S-Methoprene

Product-type 18

List of endpoints – updated June 2016

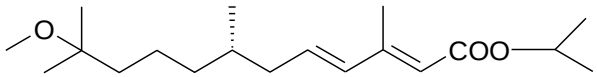
following the submission of data after active substance approval

CHAPTER 1: IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, CLASSIFICATION AND LABELLING

Active substance (ISO Common Name)	S-Methoprene
Function (*e.g.* fungicide)	Insecticide

Rapporteur Member State	Ireland

Identity (Annex IIA, point II.)

Chemical name (IUPAC)	Isopropyl-(2E,4E,7S)-11-methoxy-3,7,11-trimethyl-2,4. – dodecadienoate
Chemical name (CA)	(S)-methoprene
CAS No	65733-16-6
EC No	None
Other substance No.	Not applicable
Minimum purity of the active substance as manufactured (g/kg or g/l)	≥ 950 g/kg
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	None identified.
Molecular formula	$C_{19}H_{34}O_3$
Molecular mass	310.48
Structural formula	

Physical and chemical properties (Annex IIA, point III, unless otherwise indicated)

Freezing point (state purity)	Purity: 98.3% < -22°C
Boiling point (state purity)	Purity: 99.6% 279.9 °C
Temperature of decomposition	Not applicable as the boiling point was estimated.
Appearance (state purity)	Purity: > 95% A transparent pale yellow liquid at 24°C with a faint, fruity, waxy odour.
Relative density (state purity)	Purity: > 95% 0.924 g/ml at 20°C
Surface tension	Purity: 98.3% 50.1 mN/m at 20°C (1 mg/l)
Vapour pressure (in Pa, state temperature)	Purity: 98.1 % 0.623 mPa at 20°C 1.08 mPa at 25°C
Henry's law constant (Pa m^3 mol^{-1})	0.0306 Pa x m^3/mol at 20°C
Solubility in water (g/l or mg/l, state temperature)	Purity: > 95% 6.85 mg/l at 20 °C
Solubility in organic solvents (in g/l or mg/l, state temperature) (Annex IIIA, point III.1)	Purity: 98.1% Hexane: > 5 10^5 mg/l Methanol: > 4.5 10^5 mg/l Acetone: > 5 10^5 mg/l Temperature: 20 ± 1 °C
Stability in organic solvents used in biocidal products including relevant breakdown products (IIIA, point III.2)	Not required as no organic solvents are present in the technical.
Partition coefficient (log P_{OW}) (state temperature)	LogKow = 6.34 (calculated)
Hydrolytic stability (DT_{50}) (state pH and temperature) (point VII.7.6.2.1)	pH 1.2: 17 hours at 37 ± 0.5°C
	pH 4: Stable at 25 ± 0.5°C, 37 ± 0.5°C and 50 ± 0.5°C
	pH 7: Stable at 25 ± 0.5°C, 37 ± 0.5°C and 50 ± 0.5°C
	pH 9: Stable at 25 ± 0.5°C, 37 ± 0.5°C and 50 ± 0.5°C
Dissociation constant (not stated in Annex IIA or IIIA; additional data requirement from TNsG)	Not required as S-methoprene does not dissociate in water.
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	Purity: 95% 90% Neutral Methanol: λ_{max} 264 nm; ε 26,700 90% Acidified Methanol: λ_{max} 264 nm; ε 26,600 90% Alkalinized Methanol: λ_{max} 266 nm; ε 27,450
Photostability (DT_{50}) (aqueous, sunlight, state pH) (point VII.7.6.2.2)	DT_{50} at pH 7: 4.8 hours (continuous irradiation)

Quantum yield of direct phototransformation in water at Σ > 290 nm (point VII.7.6.2.2)	1.1
Flammability	263 °C
Explosive properties	The molecular structure of S-Methoprene indicates that the substance has little or no explosive properties.

Classification and Proposed Labelling

With regard to physical/chemical data	None
With regard to toxicological data	None
With regard to fate and behaviour data	None
With regard to ecotoxicological data	N, R50/53, S35 CLP Labelling: Chronic Category 1, H410, P273, P391, P501

CHAPTER 2: METHODS OF ANALYSIS

Soil (principle of method and LOQ) (Annex IIA, point 4.2)	Not required
Air (principle of method and LOQ) (Annex IIA, point 4.2)	Not required
Water (principle of method and LOQ) (Annex IIA, point 4.2)	GC-MS LOQ: 0.1µg/l
Body fluids and tissues (principle of method and LOQ) (Annex IIA, point 4.2)	S-Methoprene is not classified as being toxic or highly toxic. It is therefore proposed that analytical methods in animal and human body fluids and tissues are not required.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	Not required
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	Not required

CHAPTER 3: IMPACT ON HUMAN HEALTH

Absorption, distribution, metabolism and excretion in mammals (Annex IIA, point 6.2)

Rate and extent of oral absorption:	Peak plasma concentration: Low dose group 6 hours (male) and 12 hours (female) High dose group 4 hours (male) and 6 hours (female) Indicating S Methoprene is systemically absorbed in 4 to 12 hours Oral absorption 35%
Rate and extent of dermal absorption:	2.86 %
Distribution:	Low dose; stomach, liver, adrenals and white fat . High dose; (after 6 hours) stomach, GI tract, liver, white fat and kidney. Multiple dose; GI tract, liver, stomach, kidney and white fat (highest in males)
Potential for accumulation:	Tissue radioactivity negligible at 96 hours in most tissues with the exception of white fat following single dosing. (1-4% remaining at 96 hours). The same pattern applied to repeat dose group. S-Methoprene does not bioaccumulate
Rate and extent of excretion:	Majority of S-Methoprene excreted within 24-48 hours (34-69% in faeces; 14-28% in expired air; 8-20% in urine).
Toxicologically significant metabolite	Chromatographic analysis of urine, faeces, and bile samples indicated at least 22, 23, and 11 radioactive components, respectively, all more polar than the parent compound.

Acute toxicity (Annex IIA, point 6.1)

Rat LD_{50} oral	> 5050 mg/kg bw/day
Rat LD_{50} dermal	> 5050 mg/kg bw/day
Rat LC_{50} inhalation	> 2.38 mg/L
Skin irritation	Not irritating
Eye irritation	Not irritating
Skin sensitization (test method used and result)	Not a sensitiser (Buehler test)

Repeated dose toxicity (Annex IIA, point 6.3)

Species/ target / critical effect	Dog 90-day study: Clinical signs such as thin faeces and diarrhoea, increased liver weight in males and females and raised ALKP values in females Rat 104 weeks study: Liver histopathology
Lowest relevant oral NOAEL / LOAEL	Dog: LOAEL = 300 mg/kg bw/day

	NOAEL = 100 mg/kg bw/day Rat: LOAEL = 130.8 mg/kg bw/day NOAEL = 65.4 mg/kg bw/day
Lowest relevant dermal NOAEL / LOAEL	Not relevant
Lowest relevant inhalation NOAEL / LOAEL	Not relevant

Genotoxicity (Annex IIA, point 6.6)

	Non genotoxic in an *in vitro* bacterial mutation assay, an *in vitro* chromosomal aberration assay and an *in vitro* gene mutation mammalian assay

Carcinogenicity (Annex IIA, point 6.4)

Species/type of tumour	Rat / No carcinogenic potential. Mouse / No carcinogenic potential.
Lowest dose with tumours	Not relevant

Reproductive toxicity (Annex IIA, point 6.8)

Species/ Reproduction target /critical effect	Rat; Reduction in body weight in both parents and offspring
Lowest relevant reproductive NOAEL / LOAEL	LOAEL = 130.8 mg/kg bw/day NOEL = 8.15 mg/kg bw/day
Species/Developmental target /critical effect	Rat: Reduction in weight gain (maternal), intrauterine mortality and low pregnancy rate Rabbit: Intrauterine foetal growth retardation, maternal death, increase in abortions, reduced activity and vaginal bleeding, decreased weight gain
Lowest relevant developmental NOAEL / LOAEL	LOAEL (rat) = 1000 mg/kg bw/day NOAEL (rat) = 250 mg/kg bw/day LOAEL (rabbit) = 1000 mg/kg bw/day NOAEL (rabbit) = 100 mg/kg bw/day

Neurotoxicity / Delayed neurotoxicity (Annex IIIA, point VI.1)

Species/ target/critical effect	Not applicable
Lowest relevant developmental NOAEL / LOAEL.	Not applicable

Other toxicological studies (Annex IIIA, VI/XI)

.....	Not applicable

Medical data (Annex IIA, point 6.9)

	Workers producing S-Methoprene for Báblona

.....	Bioenvironmental Centre Ltd. Over the past 25years have reported no incidences of adverse effects. Workers have reported no incidences of adverse effects, accidents, poisonings or clinical cases during the synthesis of S-Methoprene and the production of the biocidal product. No clinical cases, poisoning or incidents have been reported. No observations of sensitisation or allergenicity have been made following use of S-Methoprene.

Summary (Annex IIA, point 6.10)	Value	Study	Safety factor
ADI (if residues in food or feed)	Not applicable	Not applicable	Not applicable
AOEL (Operator/Worker Exposure)	Not applicable	Not applicable	Not applicable
Drinking water limit	Not applicable	Not applicable	Not applicable
ARfD (acute reference dose)	Not applicable	Not applicable	Not applicable
AEL acute	0.35 mg/kg bw/day	Rabbit developmental study	100
AEL medium-term	0.35 mg/kg bw/day	90 day dog study	100
AEL long-term	0.076 mg/kg bw/day	2-year rat study	100

Acceptable exposure scenarios (including method of calculation)

Professional users	Oral and Inhalation exposure are not applicable. Dermal exposure was assessed using reverse reference scenario, as there is no suitable model to assess exposure. To achieve the NOAEL a 60 kg adult would need to be dermally exposed to the contents of 119.8 bait stations/day. Exposure is acceptable
Non-professional users	Oral and Inhalation exposure are not applicable. Dermal exposure was assessed using reverse reference scenario, as there is no suitable model to assess exposure. To achieve the NOAEL a 60 kg adult would need to be dermally exposed to the contents of 119.8 bait stations/day. Exposure is acceptable
Indirect exposure as a result of use	Dermal short-term exposure is considered for infant, children and adults. Oral short-term exposure is considered for infants. Inhalation long-term exposure is considered for infant, children and adults. All exposure to each group was considered acceptable. Indirect exposure to S-Methoprene *via* the environment i.e. via drinking water or foodstuffs is negligible.

CHAPTER 4: FATE AND BEHAVIOUR IN THE ENVIRONMENT

Route and rate of degradation in water (Annex IIA, point 7.6, IIIA, point XII.2.1, 2.2)

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	S-Methoprene technical was found to be hydrolytically stable at pH 4, 7 and 9 (examined at 25, 37 and 50ºC). In strong acid solution (pH 1.2), hydrolysis is rapid with a half-life of 17 hours at 37ºC.
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	DT_{50} at pH 7: 4.8 hours (15 d continuous irradiation with a Xe lamp, pH 7, sterilised, 22 ± 2 ºC) A number of submitted journal articles indicated that Methoprene rapidly decomposes in aqueous solution when exposed to sunlight. In sterilised water buffered to pH 7 the DT_{50} of Methoprene was reported to be between <1 day and 5 days (Quistad et al. 1975, Schooley et al. 1975). Sixteen transformation products detected, with the methoprene isomer [E,Z]-S-Methoprene and seven unidentified components each individually exceeding 10% of applied radioactivity.
Readily biodegradable (yes/no)	No
Inherent biodegradable (yes/no)	Yes (OECD 302C)
Biodegradation in seawater	Not relevant
Non-extractable residues	Aerobic water-sediment study - two systems presented River system: 36.9% @ 100days Pond system: 41.0% @ 100days
Distribution in water / sediment systems (active substance)	Aerobic water-sediment study - two systems presented <u>River system:</u> Water phase: 95.9% immediately after dosing to <LOQ by day 14; $DisT_{50}$ = 1.48d @ T=12°C (SFO) Sediment phase: max of 16.6% on day 2 to 3.3% by day 49; $DisT_{50}$ = 7.09d @ T=12°C (SFO) Whole system: 95.9% immediately after dosing to 3.3% by day 49; DT_{50} = 2.50d @ T=12°C (SFO) <u>Pond system:</u> Water phase: 99.1% immediately after dosing to 0.3% by day 49; DT_{50} = 1.02d @ T=12°C (SFO) Sediment phase: max of 20.8% on day 2 to 1.7% by day 49; DT_{50} = 12.8d @ T=12°C (SFO) Whole system: 99.1% immediately after dosing to 2.0% by day 49; DT_{50} = 1.65d @ T=12°C (DFOP, k_1 = 0.109, k_2 = 1.223, g = 0.2756) <u>Note</u>: Comparison of biphasic kinetic parameters with trigger cutoffs is not ideal. Therefore calculation of the DT_{50} from the slow phase of the degradation yields a more conservative estimate of degradation: $DT_{50} = \ln 2/k_1 = 0.6931/0.1089 = 6.4$ days @ T = 20 °C or 12.1 days @ T = 12 °C.
Distribution in water / sediment systems	Aerobic water-sediment study - two systems presented

(metabolites)	Metabolite M2 (River system): Water phase: max of 7.8% @ day 2 to1.0% by day 21; DT_{50} not reported Sediment phase: max of 1.6% on day 2 to 0.3% by day 49; DT_{50} not reported Whole system: max of 9.4% @ day 2 to 0.3% by day 49; DT_{50} = 5.40d @ T=12°C (SFO) Metabolite M2 (Pond system): Water phase: max of 6.2% @ day 2 to 0.8% by day 21; DT_{50} not reported Sediment phase: max of 1.9% on day 2 to 0.6% by day 49; DT_{50} not reported Whole system: max of 8.1% @ day 2 to 0.6% by day 49; DT_{50} = 9.88d @ T=12°C (SFO) Metabolite M3 (River system): Water phase: max of 10.2% @ day 2 to < LOQ by day 14; DT_{50} not reported Sediment phase: max of 2.0% @ day 2 to 0.3% by day 49; DT_{50} not reported Whole system: max of 10.2% @ day 2 to 0.3% by day 49; DT_{50} = 2.29d @ T=12°C (SFO) Metabolite M3 (Pond system): Water phase: max of 5.8% @ day 2 to <LOQ by day 7; DT_{50} not reported Sediment phase: max of 1.9% @ day 2 to 0.3% by day 49; DT_{50} not reported Whole system: max of 7.7% @ day 2 to 0.3% by day 49; DT_{50} = 3.64d @ T=12°C (SFO)

