat 21-day dermal repeat dose study Schering AG, Berlin, Germany Bayer CropScience, Report No.: A85442, Edition Number: M-157653-01-1 Date: 1992-07-13 GLP/GEP: no, unpublished	Y	Bayer
Hoberg, J. R.	2001	Propamocarb hydrochloride - Toxicity to the freshwater green alga, Pseudokirchneriella subcapitata Springborn Laboratories, Inc. (SLS), USA Bayer Report No.: 13726.6139; B003349 Report includes Trial Nos.: 13726.6139 Edition Number: M-240390-01-1 Date: 2001-06-21 GLP/GEP: Yes, unpublished	Y	Bayer
Holmes, C. M.; Peters, G. T.	1991	Propamocarb-HCl: A 96-hour shell deposition test with the eastern oyster (Crassostrea virginica) Wildlife International, Ltd., Easton, MD, USA Bayer Report No.: A85568; 244A-102A Report includes Trial Nos.: 503 AV Edition Number: M-157857-01-1 MRID#: 42083104 Date: 1991-10-18 GLP/GEP: Yes, unpublished	Y	Bayer

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Anonymous	1980	Micronucleus test on CP 604 (SN 66 752, Previcur N) propamocarb hydrochloride Huntingdon Research Centre Ltd., Huntingdon, United Kingdom Bayer CropScience, Report No.: A85367, Edition Number: M-157582-01-1 EPA MRID No.: 00101643 Date: 1980-02-26 GLP/GEP: no, unpublished	N	Bayer
Anonymous	1998	Mouse dietary 90 day toxicity range finding study Propamocarb hydrochloride liquid concentrate Code: HOE 102791 00 LC72 A101 CIT Centre Internationale de Toxicologie, Evreux, France Bayer CropScience, Report No.: A91845, Report includes Trial Nos.: TOX94156 Edition Number: M-168498-01-1 EPA MRID No.: 44810402 Date: 1998-12-17 GLP/GEP: yes, unpublished	Y	Bayer
Anonymous	1998	Rat dietary 90-day toxicity range finding study propamocarb hydrochloride liquid concentrate 102791 00 LC72 A101 CIT Centre Internationale de Toxicologie, Evreux, France Bayer CropScience, Report No.: A91844, Report includes Trial Nos.: 12370 Tox94155 Edition Number: M-168497-01-1 Date: 1998-12-17 GLP/GEP: yes, unpublished	Y	Bayer
Anonymous	1983	Previcur N (SN 66752): Toxicity and potential tumorigenicity in dietary administration to rats for 104 weeks Huntingdon Research Centre Ltd., Huntingdon, United Kingdom Bayer CropScience, Report No.: A85386, Edition Number: M-157599-01-1 Date: 1983-08-30 GLP/GEP: no, unpublished **...also filed: KCA 5.5 /01**	Y	Bayer

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Anonymous	1983	Previcur N (SN 66752): Potential tumorigenicity to mice in dietary administration for 104 weeks Huntingdon Research Centre Ltd., Huntingdon, United Kingdom Bayer CropScience, Report No.: A85391, Edition Number: M-157604-01-1 Date: 1983-08-30 GLP/GEP: no, unpublished	Y	Bayer
Anonymous	1987	Technical propamocarb hydrochloride: Microbial metabolic activation test to assess mutagenic potential Huntingdon Research Centre Ltd., Huntingdon, United Kingdom Bayer CropScience, Report No.: A85431, Edition Number: M-157642-01-1 Date: 1987-08-11 GLP/GEP: no, unpublished	N	Bayer
Klehr, M.	1980	Photolysis experiments with propamocarb HCL (SN 66 752) in heat sterilised aqueous solution Schering AG, Berlin, Germany Bayer Report No.: A85466 Edition Number: M-157698-01-1 MRID#: 00071296 MRID#: ACC.71296 Date: 1980-06-19 GLP/GEP: No, unpublished	Y	Bayer
Klehr, M.	1978	Photolysis of propamocarb. HCl (SN 66 752) in aqueous solution Schering AG, Berlin, Germany Bayer Report No.: APC 06/78; A85564 Edition Number: M-157849-01-1 MRID#: ACC.47369 Date: 1978-02-17 GLP/GEP: No, unpublished	Y	Bayer
Anonymous	1982	Previcur N: Three month sub-chronic oral toxicity study in rats An-Pyo Center, Japan Bayer CropScience, Report No.: A85400, Edition Number: M-157612-01-1 Date: 1982-04-30 GLP/GEP: no, unpublished	Y	Bayer