Route and rate of degradation in soil (Annex IIIA, point VII.4, XII.1.1, XII.1.4; Annex VI, para. 85)

Mineralisation (aerobic)	Aerobic soil degradation study - four soils, one radiolabel: Max 51.1% on day 118 for Soil I Max 61.5% on day 118 for Soil I Max 52.4% on day 118 for Soil I Max 52.8% on day 62 for Soil I

Laboratory studies (range or median, with number of measurements, with regression coefficient)	Aerobic soil degradation study - four soils, one radiolabel: DT_{50} values @ 20°C = 0.93 (soil 1), 0.73 (soil 2), 0.79 (soil 3) and 0.83 (soil 4) with correlation values of 0.9888 (soil 1), 0.9922 (soil 2), 0.999 (soil 3) and 0.9691 (soil 4). DT_{50} values @ 12°C = 1.76d (soil 1), 1.38d (soil 2), 1.50d (soil 3) and 1.57d (soil 4). These were calculated from the 20°C above using the equation: $DT_{50}(12\ °C) = DT_{50}(20\ °C) \bullet e^{(0\ 08\ (20\ -12))}$ Geomean DT50 = 1.55 days
Field studies (state location, range or median with number of measurements)	Not relevant
Anaerobic degradation	Not relevant
Soil photolysis	Not relevant
Non-extractable residues	Aerobic soil degradation study - four soils, one radiolabel: Max 48.6% on day 7 for Soil I Max 48.8% on day 7 for Soil I Max 54.3% on day 3 for Soil I Max 52.2% on day 7 for Soil I
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	Not relevant
Soil accumulation and plateau concentration	Not relevant

Adsorption/desorption (Annex IIA, point XII.7.7; Annex IIIA, point XII.1.2)

Ka , Kd	K_a adsorption values (L/kg): 5.5, 6.5, 7.9 (mean = 6.6, n = 3 soils)
Ka_{oc} , Kd_{oc}	Adsorption coefficients (L/kg) of 537, 684 and 1407, with a mean of 876.
pH dependence (yes / no) (If yes, state type of dependence)	pH dependent: No

Fate and behaviour in air (Annex IIIA, point VII.3, VII.5)

Direct photolysis in air	Not relevant
Quantum yield of direct photolysis	Not relevant

Photo-oxidative degradation in air	Not relevant
Volatilization	Not relevant

Monitoring data, if available (Annex VI, para. 44)

Soil (indicate location and type of study)	No data is provided
Surface water (indicate location and type of study)	No data is provided
Ground water (indicate location and type of study)	No data is provided
Air (indicate location and type of study)	No data is provided

CHAPTER 5: EFFECTS ON NON-TARGET SPECIES

Toxicity data for aquatic species (most sensitive species of each group)
(Annex IIA, point 8.2, Annex IIIA, point 10.2)

Species	Time-scale	Endpoint	Toxicity
Fish			
Zebrafish, *Brachydanio rerio,*	96 h	LC_{50} NOEC	An LC_{50} value of 4.26 mg/l and NOEC value of 1.25 mg/l was determined.
Invertebrates			
Daphnia magna	48 h	EC_{50}	A 48-Hour EC_{50} value of 0.22mg/l was determined.
Daphnia magna	21d	NOEC	0.019 mg/L measured
Algae			
Selenastrum capricornutum	72 h	ErC_{50}	An ErC_{50} value of 2.264 mg/l was determined.
Microorganisms			
Activated sewage sludge	3 h	EC_{50}	A 3-Hour EC_{50} value of 6.85 mg/l was determined.

Toxicity data for aquatic species (most sensitive species of each group)
(Annex IIA, point 8.2, Annex IIIA, point 10.2)

Species	Time-scale	Endpoint	Toxicity
Fish			
Zebrafish, *Brachydanio rerio,*	96 h	LC_{50} NOEC	An LC_{50} value of 4.26 mg/l and NOEC value of 1.25 mg/l was determined.
Invertebrates			
Daphnia magna	48 h	EC_{50}	A 48-Hour EC_{50} value of 0.38 mg/l was determined.
Algae			
Selenastrum capricornutum	72 h	ErC_{50}	An ErC_{50} value of 2.264 mg/l was determined.
Microorganisms			
Activated sewage sludge	3 h	EC_{50}	A 3-Hour EC_{50} value of > 100 mg/l was determined.

Effects on earthworms or other soil non-target organisms

Acute toxicity to ……..	Not relevant

(Annex IIIA, point XIII.3.2)	
Reproductive toxicity to …… (Annex IIIA, point XIII.3.2)	Not relevant

Effects on soil micro-organisms (Annex IIA, point 7.4)

Nitrogen mineralization	Not relevant
Carbon mineralization	Not relevant

Effects on terrestrial vertebrates

Acute toxicity to mammals (Annex IIIA, point XIII.3.3)	Not relevant
Acute toxicity to birds (Annex IIIA, point XIII.1.1)	Not relevant
Dietary toxicity to birds (Annex IIIA, point XIII.1.2)	Not relevant
Reproductive toxicity to birds (Annex IIIA, point XIII.1.3)	Not relevant

Effects on honeybees (Annex IIIA, point XIII.3.1)

Acute oral toxicity	Not relevant
Acute contact toxicity	Not relevant

Effects on other beneficial arthropods (Annex IIIA, point XIII.3.1)

Acute oral toxicity	Not relevant
Acute contact toxicity	Not relevant
Acute toxicity to ……..	Not relevant

Bioconcentration (Annex IIA, point 7.5)

Bioconcentration factor (BCF)	516
Depration time (DT_{50}) (DT_{90})	Not relevant
Level of metabolites (%) in organisms accounting for > 10 % of residues	Not relevant

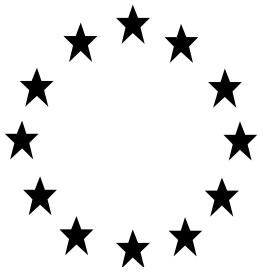
CHAPTER 6: OTHER ENDPOINTS

No other end points are available for S-Methoprene.

Regulation (EU) n°528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



S-Methoprene

Product-type 18

(Insecticides, acaricides and products to control other arthropods)

December 2013

RMS: IRELAND

S-Methoprene PT 18

Assessment Report

Finalised in the Standing Committee on Biocidal Products at its meeting on 13 December 2013

CONTENTS

1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. PRINCIPLE OF EVALUATION

This assessment report has been established as a result of the evaluation of S-Methoprene as product-type 18 (Insecticides, acaricides and products to control other arthropods), carried out in the context of the work programme for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market[1], with a view to the possible inclusion of this substance into Annex I or IA to the Directive.

The evaluation has therefore been conducted in the view to determine whether it may be expected, in light of the common principles laid down in Annex VI to Directive 98/8/EC, that there are products in product-type 18 containing S-Methoprene that will fulfil the requirements laid down in Article 5(1) b), c) and d) of that Directive.

1.2. PURPOSE OF THE ASSESSMENT

The aim of the assessment report is to support a decision on the approval of S-Methoprene for product-type 18, and should it be approved, to facilitate the authorisation of individual biocidal products in product-type 18 that contain S-Methoprene. In the evaluation of applications for product authorisation, the provisions of Regulation (EU) No 528/2012 shall be applied, in particular the provisions of Chapter IV, as well as the common principles laid down in Annex VI.

The conclusions of this report were reached within the framework of the uses that were proposed and supported by the applicant (see Appendix II). Extension of the use pattern beyond those described will require an evaluation at product authorisation level in order to establish whether the proposed extensions of use will satisfy the requirements of Regulation (EU) No 528/2012.

For the implementation of the common principles of Annex VI, the content and conclusions of this assessment report shall be taken into account.

However, where conclusions of this assessment report are based on data protected under the provisions of Regulation (EU) No 528/2012, such conclusions may not be used to the benefit of another applicant, unless access to these data has been granted.

1.3. PROCEDURE FOLLOWED

This assessment report has been established as a result of the evaluation of S-Methoprene as product-type 18 (Insecticides, acaricides and products to control other arthropods), carried out in the context of the work programme for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market.

[1] Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing of biocidal products on the market. OJ L 123, 24.4.98, p.1.

S-Methoprene (CAS no. 65733-16-6) was notified as an existing active substance, by Bábolna Bioenvironmental Centre Ltd., hereafter referred to as the applicant, in product-type 18.

Commission Regulation (EC) No. 1451/2007 of 4 December 2007[2] lays down the detailed rules for the evaluation of dossiers and for the decision-making process in order to include or not an existing active substance into Annex I or IA to the Directive.

In accordance with the provisions of Article 7(1) of that Regulation, Ireland was designated as Rapporteur Member State to carry out the assessment on the basis of the dossier submitted by the applicant. The deadline for submission of a complete dossier for s-Methoprene as an active substance in product-type 18 was 30th April 2006, in accordance with Annex V of Regulation (EC) No. 2032/2003.

On 28th April 2006, the Irish competent authorities received a dossier from the applicant. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 1st November 2006.

On 29th October 2010, the Rapporteur Member State submitted, in accordance with the provisions of Article 14(4) and (6) of Regulation (EC) No 1451/2007, to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report. The Commission made the report available to all Member States by electronic means on 4th February 2011. The competent authority report included a recommendation for the inclusion of S-Methoprene in Annex I to the Directive for PT 18.

In accordance with Article 16 of Regulation (EC) No 1451/2007, the Commission made the competent authority report publicly available by electronic means on 24 June 2013. This report did not include such information that was to be treated as confidential in accordance with Article 19 of Directive 98/8/EC.

In order to review the competent authority report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by the Commission. Revisions agreed upon were presented at technical and competent authority meetings and the competent authority report was amended accordingly.

In accordance with Article 15(4) of Regulation (EC) No 1451/2007, the present assessment report contains the conclusions of the Standing Committee on Biocidal Products, as finalised during its meeting held on 13 December 2013.

[2] Commission Regulation (EC) No 1451/2007 of 4 December 2007 on the second phase of the 10-year work programme referred to in Article 16(2) of Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. OJ L 325, 11.12.2007, p. 3

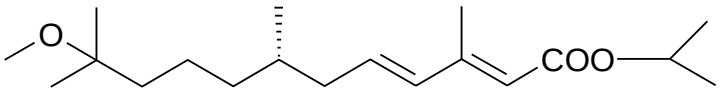
2. OVERALL SUMMARY AND CONCLUSIONS

2.1. PRESENTATION OF THE ACTIVE SUBSTANCE

2.1.1. Identity, Physico-Chemical Properties and Methods of Analysis

CAS No.	65733-16-6
EC No.	Not available
Other No. (CIPAC, ELINCS)	Not applicable
Chemical Name (IUPAC)	Isopropyl-(2E,4E, 7S)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate
Common name, synonym	S-Methoprene
Molecular formula	$C_{19}H_{34}O_3$
Purity	Specification 95% w/w, minimum

Structural formula



Molecular weight (g/mol) 310.48 g/mol

The physical chemical properties of S-Methoprene have been determined for the proposed uses. A number of data requirements have been identified and remain to be addressed.

S-Methoprene technical material is a transparent pale yellow liquid with a faint waxy and fruity odour. The boiling point of purified active substance is 279.9°C. The data for technical material of S-Methoprene indicates that it is only slightly soluble in water. Purified S-Methoprene is highly soluble in organic solvents and will be fat soluble. Surface tension of 50.1mN/m indicates that the molecule is surface active. Results of a vapour pressure study indicate that the molecule is not volatile.

It is not flammable or autoflammable up to 263°C. Based on the molecular structure it is deemed to be non explosive and non oxidising.

The product being supported is a ready to use bait, Biopren® Pharaoh's Ant Colony Eliminator.

2.1.1.1. Analysis of the active substance as manufactured

A method of analysis using Chiral HPLC-UV, was supplied to determine the S-Methoprene content in technical active substance. CIPAC/4427 Method is also available. Validated methods using GC/MS have been supplied for analysis of certain significant impurities in the technical

active substance. Certain issues have been questioned by the rapporteur. The method is broadly acceptable. See section 3.4, Demand for further information.

2.1.1.2. Formulation analysis

No acceptable method was supplied.

2.1.1.3. Residue analysis

Analytical methods for determination of S-Methoprene in soil, food and foodstuffs were not submitted based on the specific use of the product.
An acceptable method was supplied for analysis of residues of parent S-Methoprene in surface, ground and drinking water to an LOQ of 0.1µg/L.
A method for residues in air is not required based on the results of the vapour pressure study (v.p. <0.01 Pa).
Because the molecule does not classify as either toxic or very toxic, a method for residues in body fluids and tissues is not required.

2.1.2. Intended Uses and Efficacy

The assessment of the biocidal activity of the active substance demonstrates that it has a sufficient level of efficacy against the target organism(s) and the evaluation of the summary data provided in support of the efficacy of the accompanying product, establishes that the product may be expected to be efficacious.

In addition, in order to facilitate the work in granting or reviewing authorisations, the intended uses of the substance, as identified during the evaluation process, are listed in Appendix II.

2.1.2.1. Field of use envisaged / Function and organism(s) to be controlled

Insecticide (Product-Type 18).

S-Methoprene is intended for indoor use by professional and non-professional users. It is used for the control of Pharaoh's ants (*Monomorium pharaonis*). The reference product Biopren® Pharaoh's Ant Colony Eliminator contains 5g/kg (0.5% w/w) of S-Methoprene.

2.1.2.2. Effects on target organism(s)

S-Methoprene acts as a juvenile hormone mimic to disrupt the normal development of insects. It displays no immediate killing effect on the target organisms but inhibits the egg-laying capacity of the queen and the development of the brood (acting on the larval stage). The granular bait containing the active substance is transported by the target organisms into the colony nest where it is fed to the colony resulting in complete extermination within 12-14 weeks. The product is contained in sealed plastic packaging and applied at a recommended dose of 2 baiting stations per $20m^2$.
Three laboratory and five field studies were carried out on S-Methoprene (0.5% w/w) containing granular ant baits. Seven of the studies demonstrated total efficacy (i.e. 100%) of the product whilst one laboratory study achieved 90-99% efficacy over a 13 week test period.

S-methoprene has shown to be effective against Pharaoh ants and the data provided is acceptable for annex I inclusion. Final conclusions regarding application rate can be drawn at the product

authorisation stage with the provision of robust field studies demonstrating the most appropriate dose depandant on the infestation level.

2.1.2.3. Humaneness

Not applicable.

2.1.2.4. Resistance

Data from published studies has indicated that S-Methoprene is unlikely to induce resistance in Pharaoh ants. The product should only be used when there is an infestation of Pharaoh's ants. This should limit any potential for resistance to occur.

2.1.3. Classification and Labelling

2.1.3.1. Proposal for the classification and labelling of the active substance

Proposal for the classification of the active substance

Hazard symbol: (for labelling)	**N**	
Indication of danger:	-	Dangerous for the environment
Risk Phrases: (for labelling)	R50/53	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
Safety Phrases: (for labelling)	S35	This material and its container must be disposed of in a safe way

Classification Proposal			**Justification**
Hazard symbols:	 GHS09		
Signal Word	Warning		Triggered by H410
Hazard Statements:	Chronic Aquatic 1 H410	Very toxic to aquatic life with long lasting effects	Triggered by study data and CLP classification tables

Precautionary Statements	P273	Avoid release to the environment	Recommended phrase.
	P391	Collect Spillage	Recommended phrase
	P501	Dispose of contents/ container in accordance with applicable regulations	Recommended phrase
EU Specific Statements	EUH401	To avoid risks to human health and the environment, comply with the instructions for use	All plant protection products subject to Regulation (EC) No 1107/2009 shall also include this wording.

Justification for the proposal:

Physical-Chemical Properties:
The active substance S-Methoprene will not classify from a physical/chemical viewpoint.

Human Health:
No classification required.

Environment:
The active substance S-Methoprene classifies as very toxic to aquatic organisms as it has chronic toxicity of ≤ 1 mg/l to invertebrates, the logKow is > 6 and S-Methoprene is not readily biodegradable. The BCF is not experimentally determined it is estimated. It is recommended that its container be disposed of in a safe place.

2.1.3.2. Proposal for the classification and labelling of the product(s)

Proposal for the classification and labeling of the product

Hazard symbol: (for labelling)	**N**	
Indication of danger:	-	Dangerous for the environment
Risk Phrases: (for labelling)	R50/53	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
Safety Phrases: (for labelling)	S35	This material and its container must be disposed of in a safe way

Classification Proposal			Justification
Hazard symbols:	 GHS09		
Signal Word	None		None triggered
Hazard Statements:	Chronic Aquatic Cat 1 H410	Very toxic to aquatic life with long lasting effects	Triggered by study data and CLP classification tables
Precautionary Statements	P391 P501	Collect spillage Dispose of contents/ container in accordance with applicable regulations	Recommended phrase Recommended phrase
EU Specific Statements	EUH401	To avoid risks to human health and the environment, comply with the instructions for use	All plant protection products subject to Regulation (EC) No 1107/2009 shall also include this wording.

Justification for the proposal:

Physical-Chemical Properties:
The product Biopren® Pharaoh's Ant Colony Eliminator will not classify from a physical/chemical viewpoint.

Human Health:
The product Biopren® Pharaoh's Ant Colony Eliminator will not classify for human health on the basis of the data presented.

Environment:
The active substance S-Methoprene classifies as very toxic to aquatic organisms as it has chronic toxicity of ≤ 1 mg/l to invertebrates, the logKow is > 6 and S-Methoprene is not readily biodegradable. The BCF is not experimentally determined it is estimated. It is recommended that this product and its container be disposed of in a safe place.

2.2. SUMMARY OF THE RISK ASSESSMENT

2.2.1. Human Health Risk Assessment

2.2.1.1. Hazard Identification

The data requirements for identification of the potential health hazard of S-Methoprene have been fully investigated.

Single and repeat dose toxicokinetic and metabolism studies conducted in rats were presented. Based on the results of these studies, [14C]-S-Methoprene is systemically absorbed between 4 and 12 hours depending on the dosing level and the sex of the animal. It has an oral absorption value of 35%. The stomach, liver, adrenals and white fat are the prominent tissues with high radioactivity concentration in low dose groups. In the high dose group, the stomach, GI tract, liver, white fat and kidney demonstrated the highest concentrations of radioactivity after six hours in males. In multiple dose groups, the GI tract, liver, stomach, kidney and white fat contained significant radioactivity in males. For all dosing regimens, the tissue radioactivity was negligible at 96 hours post dose, with the exception of the white fat, which contained up to 4.633 % of the administered radioactivity. However, in all other tissues the levels of radioactivity decreased between the 6 and 96 hour time points, indicating that neither the compound nor its metabolites accumulate in these tissues. S-Methoprene is mostly excreted within 24 to 48 hours of administration, indicating that it is rapidly eliminated from the body. The primary route of excretion of the compound is in the faeces and expired air, with a lesser amount recovered in urine and cage rinses. Chromatographic analysis of urine, faeces, and bile samples indicated the presence of at least 22, 23, and 11 radioactive components, respectively. All of these components were more polar than the parent compound, which may allow them to be excreted more readily from the body.

The potential dermal absorption was investigated in an *in vitro* study using human volunteer skin (split-thickness skin emebranes) and radio-labelled s-methoprene (0.125% w/w). Following topical application of the test substance to human skin *in vitro*, the absorbed dose of [^{14}C]–S–Methoprene was 0.04%. The dermal delivery of [^{14}C] – S – Methoprene was 1.61%. The majority of the applied dose was removed by washing the skin, (the total dislodgeable dose was 94.16%). The dermal absorption of S-Methoprene was therefore estimated to be 2.86% (dermal delivery and stratum corneum). An agreed dermal adsorption rate of 3.50% was established from the estimated dermal adsorption value of 2.86% based on the inclusion of tape strips (3-5) (0.58%) in the calculation of dermal adsorption.

The acute toxicity of S-Methoprene via the oral dermal and inhalation routes was appropriately tested using guideline studies. The acute oral LD_{50} and dermal LD_{50} were determined to be greater than 5050 mg/kg bw and the acute inhalation LC_{50} was greater than 2.38mg/l. Minimal and reversible eye and skin irritation were observed and no dermal sensitisation potential was observed. No classification required for acute oral, dermal or inhalation toxicity, eye and skin irritation end-points or skin sensitisation. Accordingly, it is proposed that these endpoints are not considered further in the risk characterisation process.

There was no information to determine the potential of S-Methoprene to cause respiratory sensitisation/occupational asthma and the product did not contain any co-formulants that were classified for respiratory sensitisation. Therefore, respiratory sensitisation was not considered further in the risk characterisation process.

Several repeat oral dietary studies were conducted using Methoprene including an oral 28-day study in mice, an oral 14-day study in dog, and an oral 90-day repeat dose toxicity study in dogs. These studies using Methoprene were only included for information purposes due to their study reports low reliability and accordingly were not considered further in the risk characterisation. Repeated oral dose toxicity was evaluated for S-Methoprene in a 90-day dog study and a 90-day

rat study. Following repeated oral administration of S-Methoprene in the oral 90-day dog repeat dose study the effects noted at the mid dose of 300 mg/kg bw/day included clinical signs such as thin faeces and diarrhoea, increased liver weight in males and females and raised alkaline phosphatise (ALP) values in females. At the highest dose assessed, 1000 mg/kg bw/day, increases in liver weight and ALP activity and zonal vacuolisation of hepatocytes were noted in both sexes. In the 90-day oral repeat dose rat study increased liver weight is also noted at the lowest dose assessed. Kidney organ weight is also increased in the rat study at the lowest dose examined. The 90-day repeat dose study conducted in rats produced a LOAEL value only. Accordingly, this study was not taken forward for risk characterisation purposes.

S-Methoprene showed no genotoxic potential in in-vitro tests for bacterial cell mutation, clastogenicity and mutagenicity. As a result, in-vivo studies are not required as all in-vitro tests undertaken on S-Methoprene were negative and accordingly no classification is proposed. Similarly, no classification is proposed for Biopren® Pharaoh's Ant Colony Eliminator for this endpoint given that none of the other co-formulants are classified for genotoxicity.

Lifetime exposure studies including a 2-year study in rat and an 18-month study in mice were conducted. Following repeated oral administration of Methoprene in a combined chronic toxicity and carcinogenicity 104 week study in rat the most sensitive findings were observed at the highest dose, equivalent to 108 mg/kg bw/day S-Methoprene. This study highlighted evidence of liver toxicity such as increased incidence of hepatic lesions (bile-duct proliferation and portal lymphocyte infiltration) in males and increased absolute and relative weights of the liver in females. In an 18-month mouse study an LOAEL for toxicity of 500ppm S-Methoprene (equivalent to 65.4 mg/kg bw/day) was based on evidence of liver toxicity at 1000ppm Methoprene. The liver toxicity noted included increases in focal accumulations of macrophages with brownish foamy cytoplasm in the liver, often associated with small necrotic foci and mononuclear inflammatory cells.

The carcinogenic potential of Methoprene has been investigated in lifetime dietary studies in rats and mice. No incidences of tumours or any other changes were noted in either species at dietary levels producing general toxicity. Overall, no classification for carcinogenicity is considered appropriate for Methoprene and accordingly no classification is proposed for Biopren® Pharaoh's Ant Colony Eliminator given that none of the other co-formulants are classified as carcinogens.

Developmental toxicity studies have been conducted in rats exposed to Methoprene and rats and rabbits exposed to S-Methoprene. In the rabbit gavage study severe maternal toxicity was accompanied by significant foetolethality and foetotoxicity at the high dose of 1000 mg/kg bw/day. Noted effects include severe maternal toxicity (death, weight loss) accompanied by abortions and vaginal bleeding. There was also growth retarded foetuses and retarded ossification. There was no adverse effects at the next lowest dose, 100 mg/kg bw/day which was the NOAEL for both maternal and developmental toxicity. In a rat gavage study, decreased maternal mean body weight gain, decreased food consumption and an increase in post-implantation loss were seen at the high dose level of 1000 mg/kg/day. 250 mg/kg/day was the NOAEL for both maternal and developmental toxicity. Ultimately, it is concluded that S-Methoprene is not a developmental toxicant and no classification for developmental toxicity is considered appropriate. Accordingly no classification is proposed for Biopren® Pharaoh's Ant Colony Eliminator given that none of the other co-formulants are classified as developmental toxicants.

The potential reproductive toxicity of Methoprene was investigated in a two generation study (500 and 2500 ppm equivalent to 8.15 mg/kg bw/day and 130.8 mg/kg bw/day S-Methoprene). Insufficient parental toxicity was demonstrated in this study. Slight reduction in mean pup weights seen at day 21 of lactation in the F2 generation and throughout lactation in the F3 generation. 500 ppm (8.15 mg/kg bw/day) was a clear NOAEL. 2500 ppm (130.8 mg/kg bw/day) is considered the LOAEL. In the absence of any other data on this point, and the lack of

consistent adverse effects in the treated animals, the requirement of another study is not justifiable.

No classification for effects on fertility is considered appropriate for Methoprene and accordingly no classification is proposed for Biopren® Pharaoh's Ant Colony Eliminator given that none of the other co-formulants are classified as having an adverse effect on fertility.

No classification for neurotoxicity is considered appropriate for Methoprene or S-Methoprene and accordingly no classification is proposed for Biopren® Pharaoh's Ant Colony Eliminator given that none of the other co-formulants are classified as neurotoxicants.

A single case of accidental exposure to an insecticidal product containing (also 1% carbamate and 0.5% organophosphate) 0.15% methoprene gave rise to symptoms of organophosphate/carbamate poisoning. Methoprene was not thought to have caused any of the clinical signs. There is no other evidence available.

2.2.1.2. Effects Assessment

In the dog 90-day repeat oral dose study the NOAEL value of 100mg/kg bw/day is based on clinical signs and increased liver weight in both sexes and raised ALP in females at the mid-dose level assessed of 300mg/kg bw/day. At the highest dose level assessed the effects noted include gastrointestinal signs, increased liver weight, raised ALP levels and also zonal vacuolisation of hepatocytes. All of these effects were noted in both sexes at this dose level. This information indicates a clear dose response relationship and the effects noted including the vacuolisation of hepatocytes, which may be due to fatty or fluid balance change, may be indicative of liver toxicity. Accordingly from the results achieved, the NOAEL value of 100mg/kg bw/day obtained will be taken forward to the risk characterisation for medium-term repeated exposure and was used to establish a systemic AEL medium-term reference value of: AELmedium-term 0.35 mg/kg bw/day.

In the combined chronic toxicity and carcinogenicity study conducted in rat the NOAEL value of 21.7-mg/kg bw/day is based on evidence of liver toxicity such as increased incidence of hepatic lesions (bile-duct proliferation and portal lymphocyte infiltration) in males and increased absolute and relative weights of the liver in females obtained at the highest dose assessed which is the equivalent of 108 mg/kg bw/day S-Methoprene. The value of 21.7mg/kg bw/day S-Methoprene is taken forward to the risk characterisation for long-term repeated exposure and was used to establish a systemic AEL long-term reference value of: AELlong-term 0.076 mg/kg bw/day.

In the developmental rabbit gavage study severe maternal toxicity (including mortalities and abortion) was accompanied by significant foetolethality and foetotoxicity at the high dose of 1000 mg/kg bw/day. At the next dose level assessed, 100-mg/kg bw/day, no effects were observed. The top dose is considered to be inappropriately high and the mid-range dose provides an NOEL value. However, this is used to establish a systemic AEL acute reference value. It is recognised the value used of 100mg/kg bw/day may be overly conservative but considering the inadequate dosing in the rabbit developmental study the value is brought forward to the risk characterisation for acute exposure and was used to establish systemic AEL acute reference value of: AELacute 0.35 mg/kg bw/day.

2.2.1.3. Exposure Assessment

The active substance, S-Methoprene and the product Biopren® Pharaoh's Ant Colony Eliminator are manufactured and formulated in Hungary. No human health exposure scenarios have been assessed for the manufacture of the active substance or for the formulation of the product.

In the EU, potential exposure to S-Methoprene will occur through use and indirect exposure to the product. Exposure assessment has been carried out using Biopren® Pharaoh's Ant Colony Eliminator as the representative product.

Table 2.2.1.3-1: The exposure paths are identified in the following table for each exposure group.

Exposure path	Industrial use	Professional use	Non-professional	General Public	Via the environment
Inhalation	Not applicable	No	No	Yes**	No
Dermal	Not applicable	Yes**	Yes**	Yes**	Yes**
Oral	Not applicable	No	No	Yes*	No
* Infants ** Negligible					

Biopren® Pharaoh's Ant Colony Eliminator is a pre-prepared, ready to use insecticide product. The insecticide, S-Methoprene, is formulated in a bait matrix as granules. The granules are contained in a sealed plastic box called a bait station which is intended to be tamper-proof. The product is used to control/eliminate Pharaoh ants in indoor areas.