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Anonymous	1981	Mutagenicity testing in bacteria with Previcur N An-Pyo Center, Japan Bayer CropScience, Report No.: A85398, Edition Number: M-157610-01-1 Date: 1981-09-30 GLP/GEP: no, unpublished	N	Bayer
Anonymous.	1982	Previcur N: Acute oral toxicity study in rats Biosafety Research Center, Foods, Drugs and Pesticides, An-Pyo Center, Japan Bayer CropScience, Report No.: A85409, Edition Number: M-157621-01-1 EPA MRID No.: 41278115 Date: 1982-04-30 GLP/GEP: no, unpublished	Y	Bayer
Krips, H. J.	2000	Propamocarb hydrochloride - Statement on the oxiding properties of Proplant Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience, Report No.: 308611, Edition Number: M-310256-01-1 Date: 2000-12-05 GLP/GEP: yes, unpublished	N	Arysta LifeScience
Lambert, M.	1979	Corrosion tests with Previcur N Schering AG, Berlin, Germany Bayer CropScience, Report No.: A84967, Edition Number: M-157163-01-1 Date: 1979-02-07 GLP/GEP: no, unpublished	N	Bayer
Lasserre, D.	2012	Propamocarb - Rebuttal of R63 labelling of the formulations Previcur Energy (reg. No. 18-544) and Proplant (reg. No. 361-1) in Denmark - Position paper from Agriphar S.A. and Bayer CropScience Bayer CropScience Bayer CropScience, Report No.: M-425291-01-1, Edition Number: M-425291-01-1 Date: 2012-02-14 GLP/GEP: n.a., unpublished	N	Bayer
Lecocq, V.	2010	Viscosity of liquids of propamocarb-HCI 722 g/L SL Centre wallon de Recherches agronomiques (CRA-W), Gembloux, Belgium Report No.: 221312, Edition Number: M-541525-01-1 Date: 2010-06-29 GLP/GEP: yes, unpublished	N	Arysta LifeScience

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Lehne, V.	1990	Propamocarb hydrochloride - melting point Schering AG, Berlin, Germany Bayer CropScience, Report No.: A89312, Edition Number: M-164549-01-1 Date: 1990-10-15 GLP/GEP: no, unpublished	N	Bayer
Lehne, V.	1990	Previcur N - determination of viscosity Schering AG, Berlin, Germany Report No.: A85050, Edition Number: M-157246-01-1 Date: 1990-10-16 GLP/GEP: no, unpublished	N	Bayer
Anonymus	2001	Bioconcentration of Proplant to zebrafish (Danio rerio) BIOAGRI Laboratorios Ltda., Piracicaba, SP, Brazil Arysta LifeScience Report No.: RF-0998.210.022.01 Edition Number: M-310727-01-1 Date: 2001-09-26 GLP/GEP: Yes, unpublished ... also filed: 11 / 39	Y	Arysta LifeScience
Anonymous	1998	Rat combined chronic toxicity and ongenicity (dietary) Propamocarb Hydrochloride liquid concentrate Code: AE B066752 00 TK72 A101 AgrEvo UK Crop Protection Ltd., Chesterford Park, United Kingdom Bayer CropScience, Report No.: C001777, Report includes Trial Nos.: Tox94145 Edition Number: M-183340-01-1 Date: 1998-12-17 GLP/GEP: yes, unpublished	Y	Bayer
Anonymous	2001	Evaluation of the ability of Proplant (Propamocarb HCl 722 g/l) to induce chromosome aberrations in cultured peripheral human lymphocytes Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience, Report No.: 295548, Edition Number: M-310453-01-1 Date: 2001-10-27 GLP/GEP: yes, unpublished	N	Arysta LifeScience