The product is proposed for use by professionals and non-professionals. The primary exposure scenario for the use of the product considered in the risk assessments is the same for the professional and the non-professional user. However, there are differences in the amount of product handled by the professional and the non-professional user. It is envisaged that professional operators could handle 75 bait stations per day, most working days. Exposure for professionals is considered medium term. Non-professionals are predicted to carry out two placements of the product per site in a once off manner. Exposure for non-professionals is considered short-term.

Table 2.2.1.3-2 Description of primary exposure for professional and non-professional users

Intended use (MG / PT)	Exposure scenario	Inhalation uptake Exposure concentration (mg/m3)	Dermal uptake Exposure concentration (mg/m2)	Oral uptake Exposure concentration (mg/event)
MG-03 / PT-18				
Task 1	Professional and non-professional user preparing and applying the product indoors	Not applicable	Yes Negligible	Not applicable
Task 2	Professional and non-professional user removing the product post application of the product indoors	Not applicable	Yes Negligible	Not applicable

Indirect exposure to the active substance as a result of use in the biocide product may involve dermal exposure to the general public and is considered for infants, children and adults. This indirect exposure is considered short-term. Indirect oral exposure involving ingesting bait is considered possible for infants. This indirect exposure is considered short-term. Inhalation

exposure from the product is considered as occupants of treated premises could be exposed to vapours volatilised from the bait. This indirect exposure is considered long-term.

Table 2.2.1.3-3 Description of secondary indirect exposure

Intended use (MG / PT)	Exposure scenario	Inhalation uptake Exposure concentration (mg/m^3)	Dermal uptake Exposure concentration (mg/m^2)	Oral uptake Exposure concentration (mg/event)
MG-03 / PT-18				
1	Short-term dermal exposure potentially involving infant, child or adult coming in contact with the bait.	Not applicable	Yes	Not applicable
2	Short-term oral exposure potentially involving an infant coming in contact with the bait and ingesting it.	Not applicable	Not applicable	Yes
3	Long-term inhalation exposure involving occupants such as infants, children or adults in enclosed unventilated spaces inhaling the vapours of S-Methoprene volatilised from the bait.	Yes	Not applicable	Not applicable

Primary Exposure:

Reverse reference scenarios using the AEL for medium term exposure were considered. The results are presented in the table below:

Table 2.2.1.3-4: Considering primary dermal exposure for the professional user including reverse reference scenarios using the AEL for medium term exposure

Exposure assessment for Professional use	Default values used in exposure calculations	Exposure
Tier 1 Reverse reference scenario Compared to the $AEL_{MEDIUM-TERM}$ Tier 2 Reverse reference scenario Compared to the $AEL_{MEDIUM-TERM}$	- No PPE 3.50% dermal absorption Compared to the $AEL_{MEDIUM-TERM}$ - Gloves 3.50% dermal absorption Compared to the $AEL_{MEDIUM-TERM}$	To achieve the $AEL_{MEDIUM-TERM}$ a 60 kg adult would need to be dermally exposed to the contents of 34 bait stations/day. To achieve the $AEL_{MEDIUM-TERM}$ a 60 kg adult would need to be dermally exposed to the contents of 34 0bait stations/day.

Reverse reference scenarios using the AEL for short-term exposure to non-professionals were considered. The results are presented in the table below:

Table 2.2.1.3-4: Considering primary dermal exposure for non-professional users including reverse reference scenarios using the AEL for short term exposure

Exposure assessment for Professional use	Default values used in exposure calculations	Exposure
Tier 1 Reverse reference scenario $AEL_{SHORT-TERM}$	- No PPE 3.50% dermal absorption $AEL_{SHORT-TERM}$	To achieve the $AEL_{SHORT-TERM}$ a 60 kg adult would need to be dermally exposed to the contents of 34 bait stations/day.

Secondary Indirect Exposure:

For Biopren® Pharaoh's Ant Colony Eliminator an infant needs to be dermally exposed to 20g of bait (equivalent to 6 bait stations) to achieve a body burden equivalent to the systemic AEL for short-term exposure. Similarly, a child or adult would need to be dermally exposed to 69g (equivalent to 20 bait stations) or 120g (equivalent to the contents of 34 bait stations) to achieve a body burden equivalent to the systemic AEL for short-term exposure.

Table 2.2.1.3-5: The following table summarises the potential secondary indirect dermal exposure for humans that could occur from the use of Biopren® Pharaoh's Ant Colony Eliminator.

Exposures scenarios for	**Default values used in**	**Exposures**

secondary (indirect) exposure	**calculations**	Infant (bw = 10kg)	Child (bw = 34.4kg)	Adult (bw = 60kg)
Dermal Exposure				
Tier 1: Assessment using reverse reference scenario	- 3.50% Dermal absorption - $AEL_{SHORT-TERM}$	20g of bait (Equivalent to 6 bait stations)	69g of bait (Equivalent to 20 bait stations)	120g of bait (Equivalent to 34 bait stations)

For oral exposure to Biopren® Pharaoh's Ant Colony Eliminator infants are considered to be the only group which is likely to consume non-foodstuffs from surfaces, accordingly the potential oral exposure only focuses on this group. For Biopren® Pharaoh's Ant Colony Eliminator an infant needs to be orally exposed to 2g of bait (equivalent to 60% of a bait station) to achieve a body burden equivalent to the systemic NOAEL for short-term exposure.

Table 2.2.1.3-6: The following table summarises the potential secondary indirect human oral exposure that could occur from the use of Biopren® Pharaoh's Ant Colony Eliminator.

Exposures scenarios for secondary (indirect) exposure	**Default values used in calculations**	**Exposures**		
		Infant (bw = 10kg)	Child (bw = 34.4kg)	Adult (bw = 60kg)
Oral Exposure				
	- 35% Oral absorption -	2g (Equivalent to 60% of a bait station) 0.01g (Bittering agent) ingested would be 0.5 % of 2g	Not applicable	Not applicable

According to Curry et al (1995), a substance should be considered volatile if it has a vapour pressure >10 mPa at 20°C. The vapour pressures of S-Methoprene is less than 10 mPa at 20°C and therefore the substance is not considered to be volatile and is not of concern via inhalation.

Table 2.2.1.3-7: The following table summarises the potential secondary indirect inhalation exposure for humans that could occur from the use of Biopren® Pharaoh's Ant Colony Eliminator.

Exposures scenarios for secondary (indirect) exposure	**Default values used in calculations**	**Exposures**		
		Infant (bw = 10kg)	Child (bw = 34.4kg)	Adult (bw = 60kg)
Inhalation Exposure				
S-Methoprene Inhalation of vapour	100 % absorption via inhalation	60.75×10^{-3} mg/kg bw/day	54.94×10^{-3} mg/kg bw/day	34.2×10^{-3} mg/kg bw/day

2.2.1.4. Risk Characterisation

For the risk characterisation of Biopren® Pharaoh's Ant Colony Eliminator the critical endpoints are toxicity following the 90-day dog repeat exposure study, the 2-year rat combined chronic and carcinogenicity study and the rabbit developmental study. Following repeated exposure liver toxicity is observed in studies in rats, mice and dogs.

2.2.1.4.1. Uncertainties

Setting of an assessment factor:

There is no definitive data or information available to identify the relative sensitivities of humans compared to experimental animals in relation to the ability of S-Methoprene to cause liver toxicity. Similarly, there is no data to reliably inform on the potential inter individual variability in susceptibility to these effects. Given these uncertainties, standard default factors of 10 to account for potential inter-species (human compared to rats) and of 10 to account for intra-species (human to human) variability will be included in the risk characterisation. Therefore, an assessment factor of 100 will be applied for both primary and secondary exposure scenarios.

Route-to-route extrapolation:

No short-term or subchronic repeat dose dermal or inhalation studies have been conducted. It is concluded that due to a lack of information it is considered that systemic toxicity following repeated dermal or inhalation administration will be considered the same as that observed by the oral administration route.

Dose response:

The study selected for use in the risk characterisation for medium-term systemic toxicity exhibits a clear dose-response relationship. The studies selected for use in the risk characterisation for acute and long-term systemic toxicity do not exhibit clear dose-response relationships. The lack of clear dose response relationship is due to issues related to dose spacing used in the particular studies.

Primary Exposure for Professionals:

In a reverse reference scenario, which applies a 100-fold assessment factor from the NOAEL (Medium-term AEL), a 60kg adult would need to become dermally exposed to 34 complete bait stations per day before reaching a systemic exposure equivalent to the AEL_{MEDIUM_TERM}. If gloves are worn the number of bait stations the operator has to be exposed to reach $AEL_{MEDIUM\text{-}TERM}$ is 340.

Reverse reference scenarios considered the amount of S-Methoprene a professional user has to become dermally exposed to, with and without an assessment factor, before achieving the medium-term NOAEL. Results indicate that when an AF of 100 is not applied, a 60kg adult would have to become exposed to the contents of 11988 bait stations/day before reaching a systemic exposure equivalent to the NOAEL. In a reverse reference scenario, which applies a 100-fold assessment factor, a 60kg adult would need to become dermally exposed to 119.88 complete bait stations per day before reaching a systemic exposure equivalent to the AEL_{MEDIUM_TERM}.

In conclusion, professional users of the product are assumed as trained, skilled, healthy adults with workplace risk assessments and controls for residual risk in place and with access to personal protective equipment. In addition, the fact the product is contained within a child resistant bait station and the professional user will not attempt to gain access to the contents of the bait station is considered. Accordingly, taking the reverse reference scenario information into account, which demonstrates that an unrealistic amount of bait would need to be dermally absorbed to reach the systemic exposure equivalent to the AEL_{MEDIUM_TERM} it is concluded any risk to the professional user is deemed acceptable.

Primary Exposure for Non-Professionals:

Reverse reference scenarios considered the amount of S-Methoprene a non-professional user has to become dermally exposed to exceed the AEL_{SHORT_TERM}, In a reverse reference scenario, which applies a 100-fold assessment factor from the NOAEL (Medium-term AEL), a 60kg adult would need to become dermally exposed to 34 complete bait stations per day before reaching a systemic exposure equivalent to the AEL_{SHORT_TERM}.

In conclusion, considering that non-professional users of the product are usually consumers, who may or may not read a product label, there is an expectation, but no guarantee, that non-professionals will comply with instructions for use of a product. They have no access to controls or formal PPE, though they may use household protective equipment (e.g. gardening or kitchen gloves). In addition, the product is contained within a child resistant bait station and it is reasonable to expect that the non-professional user will not attempt to gain access to the contents of the bait station. Accordingly, taking the reverse reference scenario information into account, which demonstrates that an unrealistic amount of bait would need to be dermally absorbed to reach the systemic exposure equivalent to the $AEL_{SHORT\text{-}TERM}$ it is concluded that any risk to the non-professional user is deemed acceptable.

Secondary Exposure:

Indirect contact involving ingesting bait is considered possible for infants of the general public. Using the reverse reference scenario for secondary oral exposure, an infant would need to be orally exposed to 2g of bait (equivalent to 60% of a bait station) before achieving a body burden equivalent to the systemic AEL for short-term exposure. Overall, it is conceivable that an infant could come into oral contact with a bait station. However, in the TNsG Human exposure to Biocidal products – Guidance on Exposure Estimation Part 3 June 2002 / Final Appendix 7.2.1 it

is indicated that an infant involved in the transient mouthing of poison bait treated with repellent will ingest the equivalent of 0.01g of material. In the case of Biopren® Pharaoh's Ant Colony Eliminator the product contains a bittering agent which acts as a repellent and deterrent to ingestion. Therefore 0.01g ingested would be 0.5% of 2g, the amount required to reach the $AEL_{SHORT-TERM}$ level. On the basis of this fact but including examination of all the other information and evidence it is concluded any risk to infants from oral exposure is considered acceptable.

Inhalation exposure from the product is considered, as occupants of treated premises could be exposed to vapours volatilised from the bait. However, the risks from secondary exposure to adults, children and infants via inhalation are considered negligible as the active substance within Biopren® Pharaoh's Ant Colony Eliminator is considered non-volatile and large MOE values indicate that there is no cause for concern.

For Biopren® Pharaoh's Ant Colony Eliminator dermal exposure may occur by ants taking the substance out of the bait station after which the general public including infants, children or adults may come into contact with the substance indirectly. Using the reverse reference scenarios for secondary exposure an infant would need to be dermally exposed to 20g of bait (6 bait stations), a child 69g of bait (20 bait stations) and an adult 120g of bait (34 bait stations) before achieving a body burden equivalent to the systemic $AEL_{SHORT-TERM}$. Therefore, it is not conceivable that an infant, child or adult could come into contact with a sufficient number of bait stations to remotely cause any concern.

Combined Exposure:

It is not considered that oral, dermal or inhalation exposures need to be combined for assessment purposes.

2.2.2. Environmental Risk Assessment

2.2.2.1. Fate and Distribution in the Environment

Biodegradation

S-Methoprene technical, at a concentration of 2 mg/L and 8 mg/L, attained 49.45% and 20.99% degradation, respectively, after 28 days. The CA notes the higher test concentration of 8 mg/L lies above the water solubility of S-Methoprene (6.85 mg/L at 20°C). In these samples less degradation was observed compared to samples treated with 2 mg/L of test item. The CA notes that the OECD 301 guideline states "*If inhibition due to toxicity is to be avoided, it is suggested that the test substance concentrations used in ready biodegradability testing should be less than 1/10 of the EC50 values (or less than EC_{20} values) obtained in toxicity testing)"*. For s-Methoprene the EC_{50} for activated sludge is reported as >100 mg/L (3 hr). In light of the previous statements the results at 2 mg/L are considered to be more reliable than the results observed at 8 mg/L. The reference substance, Sodium acetate, attained 96.09% degradation after 28 days. Apart from the concentration effect observed at 8 mg/l, no inhibitory effects of S-Methoprene were observed (oxygen depletion was greater in the control group containing s-Methoprene and sodium acetate than the control group containing sodium acetate only). The validity criteria for the test were fulfilled. S-Methoprene is not readily biodegradable.

No studies were submitted on the fate and behaviour of S-Methoprene in freshwater and soil based on the justification of limited exposure for the use pattern being evaluated. Experimental data on degradation in soil and water-sediment systems may be required for products with different use patterns.

Abiotic degradation

Hydrolysis of the active substance, S-Methoprene, is not expected to be a significant process in the environment. S-Methoprene was found to be hydrolytically stable at pH 4, 7 and 9 at all temperatures examined. In strong acid solution (pH 1.2), hydrolysis is rapid with a DT_{50} of 17 h; however, this level of acidity is unlikely to be encountered under normal environmental conditions. Therefore, under normal environmental and proposed use conditions S-Methoprene is considered stable to hydrolysis.

In a laboratory study on aqueous phototransformation (15 d continuous irradiation with a Xe lamp, pH 7, sterilised, 22 ± 2 ºC), a DT_{50} value of 4.8 hours was measured for S-methoprene. This value relates to laboratory test conditions and was not extrapolated to correspond to the light intensities and spectral distribution from northern to southern European regions (average 50 °N) during spring and autumn. A number of journal articles were also submitted indicating that methoprene rapidly decomposes in aqueous solution when exposed to sunlight. In sterilised water buffered to pH 7 the DT_{50} of methoprene was reported to be between <1 day and 5 days (Quistad et al. 1975, Schooley et al. 1975). However, under field conditions, photolysis in water may only be relevant in the upper few centimetres of a water body.

Distribution and mobility

S-Methoprene is readily adsorbed to and desorbed from soil. Adsorption Koc values of 537 L/kg, 684 L/kg and 1407 L/kg were reported in three soil types and an average of 876 L/kg was determined.

Bioaccumulation

S-Methoprene has a calculated log Kow of 6.34 indicating bioaccumulation potential.. Due to the difficulties encountered in experimentally determining the BCF for s-Methoprene the US EPA BCFBAF EPI Suite, based on the Arnot-Gobas Method, was used for this determination. This program estimates a chemical's BCF based on its Kow and structural features (e.g. functional groups and elemental composition). Structures are entered into the BCFBAF through SMILES (Simplified Molecular Input Line Entry System). The calculated BCF is 516. This result is consistent with literature values of the BCF of s-Methoprene. The UK Pesticide Database and the US EPA Integrated Pest Management Plan, 2006, both report a BCF of 457 for s-Methoprene.According to Regulation (EC) No. 1907/2006, REACH Annex XIII, the criteria for a substance to be considered as bio-accumulative, the BCF value must be higher than 2000. From the calculation the BCF of s-Methoprene is 516, therefore, based on these results, s-Methoprene does not meet the B criterion.

2.2.2.2. Effects Assessment

Effects on aquatic organisms

S-Methoprene, applied as 'Biopren® Pharaoh's ant Colony Eliminator' is acutely toxic to fish (LC50 at 96h is 4.26 mg/l) and to algae (ErC50 at 72 hrs 2.264 mg/l). S-Methoprene is very toxic to Daphnia (LC50 at 48h is 0.22 mg/l). S-Methoprene displays chronic toxicity to Daphnia **(**NOEC 0.019 mg/L).

Acute toxicity studies indicated that Daphnia is the most sensitive indicator of toxicity to S-Methoprene (Biopren® Pharaoh's ant Colony Eliminator) (LC50 at 48h is 0.22 mg/l.). Chronic toxicity studies indicated that Daphnia is the most sensitive indicator of toxicity to Biopren® Pharaoh's ant Colony Eliminator (NOEC 0.019 mg/L). Thus the PNEC for aquatic organisms was calculated using the reproduction, growth and mortality of *Daphnia magna* as this was the most sensitive aquatic organism tested. Based on these data, the PNECaquatic of S-Methoprene to

aquatic invertebrates, following application of an assessment factor of 100, was established to be 0.00019 mg/L.

The effect of S-Methoprene at 100 mg a.s./L on the respiration of micro-organisms was examined. . This test was performed above the level of water solubility (6.85 mg/L). The solvent DMF was used. As the test substance was not monitored it cannot be assumed that the maximum concentration was really dissolved. Therefore, the results of this test conclude that no adverse effect is expected in wastewater treatment plants up to 6.85 mg/L S-Methoprene.

Effects on terrestrial organisms

Data to address this point was not submitted as S-Methoprene is to be used indoors as an ant bait. The product is contained in a plastic baiting station accessible to ants via holes in the baiting station and will not be directly released to soil in significant amounts. Therefore, according to the recommended use of the product, exposure of the terrestrial environment to S-Methoprene is expected to be negligible.

2.2.2.3. PBT and POP Assessment

PBT assessment

Persistence

A substance is considered to fulfil the persistence criterion (P) when the degradation half-life is –

> 60 days in marine water, or
> 40 days in freshwater or estuarine water, or
> 180 days in marine sediment, or
> 120 days in freshwater sediment or estuarine water sediment, or
> 120 days in soil.

The criteria for a substance to be considered as very persistent (vP) are when the degradation half-life is –

> 60 days in marine water or freshwater or estuarine water, or
> 180 days in marine or freshwater sediment or estuarine water sediment, or
> 180 days in soil.

S-Methoprene is the biologically active enantiomer in the racemic mixture methoprene. With regard to abiotic degradation, experimental evidence relevant to the consideration of persistence is available in the results from a hydrolysis study. In this study, S-methoprene was found to be stable at relevant environmental pH levels of pH 4, 7 and 9 at a range of environmentally applicable temperatures.

Results from an aqueous photolysis study showing potential for rapid aqueous degradation (DT_{50} = 4.8 hours - 15 days continuous irradiation with a Xe lamp, pH 7, sterile conditions, 22 ± 2 ºC), and accompanying literature data reporting DT_{50} values between <1 day and 5 days in sterilised water buffered to pH 7, are not considered relevant for the assessment of persistence in the environment. Under field conditions photolysis in water would only be relevant for the upper few centimetres of non-turbid water bodies.

With regard to biodegradation, S-methoprene was found to be not ready biodegradable in a study conducted in accordance with the requirements of OECD Test Guideline 301D.

No studies were submitted on biodegradation in soil or aquatic systems. In order to address these areas the applicant submitted a number of papers published in the scientific literature, information from other regulatory evaluations in the public domain (California Department of Pesticide

Regulation, FAO/WHO, Health Canada, Massachusetts Pesticide Bureau, New Zealand Ministry of Health, US EPA), and a position paper. This information was not provided in the form of robust study summaries, and consequently is not included in Document IIIA. It should also be noted that the information refers to studies conducted with methoprene as the racemic mixture. However the conclusions are also assumed to apply to the S-methoprene enantiomer.

The information provided for soil and aquatic systems consists of the following:

1. Antunes-Kenyon, Steven, and Gerard Kennedy. 2001. Methoprene: A Review of the Impacts of the Insect Growth Regulator Methoprene on Non-Target Aquatic Organisms in Fish Bearing Waters (ver. 2.0). Report for Massachusetts Pesticide Bureau, Department of Food and Agriculture, Boston.

2. Csondes, Angela. 2004. Environmental Fate of Methoprene. Report for California Department of Pesticide Regulation, Sacramento. http://www.cdpr.ca.gov/docs/emon/pubs/methofate.pdf (checked on 13 February 2013).

3. FAO and WHO (JMPR). 2005. Pesticide residues in food - 2005, Evaluations, Part I - Residues, volume 1-2 (Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues, Rome, Italy, 20-29 September 2005). Methoprene evaluation by Dr Yibing He (volume 2, pages 733-796). http://www.fao.org/ag/AGP/AGPP/Pesticid/JMPR/Download/2005_eva/2005 Methoprene1.pdf (checked on 13 February 2013).

4. Glare, Travis R, and Maureen O'Callaghan. 1999. Environmental and Health Impacts of the Insect Juvenile Hormone Analogue, S-methoprene. Report for New Zealand Ministry of Health. http://www.moh.govt.nz/notebook/nbbooks.nsf/0/7A939F67CF39FA134C25674D0011D402/$file/s-methoprene.pdf (checked on 12 February 2013).

5. Hangartner, Walter W, Milos Suchy, Hans K. Wipf, and Rene C Zurflueh. 1976. "Synthesis and Laboratory and Field Evaluation of a New, Highly Active and Stable Insect Growth Regulator." Journal of Agricultural and Food Chemistry 24 (1) (January): 169–175. doi:10.1021/jf60203a019.

6. Health Canada (Pest Management Regulatory Agency). 2007. Proposed Acceptability for Continuing Registration: Re-evaluation of S-methoprene. http://publications.gc.ca/collections/Collection/H113-18-2007-1E.pdf (checked on 13 February 2013).

7. Madder, D J, and W. L. Lockhart. 1980. "Studies on the Dissipation of Diflubenzuron and Methoprene from Shallow Prairie Pools." The Canadian Entomologist 112 (2) (February): 173–177. doi:10.4039/Ent112173-2.

8. Menzie, C M. 1980. Metabolism of Pesticides. Update III. Special Scientific Report - Wildlife No. 232, pp.333-339. United States Department of the Interior, Fish and Wildlife Service.

9. PPDB (2013). The Pesticide Properties DataBase (PPDB) developed by the Agriculture & Environment Research Unit (AERU), University of Hertfordshire, funded by UK national sources and through EU-funded projects, 2006-2013. http://sitem.herts.ac.uk/aeru/footprint/en/Reports/1457.htm (checked on 13 February 2013).

10. Quistad, G B, Luana E. Staiger, and David A. Schooley. 1975. "Environmental Degradation of the Insect Growth Regulator Methoprene (isopropyl (2E, 4E)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate). III. Photodecomposition." Journal of Agricultural and Food Chemistry 23 (2) (March): 299–303. doi:10.1021/jf60198a002.

11. Ross, D. H., P. Cohle, P. R. Blase, J. B. Bussard, and K. Neufeld. 1994. "Effects of the Insect Growth Regulator (S)-Methoprene on the Early Life Stages of the Fathead Minnow *Pimephales Promelas* in a Flow-Through Laboratory System." Journal of the American Mosquito Control Association 10 (2): 211–221.

12. Schaefer, C H, and E F Dupras. 1973. "Insect Developmental Inhibitors. 4. Persistence of ZR-515 in Water." Journal of Economic Entomology 66 (4) (August): 923–5.

13. Schooley, David A., B. John. Bergot, Loren L. Dunham, and John B. Siddall. 1975a. "Environmental Degradation of the Insect Growth Regulator Methoprene (Isopropyl (2*E*,4*E*)-11-Methoxy-3,7,11-trimethyl-2,4-dodecadienoate). II. Metabolism by Aquatic Microorganisms." Journal of Agricultural and Food Chemistry 23 (2) (March): 293–298. doi:10.1021/jf60198a059.

14. Schooley, David A., Karen M. Creswell, Luana E. Staiger, and Gary B. Quistad. 1975b. "Environmental Degradation of the Insect Growth Regulator Isopropyl (2*E*,4*E*)-11-Methoxy-3,7,11-trimethyl-2,4-dodecadienoate (Methoprene). IV. Soil Metabolism." Journal of Agricultural and Food Chemistry 23 (3) (May): 369–373. doi:10.1021/jf60199a067.

15. US EPA. 1991. Methoprene Reregistration Eligibility Document (RED). http://www.epa.gov/oppsrrd1/REDs/old_reds/methoprene.pdf (checked on 13 February 2013).

16. US EPA. 2001. Pesticide Fact Sheet - Methoprene (June 2001 Update of the March 1991 Methoprene R.E.D. Fact Sheet). http://www.epa.gov/pesticides/chem_search/reg_actions/reregistration/fs_PC-105401_1-Jun-01.pdf (checked on 13 February 2013).

17. Wright, J E. 1976. "Environmental and Toxicological Aspects of Insect Growth Regulators." Environmental Health Perspectives 14 (51) (April 20): 127–32. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1475109/pdf/envhper00489-0125.pdf (checked on 12 February 2013).

The above information was considered by the CA evaluator but has not been assessed in detail since robust study summaries were not provided.

Information on the half-life in soil is given in references 2, 3, 4, 6, 8, 9, 14, 15, 16 and 17. Reference number 14 (Schooley et al., 1975b) is the source reference. The other references dealing with soil ultimately refer back to this reference. References 2, 3, 4, 8, 9, 15, 16 and 17 report an aerobic half-life value in soil of approximately 10 days, for a sandy loam treated with methoprene at a rate of 1 kg/ha. This information was originally reported by Schooley et al., 1975b. Reference 6 reports a field half life value of up to 14 days but does not give an explicit source for this value. However it appears that this information is also derived from Schooley et al., 1975b.

The paper by Schooley et al. (1975b) describes a study on the metabolic fate of methoprene (the racemic mixture) in illuminated soils under fluorescent lamps. A half-life of approximately 10 days is reported for a sandy loam soil treated at a rate of 1 kg a.i./ha and incubated aerobically for 60 days in an indoor plant growth chamber (temperature: 22 °C by day (16 hr), 19° C by night (8

hr); relative humidity: about 50%; luminescence (fluorescent lamps): 4000 lx). Degradation was slower for another incubation in the same soil treated at a rate of 10 kg a.i./ha but no half-life value was reported for this latter case. The half-life value of 10 days for the 1 kg/ha treatment appears to have been obtained from visual inspection of Figure 4 in the paper (showing residue levels as a function of time). Extractable metabolites formed in soil accounted collectively for a maximum of 5.4% of applied radioactivity after seven days. Only one of these metabolites was positively identified, which was the hydroxy ester resulting from O-demethylation of methoprene. Mineralisation (determined in a separate incubation with a treatment rate of 0.7 kg a.i./ha) was extensive, with $^{14}CO_2$ accounting for greater than 50% of applied radioactivity by the end of the study.

It seems that the degradation in soil was mainly microbially mediated but there could have been a photolytic contribution given the propensity of methoprene to photodegrade. However any such photochemical contribution in this instance is considered to have been limited, since the luminescence experienced was low in comparison to that from natural sunlight. The half life could have been longer for an incubation in the dark but overall the study can be regarded as providing an indication that methoprene would not be expected to be persistent in soil, since it is thought that the photolytic contribution to degradation in this case, if any, was quite small.

In relation to persistence in aquatic systems, original source data is reported in references 5, 7, 10, 12, and 13. However much of the submitted information is of limited relevance. Many of the reported values are for incubations under photolysing conditions, while in some cases the values refer to dissipation rather than degradation and in other cases the information was obtained for a formulated product. According to reference 4 (Glare and O'Callaghan, 1999), formulation has a significant effect on methoprene persistence, especially in water. Pertinent information for assessing persistence in aquatic systems is reported in references 12 (Schaefer and Dupras, 1973) and 13 (Schooley et al., 1975 a).