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Anonymus	2001	96-hour acute toxicity study in bluegill sunfish with Proplant (propamocarb HCL 722 g/l) (static) Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience Report No.: 329748 Edition Number: M-310734-01-1 Date: 2001-12-19 GLP/GEP: Yes, unpublished ... also filed: 11 / 28	Y	Arysta LifeScience
Anonymus	2000	96-hour acute toxicity study in carp with Proplant Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience Report No.: 308622 Edition Number: M-310773-01-1 Date: 2001-12-12 GLP/GEP: Yes, unpublished ... also filed: 11 / 25	Y	Arysta LifeScience
Miklautz, H.	1991	The acid dissociation constant of ZK 66 752 (Propamocarb-HCl) Schering AG, Berlin, Germany Bayer CropScience, Report No.: A85060, Edition Number: M-157256-01-1 EPA MRID No.: 42083101 Date: 1991-05-28 GLP/GEP: no, unpublished	N	Bayer
Miklautz, H.	1990	The temperature dependence of the vapor pressure of Propamocarb-HCl (ZK 66752) Schering AG, Berlin, Germany Bayer CropScience, Report No.: A85057, Report includes Trial Nos.: 90/064 Edition Number: M-157253-01-1 Date: 1990-11-28 GLP/GEP: no, unpublished	N	Bayer
Anonymous.	1997	[14C] Propamocarb Hydrochloride toxicokinetic studies in the rat; Code:AE B066752 00 1E72 0001- AgrEvo UK Crop Protection Ltd., Chesterford Park, United Kingdom Bayer CropScience, Report No.: A83866, Report includes Trial Nos.: TOX 96219 Edition Number: M-156084-03-1 Date: 1997-05-30 **...Amended: 1998-10-22** GLP/GEP: yes, unpublished	Y	Bayer

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Muehlberger, B.	2004	AE B066752 - Water solubility in the pH-range 1.6 - 9.6 - Statement to the study PA01/009 - Code: AE B066752 - Propamocarb hydrochloride Bayer CropScience GmbH, Frankfurt am Main, Germany Report No.: C042353, Edition Number: M-232456-01-1 Date: 2004-06-24 GLP/GEP: n.a., unpublished	N	Bayer
Muehlberger, B.	2001	Partition coefficient N-octanol / water (Flash-shaking method) Propamocarb hydrochloride Code: AE B066752 00 1B97 0001 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C012642, Edition Number: M-203110-01-1 Date: 2001-04-24 GLP/GEP: yes, unpublished	N	Bayer
Muehlberger, B.	2001	Water solubility in the pH-range 1.6 - 9.6 - Propamocarb hydrochloride - Code: AE B066752 00 1B97 0001 Aventis CropScience GmbH, Frankfurt am Main, Germany Report No.: C012641, Edition Number: M-203108-01-1 Date: 2001-04-23 GLP/GEP: yes, unpublished	N	Bayer
Muehlberger, B.	2001	Partition coefficient N-octanol / water (Flash-shaking method) Propamocarb hydrochloride Code: AE B066752 00 1B97 0001 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer Report No.: C012642 Edition Number: M-203110-01-1 Date: 2001-04-24 GLP/GEP: Yes, unpublished confidential	Y	Bayer
Muehlberger, B.; Lemke, G.	2004	AE B066752 Propamocarb hydrochloride; substance, pure Surface tension Code: AE B066752 00 TK77 A101 Bayer CropScience, Report No.: C044112, Edition Number: M-235782-01-1 Date: 2004-09-21 GLP/GEP: yes, unpublished	N	Bayer