The paper by Schaefer and Dupras (1973) describes an investigation into how sunlight and temperature affected the rate of decline of the methoprene formulation ZR-515 in various water samples. One of the experiments was performed in the dark using tap water and distilled water samples treated with an acetone solution of technical ZR-515 at a rate of 0.1 ppm and incubated at 10 ºC, 24 ºC and 38 ºC. The results, presented in Figure 1 of the paper, show that by 120 hours the decrease in methoprene was greater than 90% in the 38 ºC incubations, approximately 70-80% in the 24 ºC incubations and approximately 35% in the 10 ºC incubations. Presumably the decreases were due to microbial degradation, given the hydrolytic stability of methoprene.

The paper by Schooley et al. (1975a) provides some further information in support of a microbial contribution to degradation in aquatic systems. One of the reported experiments involved incubation outdoors under natural sunlight of autoclaved and non-autoclaved samples of collected pond water, containing sediment, that were treated with methoprene at a rate of 0.65 ppm. Methoprene was not detected after 13 days in the non-autoclaved samples but was present in the autoclaved samples at 10-20%. One major metabolite, reaching 29% of the applied dose, was identified in both incubations as 7-methoxycitronellic acid. It was speculated that this metabolite was formed by a combination of microbial and photolytic processes. Low recovery of applied radioactivity in the non-autoclaved samples (48%), as compared to 98% in the autoclaved samples, was considered evidence of CO_2 evolution in the non-autoclaved samples, since an open incubation system was used in both cases. On this basis it was considered that aquatic microorganisms can make an important contribution to the degradation of methoprene. The relative importance of photolytic and biotic contributions to degradation in field situations would depend on factors such as temperature, degree of exposure to photolysing conditions and the nature of the microbial population.

An additional indication of microbial degradation in water can be found in hydrolysis results reported in the Schooley et al. (1975a) paper. Hydrolysis incubations were performed in the dark

at 20 ºC using sterile samples, with the exception of pH 5 buffered samples in which sterility was accidentally lost between day 21 and day 30. No observable degradation was found in the incubations where sterility was maintained, whereas degradation of 59% was found in the incubation which experienced a loss of sterility over 9 days.

There is another literature paper worth noting in relation to aquatic persistence. This paper (Pree and Stewart, 1975) has the following citation –

- Pree, D. J., and D. K. R. Stewart. "Persistence in water of formulations of the insect developmental inhibitor ZR515." Bulletin of environmental contamination and toxicology 14, no. 1 (1975): 117-121.

It was not submitted by the applicant but is mentioned or indirectly referred to by three of the submitted references (references, 4, 8 and 15).

The paper by Pree and Stewart (1975) describes an investigation on the stability of two methoprene formulations in fresh and salt water at 4.5 ºC and 20 ºC. The incubations were performed in stoppered, foil-covered flasks. One of the formulations used was an emulsifiable concentrate, while the other was a slow release formulation. Only the results for the emulsifiable concentrate are considered here. Reported half life values for fresh and salt water respectively are 10-35 days for the 20 ºC incubation and 35-100 days for the 4.5 ºC incubation.

Taken together, the pertinent information on behaviour of methoprene in aquatic systems provides an indication of the potential for extensive microbial degradation to occur.

Conclusion of PBT assessment with respect to persistence

Overall it is considered that there are indications from the literature data supplied that microbial degradation could be expected to be sufficiently rapid such that methoprene would not be persistent in either soil or aquatic systems. This conclusion is also assumed to apply to the S-methoprene enantiomer. Due to deficiencies in the data relied upon, and the fact that the data refers to the racemic mixture of methoprene rather than S-methoprene alone, the P assessment should be regarded as provisional in nature. It could be updated to take account of experimental degradation data on S-methoprene that may be required for product authorisations, which would then allow for a definitive P classification of S-methoprene.

Bioaccumulation

Bioaccumulation of s-methoprene was calculated due to the difficulties encountered in experimentally determining the BCF because of the surface activity and lipophilic characteristics of the substance.

S-Methoprene has a calculated log Kow of 6.34 indicating bioaccumulation potential. Therefore, a calculated BCF value was initially determined using the log Kow value and the TGD equation for substances with a log Kow > 6 (TGD, part II, eq. 75, p. 126) as indicated below:

log BCF = -0.20 log KOW2 + 2.74 log KOW - 4.72

The resultant log BCF fish value for s-methoprene using the above equation is 4.61 (which is equivalent to a BCF of 40,738) which is considered to be unrealistic physiologically.

However, the above equation is considered to have limitations for substances, such as s-methoprene, since only the log Kow is taken in to account. For this reason, any substance with a log Kow between 4.3 and 9.3 used in the above calculation tends to result in a calculated BCF values >2,000 and be considered potentially bioaccumulative regardless of other substance parameters such as the functional groups, molecular structure or any other biodegradation or metabolic properties that may affect the bioacummulation characteristics of the substance.

Since, the TGD also indicates that other approaches are in existence that can be utilised for determining the BCF and owing to difficulties encountered in experimentally determining the BCF for s-Methoprene and the limitations of the TGD equation the RMS considered a QSAR system was considered more appropriate, since additional input parameters are utilised to calculate the BCF. The QSAR model used was the BCFBAF suite within the USEPA EPIWIN program. This model was considered more appropriate since the calculation follows the methodology explained and reported in Arnot-Gobas (2003). This model estimates a chemical's BCF based on its Kow and also takes into account structural properties features (such as functional groups and elemental composition of the substance) of the substance and how these will affect metabolic half-life and degradation rates. Structures are entered into the BCFBAF through SMILES (Simplified Molecular Input Line Entry System). The BCF calculation uses the following equation:

$$BCF = (1 - L_B) +$$

Where:
LB: Median fish whole body lipid content
Φ: Bioavailable solute fraction
k1: Gill uptake rate constant
k2: Gill elimination rate constant
kE: Fecal egestion rate constant
kG: Growth rate constant
kM: Metabolic biotransformation rate constant (default value: 0)

The Arnot-Gobas model estimates steady-state bioconcentration factor (BCF; L/kg) and bioaccumulation factor (BAF; L/kg) values for non-ionic organic chemicals in three general trophic levels of fish (i.e., lower, middle and upper) in temperate environments. The model calculations represent general trophic levels (i.e., not for a particular fish species) and are derived for "representative" environmental conditions (e.g., dissolved and particulate organic carbon content in the water column, water temperature). Thus, it provides general estimates for these conditions in absence of site-specific measurements or estimates. The default temperature for the BCF and BAF calculations is 10°C (temperate regions). The Arnot Gobas BCF BAF Model is recommended and fully supported by the US EPA for an update to the BCF WIN model due to the fact that it is based on first principles and it is based ona large database.
The BCFBAF Program is an update and expansion of the previous BCFWIN Program that was part of the EPI Suite version 3.20. The update pertains to estimation of bioconcentration factor (BCF). The BCFBAF program estimates BCF of an organic compound using the compound's log octanol-water partition coefficient (Kow). For the update, a more recent and better evaluated database of BCF values was used for both training and validation. The BCF data were reregressed using the same methodology as in the original BCFWIN program. The update is based on information obtained from a paper called "A Generic QSAR for Assessing the Bioaccumulation Potential of Organic Chemicals in Aquatic Food Webs" (Arnot, J., Gobas F.2003).

The original estimation methodology used by the original BCFWIN program is described in a document prepared for the U.S. Environmental Protection Agency which can be found in the Meylan, W.M. (1997). BCFBAF requires only a chemical structure to estimate BCF, Bio-accumulation factor (BAF) and a rate constant for metabolic biotransformation (kM). Structures are entered into BCFBAF through SMILES (Simplified Molecular Input Line Entry System). The six available methods of entering a SMILES formula into BCFBAF are listed in the Entering SMILES section. BCFBAF estimates a log Kow for every SMILES notation by using the estimation module of the KOWWIN program (which is part of the EPI Suite). BCFBAF also automatically retrieves experimental log Kow values from a database containing more than 13,200 organic compounds with reliably measured values. When a SMILES structure matches a database structure (via an exact atom-to-atom connection match), the experimental log Kow value

is retrieved and used to predict BCF, BAF and kM rather than the estimated value. As a consequence the potential for bioaccumulation is assessed by expert judgement on the basis of the log Kow value and the estimated BCF using the available BCF models.

The resultant BCF calculated value based on the BCFBAF QSAR model is 516. This result is consistent with literature values of the BCF of s-Methoprene. The UK Pesticide Database and the US EPA Integrated Pest Management Plan, 2006, both report a BCF of 457 for s-Methoprene.

According to Regulation (EC) No. 1907/2006, REACH Annex XIII, the criteria for a substance to be considered as bio-accumulative, the BCF value must be higher than 2000. From the calculation the BCF of s-Methoprene is 516, therefore, based on these results, s-Methoprene does not meet the B criterion.

The information provided above relies on the following:

1. Arnot JA, Gobas FAPC. 2003. A generic QSAR for assessing the bioaccumulation potential of organic chemicals in aquatic food webs. QSAR and Combinatorial Science 22: 337-345.

2. Meylan, W. M., Howard, P. H., Boethling, R. S., Aronson, D., Printup, H., Gouchie, S., ImprovedMethod For Estimating Bioconcentration/Bioaccumulation Factor From Octanol/Water Partition Coefficient, Environ. Toxicol. Chem. 18(4), 664 - 672 (1999).

Toxicity

According to REACH legislation (Annex XIII) a substance is considered to fulfil the toxicity (T) criterion for when '*the long-term no-observed effect concentration (NOEC) for marine and freshwater organisms is less than 0.01 mg/L*'. The chronic toxicity of S-Methoprene to Daphnia magna in a robust 21-day reproduction test resulted in a NOEC of 0.019 mg/L and a LOEC of 0.027mg/L. Based on these results s-Methoprene does not meet the T criterion.

PBT conclusion

S-Methoprene is not a PBT candidate and does not meet any of the individual screening criteria.

POP assessment

Persistence

In relation to the POPs persistence screening criteria as set out in Annex D to the Stockholm Convention (evidence that the half-life of the chemical in water is greater than two months, or that its half-life in soil is greater than six months, or that its half-life in sediment is greater than six months), it is considered that S-methoprene can be regarded as non-persistent on the basis of literature information supplied for methoprene indicating that microbial degradation could be expected to be sufficiently rapid such that it would not be persistent in either soil or aquatic systems. Experimental degradation data on S-methoprene that may be required for product authorisations could be used to update the persistence assessment, if necessary.

Bio-accumulation

S-Methoprene has a calculated log Kow of 6.34 indicating bioaccumulation potential.. Due to the difficulties encountered in experimentally determining the BCF for s-Methoprene the US EPA BCFBAF EPI Suite, based on the Arnot-Gobas Method, was used for this determination. This program estimates a chemical's BCF based on its Kow and structural features (e.g. functional groups and elemental composition). Structures are entered into the BCFBAF through SMILES (Simplified Molecular Input Line Entry System). The calculated BCF is 516. This result is consistent with literature values of the BCF of s-Methoprene. The UK Pesticide Database and the

US EPA Integrated Pest Management Plan, 2006, both report a BCF of 457 for s-Methoprene. According to Regulation (EC) No. 1907/2006, REACH Annex XIII, the criteria for a substance to be considered as bio-accumulative, the BCF value must be higher than 2000. From the calculation the BCF of s-Methoprene is 516, therefore, based on these results, s-Methoprene does not meet the B criterion.

Long-range environmental transport

The vapour pressure (0.623 mPa at 20 ºC) and molecular weight (310.5) indicate that S-Methoprene will not readily volatilise into the atmosphere at ambient temperature and pressure. If atmospheric exposure did occur a very short half life would be expected given the propensity for S-methoprene to undergo rapid photodegradation. It is not expected that the substance will fulfil the screening criteria for the potential for long-range environmental transport. Furthermore, there is no monitoring data available or other evidence indicating potential for long-range environmental transport.

Adverse Effects (includes ED Assessment)
S-Methoprene is not included in the Commission staff working document on implementation of the EU Strategy for Endocrine Disrupters. Whilst s-Methoprene is a juvenile (insect) hormone analogue, there is no evidence of any endocrine disruption potential in the human health or ecotoxicological studies presented in the dossier.

As such it has been agreed that S-methoprene should be further assessed with regards to its potential endocrine disruptor properties once further guidance is available and preferably before the product authorisation stage. The conclusion of that assessment might lead to review the active substance approval.

POP Conclusion
S-Methoprene does not fulfil the POP criteria.

2.2.2.4. Exposure Assessment

In accordance with the guidance given in the PT18 ESD for household and professional uses, it is expected that use of the supported product (a ready-to-use bait station placed indoors) would result in negligible environmental exposure of S-methoprene. Therefore PEC values for the aquatic, atmospheric and terrestrial compartments are all considered to be effectively zero.

The product *Biopren® Pharaoh's Ant Colony Eliminator* is intended for indoor use by professional and non-professional users for the control of Pharaoh ants (*Monomorium pharaonis*) where nests are established in cracks and crevices. The granular bait containing the active substance is applied in bait boxes. The bait boxes are entirely closed boxes made of plastic, in which the user has to cut along the printed dotted line to make two entrance openings for the ants. The user must also tear off the protective foil from the sticker at the bottom of the baiting station. This sticky pad on the bottom of the blister pack ensures that the baiting station remains in a fixed position.

According to the ESD (section 2.4.9), "*In bait stations, sometimes improperly called "traps" on the market, insecticide is contained in sealed boxes and placed in the neighbourhood of insect's tracks. These are usually ready to use products. For these products, emissions to the environment during the treatment are negligible. The only possible emission is when the box is eliminated to waste during indoor uses or through flooding and insect dispersion during outdoor uses.*" There is no potential for environmental exposure via emission to the applicator, since the product is pre-prepared and ready to use. Neither does a cleaning event result in exposure since the ESD (Table 3.3-8) assumes that there is no exposure to cleaning for solid baits in bait stations. Potential for

exposure via waste disposal following use of the product is beyond the scope of this assessment and would be covered by the Hazardous Waste Directive.

It is on this basis that the environmental exposure arising from the use phase of S-methoprene in the product *Biopren® Pharaoh's Ant Colony Eliminator* is anticipated to be negligible and that PEC values for the various environmental compartments are considered to be effectively zero.

Aquatic compartment

Exposure of the aquatic environment to S-methoprene as a result of use of the product *Biopren® Pharaoh's Ant Colony Eliminator* is expected to be negligible, in accordance with the guidance given in the PT18 ESD for household and professional uses. Consequently aquatic PEC values (PEC_{stp}, PEC_{sw}, $PEC_{sediment}$, PEC_{gw}) are all considered to be effectively zero.