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Muehlberger, B.; Lemke, G.	2004	AE B066752 Propamocarb hydrochloride; substance, pure Surface tension Code: AE B066752 00 1B97 0001 Bayer CropScience, Report No.: C044111, Edition Number: M-235780-01-1 Date: 2004-09-21 GLP/GEP: yes, unpublished	N	Bayer
Mueller, T.	1988	Solubility of Propamocarb-hydrochloride in water at 20 degree C Schering AG, Berlin, Germany Bayer CropScience, Report No.: A85005, Edition Number: M-157201-01-1 EPA MRID No.: 41278103 Date: 1988-08-08 GLP/GEP: no, unpublished	N	Bayer
Mueller, T.	1990	Propamocarb hydrochloride - solubility in organic solvents Schering AG, Berlin, Germany Bayer CropScience, Report No.: A85046, Edition Number: M-157242-01-1 Date: 1990-10-05 GLP/GEP: no, unpublished	N	Bayer
Mueller, T.	1990	Previcur N - corrosion characteristics Schering AG, Berlin, Germany Bayer CropScience, Report No.: A85049, Edition Number: M-157255-01-1 Date: 1990-12-11 GLP/GEP: no, unpublished	N	Bayer
Mullee, D. M.; Bartlett, A. J.	1995	Propamocarb hydrochloride: Determination of photochemical degradation Safepharm Lab. Ltd., Derby, United Kingdom Arysta LifeScience Report No.: 722/014 Edition Number: M-310246-01-1 Date: 1995-06-13 GLP/GEP: No, unpublished ... also filed: 11 / 66	Y	Arysta LifeScience

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Anonymous	1998	Amendment to the final report - propamocarb hydrochloride liquid concentrate, 780 g/l - Code: AE B066752 00 TK72 A101 - Rat dietary two-generation reproductive toxicity study WIL Research Laboratories Inc., Ashland, OH, USA Bayer CropScience, Report No.: M-183560-02-1, Report includes Trial Nos.: TOX96131 WIL-303002 Edition Number: M-183560-02-1 Date: 1998-12-18 **...Amended: 2004-09-30** GLP/GEP: yes, unpublished	Y	Bayer
Anonymous.	1994	Propamocarb-HCI: Clearance of a single oral dose from rat tissues Schering AG, Berlin, Germany Bayer CropScience, Report No.: A85146, Edition Number: M-157339-02-1 Date: 1994-02-01 **...Amended: 1997-09-25** GLP/GEP: yes, unpublished	Y	Bayer
Anonymous	2011	Propamocarb hydrochloride - 28-day immunotoxicity study in the female Sprague-Dawley rat by dietary administration Bayer S.A.S., Bayer CropScience, Sophia Antipolis, France Bayer CropScience, Report No.: SA 10354, Edition Number: M-414757-01-1 EPA MRID No.: 48752605 Date: 2011-09-23 GLP/GEP: yes, unpublished	Y	Bayer
Poerschke, R.	2001	Statement on auto-flammability and explosive properties Propamocarb-hydrochloride technical grade active ingredient Code: AE B066752 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C014554, Edition Number: M-206828-01-1 Date: 2001-07-16 GLP/GEP: n.a., unpublished	N	Bayer

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Poerschke, R.	2001	The acid dissociation constant of AE B066752 Identity of the dissociated species Propamocarb-hydrochloride Code: AE B066752 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C014007, Edition Number: M-205699-01-1 Date: 2001-06-26 GLP/GEP: no, unpublished	N	Bayer
Anonymous.	1981	Previcur N (CP 604): Embryotoxicity including teratogenicity study in rats after daily intragastrical administration from day 6 to day 19 of gestation - Revised final report Schering AG, Berlin, Germany Bayer CropScience, Report No.: A85396, Edition Number: M-157608-02-1 Date: 1981-11-02 **...Amended: 1990-04-17** GLP/GEP: no, unpublished	Y	Bayer
Anonymous.	1981	Pevicur N (CP 604): Embryotoxicity including teratogenicity study in rabbits after daily intragastrical administration from day 6 to day 18 of gestation - Revised final report Schering AG, Berlin, Germany Bayer CropScience, Report No.: A85384, Edition Number: M-157597-02-1 Date: 1981-01-09 **...Amended: 1990-03-06** GLP/GEP: no, unpublished	Y	Bayer
Anonymous	1993	Previcur N SL: Rat subchronic (3-month) dietary neurotoxicity study Pharmaco LSR International Inc.; Bayer CropScience, Report No.: A85450, Edition Number: M-157670-01-1 Date: 1993-11-03 GLP/GEP: no, unpublished	Y	Bayer
Anonymous	1993	Previcur N SL: Rat acute oral neurotoxicity study Pharmaco LSR International Inc.; Bayer CropScience, Report No.: A85449, Edition Number: M-157666-01-1 Date: 1993-11-03 GLP/GEP: no, unpublished	Y	Bayer
Putt, A. E.	2001	Proplant (propamocarb HCL 722 g/l SL): Acute toxicity to Mysids (Americamysis bahia) under static conditions Springborn Laboratories, Inc., Wareham, MA, USA Arysta LifeScience	N	Arysta LifeScience

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
		Report No.: 13763.6101 Edition Number: M-310709-01-1 Date: 2001-08-28 GLP/GEP: Yes, unpublished ... also filed: 11 / 12		
Anonymus	2001	Proplant (propamocarb HCL 722 g/l SL): Acute toxicity to Sheepshead minnow (Cyprinodon variegatus) under static conditions Springborn Laboratories, Inc., Wareham, MA, USA Arysta LifeScience Report No.: 13763.6104 Edition Number: M-310736-01-1 Date: 2001-08-15 GLP/GEP: Yes, unpublished ... also filed: 11 / 14	Y	Arysta LifeScience
Rehme, G.	1985	Thermal stability and stability in air of propamocarb hydrochloride Schering AG, Berlin, Germany Bayer CropScience, Report No.: A84979, Edition Number: M-157175-01-1 Date: 1985-06-13 GLP/GEP: no, unpublished	N	Bayer
Renaud, D.	2004	Propamocarb Hydrochloride Statement on water solubility and its pH variation Code: AE B066752 Bayer CropScience S.A., Lyon, France Report No.: C045318, Edition Number: M-236979-01-1 Date: 2004-11-05 GLP/GEP: no, unpublished	N	Bayer
Anonymous	2005	AE B066752 00 SL67 A2 (Previcur N) - Evaluation of potential dermal sensitisation in the local lymph node assay in the mouse Bayer CropScience S.A., Sophia Antipolis, France Bayer CropScience, Report No.: SA05038, Edition Number: M-252483-01-1 Date: 2005-05-04 GLP/GEP: yes, unpublished	Y	Bayer
Anonymous	1994	Propamocarb-HCI: Absorption, distribution and elimination in the rat following single and repeated oral dosing and single intraveneous dosing Schering AG, Berlin, Germany Bayer CropScience, Report No.: A85144, Edition Number: M-157337-01-1 Date: 1994-02-02 GLP/GEP: yes, unpublished	Y	Bayer

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Anonymous.	1979	Dominant lethal study of Previcur N propamocarb hydrochloride SRI; Bayer CropScience, Report No.: A85368, Edition Number: M-157583-01-1 Date: 1979-12-03 GLP/GEP: no, unpublished	N	Bayer
Anonymous	2003	18-months oral dietary carcinogenicity study with Proplant (Propamocarb HCl 722 g/l) in CD-1 mice Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience, Report No.: 295605, Edition Number: M-310623-01-1 Date: 2003-01-31 GLP/GEP: yes, unpublished	Y	Arysta LifeScience
Anonymous	2002	52-week oral dietary toxicity study with Proplant (Propamocarb HCl 722 g/l) in wistar rats Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience, Report No.: 295583, Edition Number: M-310609-01-1 Date: 2002-09-16 GLP/GEP: yes, unpublished	Y	Arysta LifeScience
Anonymous	2001	Propamocarb HCL 722 G/L - 90-day oral dietary toxicity study in male and female beagle dogs Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience, Report No.: 295392, Edition Number: M-310439-01-1 Date: 2001-09-18 GLP/GEP: yes, unpublished	Y	Arysta LifeScience
Anonymous	2001	Propamocarb HCL 722 G/L - 90-day oral dietary toxicity study in wistar rats, followed by a 28-day recovery period Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience, Report No.: 295381, Edition Number: M-310432-01-1 Date: 2001-06-21 GLP/GEP: yes, unpublished	Y	Arysta LifeScience
Schupner, J. K.	1991	The static acute toxicity of propamocarb HCl to the mysid shrimp, Mysidopsis bahia Schering AG, Berlin, Germany Bayer Report No.: 500 AV; A85561 Edition Number: M-157843-01-1 MRID#: 41834604 Date: 1991-03-13 GLP/GEP: Yes, unpublished	Y	Bayer
Anonymus	1991	The static acute toxicity of propamocarb-HCl to the rainbow trout, Oncorhynchus mykiss	Y	Bayer

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
		Nor-Am Chemical Company, Pikeville, NC, USA Bayer Report No.: 509 AV; A85569 Edition Number: M-157858-01-1 MRID#: 42083103 Date: 1991-09-16 GLP/GEP: Yes, unpublished		
Anonymus	1991	The static acute toxicity of propamocarb-HCl to the bluegill sunfish, Lepomis macrochirus Nor-Am Chemical Company, Pikeville, NC, USA Bayer Report No.: 510 AV; A85566 Edition Number: M-157853-01-1 MRID#: 42083102 Date: 1991-09-16 GLP/GEP: Yes, unpublished	Y	Bayer

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Shepler, K.; McKemmie, T.	2001	Hydrolysis of [14C]Propamocarb at pH 4,5,7 and 9 PTRL West, Inc., USA Bayer Report No.: 882 W-1; B003419 Report includes Trial Nos.: 882W Edition Number: M-240450-01-1 Date: 2001-08-24 GLP/GEP: Yes, unpublished	Y	Bayer
Sixl, F.; Rexer, K.	1998	Determination of the physical form Propamocarb hydrochloride technical concentrate 780 g/l Code: AE B066752 00 TK72 A1 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C001717, Edition Number: M-183222-01-1 Date: 1998-11-20 GLP/GEP: no, unpublished	N	Bayer
Sixl, F.; Rexer, K.	1998	Determination of the colour Propamocarb hydrochloride technical concentrate 780 g/l Code: AE B066752 00 TK72 A110 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C001715, Edition Number: M-183218-01-1 Date: 1998-11-20 GLP/GEP: no, unpublished	N	Bayer
Anonymous	1986	Previcur N: Subacute systemic tolerance study in rats with dietary administration over a period of 5 weeks Schering AG, Berlin, Germany Bayer CropScience, Report No.: A85365, Edition Number: M-157580-01-1 Date: 1986-02-27 GLP/GEP: no, unpublished	Y	Bayer
Anonymous.	1997	Propamocarb HCl 722 g/l : Reserve mutation assay "Ames Test" using Salmonella typhimurium Safepharm Lab. Ltd., Derby, United Kingdom Arysta LifeScience, Report No.: 722/019, Edition Number: M-310446-01-1 Date: 1997-04-07 GLP/GEP: yes, unpublished	N	Arysta LifeScience

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Anonymous	2002	An oral (gavage) two-generation reproduction toxicity in rats with Proplant Springborn Laboratories, Inc., Spencerville, OH, USA Arysta LifeScience, Report No.: 3437.3, Edition Number: M-310681-01-1 Date: 2002-03-04 GLP/GEP: yes, unpublished	Y	Arysta LifeScience
Anonymous	1977	Sub-chronic (90-day) feeding study with ZK 17 296 in dogs (revised version of final report) Central Institute for Nutrition and Food Research, Zeist, Netherlands Bayer CropScience, Report No.: A85381, Edition Number: M-157595-02-1 Date: 1977-01-01 **...Amended: 1990-07-16** GLP/GEP: no, unpublished	Y	Bayer
Tremain, S. P.; Bartlett, A. J.	1995	Propamocarb hydrochloride - Determination of hazardous physico-chemical properties Safepharm Lab. Ltd., Derby, United Kingdom Arysta LifeScience, Report No.: 722/016, Edition Number: M-310252-01-1 Date: 1995-06-13 GLP/GEP: yes, unpublished	N	Arysta LifeScience
Anonymous	2002	Proplant (Propamocarb HCl 722 g/l) : Repeated dose (28-days) dermal toxicity by daily exposure in the rat Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience, Report No.: 326993, Edition Number: M-310445-01-1 Date: 2002-01-10 GLP/GEP: yes, unpublished	Y	Arysta LifeScience
Anonymous	2001	Evaluation of the mutagenic activity of Proplant (propamocarb HCl 722 g/l) in an in vitro mammalian cell gene mutation test with L5178Y mouse lymphoma cells (with independant repeat) Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience, Report No.: 295559, Edition Number: M-310551-01-1 Date: 2001-07-17 GLP/GEP: yes, unpublished	N	Arysta LifeScience

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Anonymous	2001	Evaluation of the mutagenic activity of Proplant (propamocarb HCl 722 g/l) in the Escherichi coli reverse mutation assay (with independent repeat) Notox B.V., 's-Hertogenbosch, Netherlands Arysta LifeScience, Report No.: 333348, Edition Number: M-310449-01-1 Date: 2001-10-22 GLP/GEP: yes, unpublished	N	Arysta LifeScience
Walker, A. J.; Mulle, D. M.; Barlett, A. J.	1995	Propamocarb hydrochloride : Determination of general physico-chemical properties Safepharm Lab. Ltd., Derby, United Kingdom Arysta LifeScience, Report No.: 722/013, Edition Number: M-309665-01-1 Date: 1995-06-09 GLP/GEP: yes, unpublished	N	Arysta LifeScience
Walker, A. J.; Mulle, D. M.; Barlett, A. J.	1995	Propamocarb hydrochloride : Determination of general physico-chemical properties Safepharm Lab. Ltd., Derby, United Kingdom Arysta LifeScience Report No.: 722/013 Edition Number: M-309665-01-1 Date: 1995-06-09 GLP/GEP: Yes, unpublished ... also filed: 11 / 65 13 / 02	Y	Arysta LifeScience
Weilbaecher, R.	1998	Certificate of Analysis No. AZ07563 Propamocarb hydrochloride Code: AE B066752 00 1B97 0001 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C001142, Edition Number: M-181858-01-1 Date: 1998-10-09 GLP/GEP: n.a., unpublished	N	Bayer
Anonymous	2014	A 28-day inhalation toxicity study of propamocarb hydrochloride in sprague dawley rats WIL Research Laboratories Inc., Ashland, OH, USA TF- BCS-Agriphar, Report No.: WIL-21215, Edition Number: M-494160-01-1 EPA MRID No.: 49452701 Date: 2014-08-13 GLP/GEP: yes, unpublished	Y	TF- Bayer-Agriphar

Author(s)	Year	Title Source *(where different from company)* Company name, Report No., Date, GLP status *(where relevant)*, published or not	Vertebrate study Y/N	Owner
Anonymous	2001	Previcur-N (AE B06675200 SL67 A2 - EXP 10382 A): Acute inhalation toxicity (nose only) study in the rat Safepharm Lab. Ltd., Derby, United Kingdom Bayer CropScience, Report No.: C014379, Edition Number: M-206501-01-1 Date: 2001-07-03 GLP/GEP: yes, unpublished	Y	Bayer
Weyers, A.	2008	Biodegradation with Propamocarb-hydrochloride Currenta GmbH & Co. OHG, Leverkusen, Germany Bayer Report No.: 2008/0004/01 Edition Number: M-299907-02-1 Date: 2008-04-08 ... amended: 2008-08-13 GLP/GEP: Yes, unpublished	Y	Bayer
Anonymus	1990	Previcur N (propamocarb HCl techn.): 21-day prolonged toxicity study in the rainbow trout under flow-through conditions RCC, Research and Consulting Company Ltd., Switzerland Bayer Report No.: 223086; A85548 Edition Number: M-157819-02-1 MRID#: 41834602 Date: 1990-02-06 ... amended: 1990-12-03 GLP/GEP: Yes, unpublished	Y	Bayer
Young, B. M.; Ruff, D. F.	1996	Propamocarb hydrochloride water-miscible concentrate 68.2 percent w/w (738 g/L); Code AE B066752: Effects on life-cycle of the water flea (Daphnia magna) in a static renewal system AgrEvo USA Company, USA Bayer Report No.: A89730; O008A/U037 Report includes Trial Nos.: 516AV Edition Number: M-165289-01-1 MRID#: 44557801 Date: 1996-11-26 GLP/GEP: Yes, unpublished	Y	Bayer

15 ANNEXES

Annex I is attached as a separate document.