Atmospheric compartment

Exposure of the atmospheric environment to S-methoprene as a result of use of the product *Biopren® Pharaoh's Ant Colony Eliminator* is expected to be negligible, in accordance with the guidance given in the PT18 ESD for household and professional uses. Consequently PEC_{air} values are considered to be effectively zero.

Terrestrial compartment

Exposure of the terrestrial environment to S-methoprene as a result of use of the product *Biopren® Pharaoh's Ant Colony Eliminator* is expected to be negligible, in accordance with the guidance given in the PT18 ESD for household and professional uses. Consequently PEC_{soil} values are considered to be effectively zero.

Primary and secondary poisoning

Aquatic organisms:

S-Methoprene has a log K_{ow} of 6.34 indicating bioaccumulation potential. No studies were submitted investigating the potential hazards of S-Methoprene and its metabolites on non-target aquatic organisms via secondary poisoning, and a bio-concentration study was not submitted. The use pattern of the evaluated product (indoor use in baits) should act to ensure that the potential for secondary poisoning is negligible for the use evaluated (indoor use as baits for the control of ants). The RMS thus agrees that a study is not warranted in this case. Further assessment may be required for products with different use patterns.

Terrestrial organisms:

No studies were submitted investigating the potential hazards of S-Methoprene on non-target terrestrial organisms via secondary poisoning. S-Methoprene has a log K_{ow} of6.34 indicating bioaccumulation potential.Exposure via consumption of contaminated vegetation and treated insects can be ruled out as the formulation is to be applied indoors only.

2.2.2.5. Risk Characterisation

As discussed in section 2.2.2.4, environmental exposure to S-methoprene as a result of use of the product *Biopren® Pharaoh's Ant Colony Eliminator* is expected to be negligible, in accordance with the guidance given in the PT18 ESD for household and professional uses. Therefore PEC

values for the various environmental compartments are effectively zero, and the risk quotients for S-methoprene under the proposed use conditions are all less than one.

In the absence of environmental exposure, no risk assessment is presented here. S-Methoprene environmental hazards are presented in Doc IIA along with PNEC derivations.

PNEC derivation for the aquatic compartment

PNEC's relevant to risk characterisation in the aquatic compartment (hydrosphere) are as follows:

$PNEC_{STP\ micro\text{-}organisms}$	=	6.85 mg/L
$PNEC_{aquatic\ (SW)}$	=	0.00019mg/L
$PNEC_{sediment}$	=	0.0038 mg/kg wwt At risk assessment stage, according to the TGD, the PECsed/PNECsed ratio is increased by a factor of 10 due to the log Kow >5. This results in a **$PNEC_{sediment}$ = 0.00038 mg/kg wwt.**

PNEC derivation for the terrestrial compartment

In the absence of specific data on soil organisms the PNEC for soil was estimated using the equilibrium partitioning method.

$PNEC_{soil}$	=	0.003 mg/kg At risk assessment stage, according to the TGD, the PECsoil/PNECsoil ratio is increased by a factor of 10 due to the log Kow >5. This results in a **$PNEC_{sediment}$ = 0.0003 mg/kg wwt.**

2.2.3. List of Endpoints

In order to facilitate the work of Member States in granting or reviewing authorisations the most important endpoints, as identified during the evaluation process, are listed in Appendix I.

3. PROPOSED DECISION

3.1. BACKGROUND TO THE PROPOSED DECISION

The human health risk assessment indicates that the risks for users of the biocidal product for the exposure scenarios are acceptable as long as specified procedures are followed. Principles of good working practice should be applied and label instructions and recommendations on the products respected. The risk to infants and children from dermal exposure is shown not to be of concern. The risk to infants via oral exposure to Biopren® Pharaoh's Ant Colony Eliminator was considered to be of concern in terms of the AEL acute. However, the product will be packaged in a tamper proof/child resistant bait station and may also include a bittering agent (Note: the inclusion of a bittering agent in a product does not preclude all individuals tasting/eating the product as not all individuals can taste the bittering agent. However, inclusion of a bittering agent could restrict the number of people attempting to taste/eat the product). It is considered that with these measures in place, the potential risk to infants via the oral route will be acceptable.

Considering the profile of the active substance, the provided toxicology of the preparation, the characteristics of the product, the method of application and the risk assessment for the product the RMS considers that Biopren® Pharaoh's Ant Colony Eliminator does not present an unacceptable long-term inhalatory or short-term oral or dermal risk to infants, children, and adults.

S-Methoprene has been evaluated as an insecticide for the use pattern "indoor use" by professional and non-professional users. It is intended for use in the control of Pharaoh's ants (*Monomorium pharaonis*).

S-Methoprene is not readily biodegradable. S-Methoprene technical was found to be hydrolytically stable at relevant environmental pH levels of pH 4, 7 and 9 at a range of environmentally applicable temperatures. Under strong acid solution (pH 1.2), hydrolysis was observed to be rapid with a DT_{50} value determined at 17 hours. However, these acidic conditions (~ pH 1.2) are unlikely to be encountered under the normal use proposed for the active substance. In a laboratory study on aqueous phototransformation (15 d continuous irradiation with a Xe lamp, pH 7, sterilised, 22 ± 2 ºC), a DT_{50} value of 4.8 hours was measured for S-methoprene. This value relates to laboratory test conditions and was not extrapolated to correspond to the light intensities and spectral distribution from northern to southern European regions (average 50 °N) during spring and autumn. A number of journal articles were also submitted indicating that methoprene rapidly decomposes in aqueous solution when exposed to sunlight. In sterilised water buffered to pH 7 the DT_{50} of methoprene was reported to be between <1 day and 5 days. However, under field conditions, photolysis in water may only be relevant in the upper few centimetres of a water body. S-Methoprene is readily adsorbed to and desorbed from soil. Koc adsorption values of 537 L/kg, 684 L/kg and 1407 L/kg were measured in three soil types, giving an average Koc value of 876 L/kg. The use pattern of the biocidal product is anticipated to result in negligible environmental exposure of S-Methoprene.

Given the negligible level of environmental exposure (see Doc II-B) expected in all compartments from the use of S-Methoprene as a pesticide (PEC values are considered to be effectively zero), it is considered that there is no risk to the environment and safe uses of the *Biopren® Pharaoh's Ant Colony Eliminator* product are identified.

Overall, based on the studies submitted, justifications provided, and the general level of scientific knowledge for S-Methoprene in published material, it is concluded that at the proposed level of use and considering the use pattern, S-Methoprene will not have any unacceptable effect on the environment.

3.2. PROPOSED DECISION

The overall conclusion from the evaluation of S-Methoprene for use in product-type 18 (Insecticides, acardicides, and product for the control of other arthropods), is that it may be possible to issue authorisations of products containing S-Methoprene in accordance with the conditions laid down in Article 5(1) b), c) and d) of Dir. 98/8/EC.

It is therefore proposed to approve S-Methoprene as an active substance for use in product-type 18 (Insecticides, acaricides, and product for the control of other arthropods), subject to the following specific conditions:

The product assessment shall pay particular attention to the exposures, the risks and the efficacy linked to any uses covered by an application for authorisation, but not addressed in the Union level risk assessment of the active substance.

Authorisations are subject to the following conditions:

1) For products that may lead to residues in food or feed, the need to set new or to amend existing maximum residue levels (MRLs) in accordance with Regulation (EC) No 470/2009 or Regulation (EC) No 396/2005 shall be verified, and any appropriate risk mitigation measures shall be taken to ensure that the applicable MRLs are not exceeded.

3.3. ELEMENTS TO BE TAKEN INTO ACCOUNT WHEN AUTHORISING PRODUCTS

1. For amateur uses, only ready-for-use products have been assessed. Other uses will require further evaluation.

2. When formulated as bait, only tamper resistant and secured bait boxes shall be authorised

3. At the product authorisation stage, the need to incorporate of a deterrent into baits containing s-methorpene should be considered.

4. The minimum nominal concentration of the active substance in the products shall be: 5 g/kg (0.5% w/w) S-Methoprene.

5. Products must be labelled appropriately to ensure safe storage, handling, use and disposal in accordance with national arrangements.

6. The size of the package placed on the market should be proportionate to the duration of the treatment and appropriate to the pattern of use of particular user groups.

7. Product design and use restrictions should be optimised in order to ensure efficient insect pest control while at the same time minimizing the risk for non-target organisms, such as aquatic organisms.

8. The use of S-Methoprene was not assessed as a tracking powder. Member States should be aware to fully evaluate this use pattern in relation to the risk posed to humans, animals and the environment if application is made at product authorisation.

9. The use of insecticides containing S-Methoprene must take into specific account the aquatic and soil compartments of the environment. Member States should consider the need for degradation studies, depending on the product use pattern. The potential risk of direct and

indirect emissions should also be considered for each Member State's product authorisation. In case of relevant exposure to aquatic or soil compartments higher tier studies on degradation, such as water-sediment and soil degradation studies, will need to be submitted for product authorisation. It should be noted that this requirement for higher tier environment studies may also be the case for other indoor uses which are not covered by the Union risk assessment (i.e. restricted to application in baits).

10. Application rates at the product authorisation stage must be refined utilising robust field or semi-field trial studies demonstrating the most appropriate dose dependant on the infestation level.

11. At the authorisation stage a comprehensive data set will be required to demonstrate what resistance mitigation measures and testing regimes are in place.

12. Labels and/or safety-data sheets of products authorised shall clearly indicate that products when used shall take into account the potential for exposure of humans, non-target species.

13. Used and unused products shall be disposed of properly to minimise contamination of the aquatic environment and, where appropriate, product containers should not be washed.

14. The use pattern of the evaluated product (indoor use in baits) should act to ensure that the potential for secondary poisoning is negligible for the use evaluated (indoor use as baits for the control of ants). Further assessment may be required for products with different use patterns..

15. Due to deficiencies in the data relied upon, and the fact that the data refers to the racemic mixture of methoprene rather than S-methoprene alone, the P assessment should be regarded as provisional in nature. It could be updated to take account of experimental degradation data on S-methoprene that may be required for product authorisations, which would then allow for a definitive P classification of S-methoprene.

16. Dermal absorption values used in the applications for product authorisation should be justified, if available by the submission of specific dermal absorption data on the product, or by read-across to existing data if scientifically justified, or by using default values.

17. It has been agreed that S-methoprene should be further assessed with regards to its potential endocrine disruptor properties once further guidance is available and preferably before the product authorisation stage. The conclusion of that assessment might lead to review the active substance approval.

3.4. REQUIREMENT FOR FURTHER INFORMATION

It is considered that the evaluation has shown that sufficient data have been provided to verify the outcome and conclusions, and permit the proposal for the approval of S-Methoprene in accordance with Article 9 of Regulation (EU) No 528/2012.

However, the following data requirements have been identified:

Identity of the active substance

None.

Physical and chemical properties of the active substance

None.

Physical and chemical properties of the biocidal product

The following biocidal product issues can be addressed at the product authorisation stage –

When the product LX 125-10 Formulation 0.5% was stored for 12 months at 20ºC there was a reduction of active substance content of 13.5%. The shelf life study indicates that an expiry date of 12 months should be placed on the product label. The relevant impurities formed should be identified and quantified and an explanation of why the reduction of active substance content occurred should be included.

Validation data to support the GC/FID method used to determine active substance content in the storage stability study is required. (Storage Stability with Corrosion Characteristics, Anderson W., 2003. Laboratory study no. 4817-98, MRID No. 46061501)

Results of a two year storage stability study at ambient temperature to be provided when available.

CIPAC MT178 and MT193 methods are available to determine Attrition/friability of granules. These tests should be carried out on the product, Biopren® Pharaoh's Ant Colony Eliminator, and results supplied.

Data to indicate that there is no loss of palatability on storage of product should be provided.

Methods of analysis of the active substance

No outstanding data required in relation to the active substance.

Methods of analysis of biocidal product

The following biocidal product issues can be addressed at the product authorisation stage –

An acceptable validated method will be required for analysis of the active substance S-Methoprene in the Biocidal product "Biopren® Pharoh's Ant Colony Eliminator" when the product is being registered at member state level.

Human health

No further data required for human health assessment.

Environment

Studies on the degradation of S-methoprene in soil and water-sediment systems may be required for product authorisations, for products where the use pattern could result in exposure of these compartments (either directly or indirectly).

3.5. UPDATING THIS ASSESSMENT REPORT

This assessment report may need to be updated periodically in order to take account of scientific developments and results from the examination of any of the information submitted in relation with Regulation (EU) No 528/2012. Such adaptations will be examined and

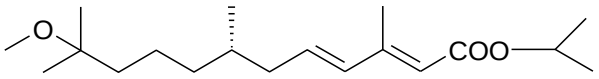
finalised in connection with any amendment of the conditions for the approval of S-Methoprene.

APPENDIX I: LIST OF ENDPOINTS

CHAPTER 1: IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, CLASSIFICATION AND LABELLING

Active substance (ISO Common Name)	S-Methoprene
Function (*e.g.* fungicide)	Insecticide
Rapporteur Member State	Ireland

Identity (Annex IIA, point II.)

Chemical name (IUPAC)	Isopropyl-(2E,4E,7S)-11-methoxy-3,7,11-trimethyl-2,4. –dodecadienoate
Chemical name (CA)	(S)-methoprene
CAS No	65733-16-6
EC No	None
Other substance No.	Not applicable
Minimum purity of the active substance as manufactured (g/kg or g/l)	≥ 950 g/kg
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	None identified.
Molecular formula	$C_{19}H_{34}O_3$
Molecular mass	310.48
Structural formula	

Physical and chemical properties (Annex IIA, point III, unless otherwise indicated)

Freezing point (state purity)	Purity: 98.3% < -22°C
Boiling point (state purity)	Purity: 99.6% 279.9 °C
Temperature of decomposition	Not applicable as the boiling point was estimated.
Appearance (state purity)	Purity: > 95% A transparent pale yellow liquid at 24°C with a faint, fruity, waxy odour.
Relative density (state purity)	Purity: > 95% 0.924 g/ml at 20°C
Surface tension	Purity: 98.3% 50.1 mN/m at 20°C (1mg/l)
Vapour pressure (in Pa, state temperature)	Purity: 98.1 % 0.623 mPa at 20°C 1.08 mPa at 25°C
Henry's law constant (Pa m^3 mol^{-1})	0.0306 Pa x m^3/mol at 20°C
Solubility in water (g/l or mg/l, state temperature)	Purity: > 95% 6.85 mg/l at 20 °C
Solubility in organic solvents (in g/l or mg/l, state temperature) (Annex IIIA, point III.1)	Purity: 98.1% Hexane: > 5 10^5 mg/l Methanol: > 4.5 10^5 mg/l Acetone: > 5 10^5 mg/l Temperature: 20 ± 1 °C
Stability in organic solvents used in biocidal products including relevant breakdown products (IIIA, point III.2)	Not required as no organic solvents are present in the technical.
Partition coefficient (log P_{OW}) (state temperature)	LogKow = 6.34 (calculated)
Hydrolytic stability (DT_{50}) (state pH and temperature) (point VII.7.6.2.1)	pH 1.2: 17 hours at 37 ± 0.5°C
	pH 4: Stable at 25 ± 0.5°C, 37 ± 0.5°C and 50 ± 0.5°C
	pH 7: Stable at 25 ± 0.5°C, 37 ± 0.5°C and 50 ± 0.5°C
	pH 9: Stable at 25 ± 0.5°C, 37 ± 0.5°C and 50 ± 0.5°C
Dissociation constant (not stated in Annex IIA or IIIA; additional data requirement from TNsG)	Not required as S-Methoprene does not dissociate in water.

UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	Purity: 95% 90% Neutral Methanol: λ_{max} 264 nm; ε 26,700 90% Acidified Methanol: λ_{max} 264 nm; ε 26,600 90% Alkalinized Methanol: λ_{max} 266 nm; ε 27,450
Photostability (DT_{50}) (aqueous, sunlight, state pH) (point VII.7.6.2.2)	DT_{50} at pH 7: 4.8 hours (continuous irradiation)
Quantum yield of direct phototransformation in water at Σ > 290 nm (point VII.7.6.2.2)	1.1
Flammability	263 °C
Explosive properties	The molecular structure of S-Methoprene indicates that the substance has little or no explosive properties.

Classification and Proposed Labelling

With regard to physical/chemical data	None
With regard to toxicological data	None
With regard to fate and behaviour data	None
With regard to ecotoxicological data	N, R50/53, S35 CLP Labelling:Chronic Category 1, H410, P273, P391, P501

CHAPTER 2: METHODS OF ANALYSIS

Soil (principle of method and LOQ) (Annex IIA, point 4.2)	Not required
Air (principle of method and LOQ) (Annex IIA, point 4.2)	Not required
Water (principle of method and LOQ) (Annex IIA, point 4.2)	GC-MS LOQ: 0.1µg/l
Body fluids and tissues (principle of method and LOQ) (Annex IIA, point 4.2)	S-Methoprene is not classified as being toxic or highly toxic. It is therefore proposed that analytical methods in animal and human body fluids and tissues are not required.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	Not required
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	Not required

CHAPTER 3: IMPACT ON HUMAN HEALTH

Absorption, distribution, metabolism and excretion in mammals (Annex IIA, point 6.2)

Rate and extent of oral absorption:	Peak plasma concentration: Low dose group 6 hours (male) and 12 hours (female) High dose group 4 hours (male) and 6 hours (female) Indicating S Methoprene is systemically absorbed in 4 to 12 hours Oral absorption 35%
Rate and extent of dermal absorption:	3.50 %
Distribution:	Low dose; stomach, liver, adrenals and white fat . High dose; (after 6 hours) stomach, GI tract, liver, white fat and kidney. Multiple dose; GI tract, liver, stomach, kidney and white fat (highest in males)
Potential for accumulation:	Tissue radioactivity negligible at 96 hours in most tissues with the exception of white fat following single dosing. (1-4% remaining at 96 hours). The same pattern applied to repeat dose group. S-Methoprene does not bioaccumulate
Rate and extent of excretion:	Majority of S-Methoprene excreted within 24-48 hours (34-69% in faeces; 14-28% in expired air; 8-20% in urine).
Toxicologically significant metabolite	Chromatographic analysis of urine, faeces, and bile samples indicated at least 22, 23, and 11 radioactive components, respectively, all more polar than the parent compound.

Acute toxicity (Annex IIA, point 6.1)

Rat LD_{50} oral	> 5050 mg/kg bw/day
Rat LD_{50} dermal	> 5050 mg/kg bw/day
Rat LC_{50} inhalation	> 2.38 mg/L
Skin irritation	Not irritating
Eye irritation	Not irritating
Skin sensitisation (test method used and result)	Not a sensitiser (Buehler test)

Repeated dose toxicity (Annex IIA, point 6.3)

Species/ target / critical effect	Dog 90-day study: Clinical signs such as thin faeces and diarrhoea, increased liver weight in males and females and raised ALP values in females Rat 104 weeks study: Liver histopathology
Lowest relevant oral NOAEL / LOAEL	Dog: LOAEL = 300 mg/kg bw/day NOAEL = 100 mg/kg bw/day Rat: LOAEL = 130.8 mg/kg bw/day

	NOAEL = 65.4 mg/kg bw/day
Lowest relevant dermal NOAEL / LOAEL	Not relevant
Lowest relevant inhalation NOAEL / LOAEL	Not relevant

Genotoxicity (Annex IIA, point 6.6)	Non genotoxic in an *in vitro* bacterial mutation assay, an *in vitro* chromosomal aberration assay and an *in vitro* gene mutation mammalian assay

Carcinogenicity (Annex IIA, point 6.4)

Species/type of tumour	Rat / No carcinogenic potential. Mouse / No carcinogenic potential.
Lowest dose with tumours	Not relevant

Reproductive toxicity (Annex IIA, point 6.8)

Species/ Reproduction target /critical effect	Rat; Reduction in body weight in both parents and offspring
Lowest relevant reproductive NOAEL / LOAEL	LOAEL = 130.8 mg/kg bw/day NOAEL = 8.15 mg/kg bw/day
Species/Developmental target /critical effect	Rat: Reduction in weight gain (maternal), intrauterine mortality and low pregnancy rate Rabbit: Intrauterine foetal growth retardation, maternal death, increase in abortions, reduced activity and vaginal bleeding, decreased weight gain
Lowest relevant developmental NOAEL / LOAEL	LOAEL (rat) = 1000 mg/kg bw/day NOAEL (rat) = 250 mg/kg bw/day LOAEL (rabbit) = 1000 mg/kg bw/day NOAEL (rabbit) = 100 mg/kg bw/day

Neurotoxicity / Delayed neurotoxicity (Annex IIIA, point VI.1)

Species/ target/critical effect	Not applicable
Lowest relevant developmental NOAEL / LOAEL.	Not applicable

Other toxicological studies (Annex IIIA, VI/XI)

.....	Not applicable

Medical data (Annex IIA, point 6.9)

.....	Workers producing S-Methoprene for Bábolna Bioenvironmental Centre Ltd. Over the past 25 years have reported no incidences of adverse effects.

	Workers have reported no incidences of adverse effects, accidents, poisonings or clinical cases during the synthesis of S-Methoprene and the production of the biocidal product. No clinical cases, poisoning or incidents have been reported. No observations of sensitisation or allergenicity have been made following use of S-Methoprene.

Summary (Annex IIA, point 6.10)	Value	Study	Safety factor
ADI (if residues in food or feed)	Not applicable	Not applicable	Not applicable
AOEL (Operator/Worker Exposure)	Not applicable	Not applicable	Not applicable
Drinking water limit	Not applicable	Not applicable	Not applicable
ARfD (acute reference dose)	Not applicable	Not applicable	Not applicable
AEL acute	0.35 mg/kg bw/day	Rabbit developmental study	100
AEL medium-term	0.35 mg/kg bw/day	90 day dog study	100
AEL long-term	0.076 mg/kg bw/day	2-year rat study	100

Acceptable exposure scenarios (including method of calculation)

Professional users	Oral and Inhalation exposure are not applicable. Dermal exposure was assessed using reverse reference scenario, as there is no suitable model to assess exposure. To achieve the $AEL_{MEDIUM-TERM}$ a 60 kg adult would need to be dermally exposed to the contents of 34 bait stations/day. Exposure is acceptable
Non-professional users	Oral and Inhalation exposure are not applicable. Dermal exposure was assessed using reverse reference scenario, as there is no suitable model to assess exposure. To achieve the $AEL_{MEDIUM-TERM}$ a 60 kg adult would need to be dermally exposed to the contents of 34 bait stations/day.Exposure is acceptable
Indirect exposure as a result of use	Dermal short-term exposure is considered for infants, children and adults. Oral short-term exposure is considered for infants. Inhalation long-term exposure is considered for infants, children and adults. All exposure to each group was considered acceptable. Indirect exposure to S-Methoprene *via* the environment i.e. via drinking water or foodstuffs is negligible.

CHAPTER 4: FATE AND BEHAVIOUR IN THE ENVIRONMENT

Route and rate of degradation in water (Annex IIA, point 7.6, IIIA, point XII.2.1, 2.2)

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	S-Methoprene technical was found to be hydrolytically stable at pH 4, 7 and 9 (examined at 25, 37 and 50°C). In strong acid solution (pH 1.2), hydrolysis is rapid with a half-life of 17 hours at 37°C.
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	DT_{50} at pH 7: 4.8 hours (15 d continuous irradiation with a Xe lamp, pH 7, sterilised, 22 ± 2 ºC) A number of submitted journal articles indicated that Methoprene rapidly decomposes in aqueous solution when exposed to sunlight. In sterilised water buffered to pH 7 the DT_{50} of Methoprene was reported to be between <1 day and 5 days (Quistad et al. 1975, Schooley et al. 1975). Sixteen transformation products detected, with the methoprene isomer [E,Z]-S-Methoprene and seven unidentified components each individually exceeding 10% of applied radioactivity.
Readily biodegradable (yes/no)	No
Biodegradation in seawater	Not relevant
Non-extractable residues	Not relevant
Distribution in water / sediment systems (active substance)	Not relevant
Distribution in water / sediment systems (metabolites)	Not relevant

Route and rate of degradation in soil (Annex IIIA, point VII.4, XII.1.1, XII.1.4; Annex VI, para. 85)

Mineralisation (aerobic)	Not relevant
Laboratory studies (range or median, with number of measurements, with regression coefficient)	Not relevant degradation in the saturated zone: Not relevant
Field studies (state location, range or median with number of measurements)	Not relevant
Anaerobic degradation	Not relevant
Soil photolysis	Not relevant
Non-extractable residues	Not relevant
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	Not relevant
Soil accumulation and plateau concentration	Not relevant

Adsorption/desorption (Annex IIA, point XII.7.7; Annex IIIA, point XII.1.2)

Ka , Kd	K_a adsorption values (L/kg): 5.5, 6.5, 7.9 (mean = 6.6, n = 3 soils)
Ka_{oc} , Kd_{oc}	Adsorption coefficients (L/kg) of 537, 684 and 1407, with a mean of 876.
pH dependence (yes / no) (If yes, state type of dependence)	pH dependent: No

Fate and behaviour in air (Annex IIIA, point VII.3, VII.5)

Direct photolysis in air	Not relevant
Quantum yield of direct photolysis	Not relevant
Photo-oxidative degradation in air	Not relevant
Volatilization	Not relevant

Monitoring data, if available (Annex VI, para. 44)

Soil (indicate location and type of study)	No data is provided
Surface water (indicate location and type of study)	No data is provided
Ground water (indicate location and type of study)	No data is provided
Air (indicate location and type of study)	No data is provided

CHAPTER 5: EFFECTS ON NON-TARGET SPECIES

Toxicity data for aquatic species (most sensitive species of each group)
(Annex IIA, point 8.2, Annex IIIA, point 10.2)

Species	Time-scale	Endpoint	Toxicity
Fish			
Zebrafish, *Brachydanio rerio,*	96 h	LC_{50} NOEC	An LC_{50} value of 4.26 mg/l and NOEC value of 1.25 mg/l was determined.
Invertebrates			
Daphnia magna	48 h	EC_{50}	A 48-Hour EC_{50} value of 0.22mg/l was determined.
Daphnia magna	21d	NOEC	0.019 mg/L measured
Algae			
Selenastrum capricornutum	72 h	ErC_{50}	An ErC_{50} value of 2.264 mg/l was determined.
Microorganisms			
Activated sewage sludge	3 h	EC_{50}	A 3-Hour EC_{50} value of 6.85 mg/l was determined.

Effects on earthworms or other soil non-target organisms

Acute toxicity to …….. (Annex IIIA, point XIII.3.2)	Not relevant
Reproductive toxicity to …… (Annex IIIA, point XIII.3.2)	Not relevant

Effects on soil micro-organisms (Annex IIA, point 7.4)

Nitrogen mineralization	Not relevant
Carbon mineralization	Not relevant

Effects on terrestrial vertebrates

Acute toxicity to mammals (Annex IIIA, point XIII.3.3)	Not relevant
Acute toxicity to birds (Annex IIIA, point XIII.1.1)	Not relevant
Dietary toxicity to birds (Annex IIIA, point XIII.1.2)	Not relevant

Reproductive toxicity to birds (Annex IIIA, point XIII.1.3)	Not relevant

Effects on honeybees (Annex IIIA, point XIII.3.1)

Acute oral toxicity	Not relevant
Acute contact toxicity	Not relevant

Effects on other beneficial arthropods (Annex IIIA, point XIII.3.1)

Acute oral toxicity	Not relevant
Acute contact toxicity	Not relevant
Acute toxicity to ……..	Not relevant

Bioconcentration (Annex IIA, point 7.5)

Bioconcentration factor (BCF)	516
Depration time (DT_{50}) (DT_{90})	Not relevant
Level of metabolites (%) in organisms accounting for > 10 % of residues	Not relevant

CHAPTER 6: OTHER ENDPOINTS

No other end points are available for S-Methoprene.

APPENDIX II: LIST OF INTENDED USES

Product-type:

Product Type 18 (insecticides, acaricides and products to control other arthropods).

Claim of the participant:
S-Methoprene is intended for indoor use by professional and non-professional users.
It is used for the control of Pharaoh's ants (*Monomorium pharaonis*).

Target organisms:
Pharaoh's ants (*Monomorium pharaonis*).

Concentration:
Biopren® Pharaoh's Ant Colony Eliminator containing 5g/kg (0.5% w/w) of S-Methoprene.

Categories of users:

Professional and non-professional users.

Type of application:

Ready to use bait (RB). A preparation designed to attract and be eaten by the target species. Each bait station contains 3.5 g of bait.

Summary of intended uses[3]

Object and/or situation	Member State or Country	Product name	Organisms controlled	Formulation		Application			Applied amount per treatment			Remarks:
(a)			(c)	Type (d-f)	Conc. of as (i)	method kind (f-h)	number min max (k)	interval between applications (min)	g as/kg min max	water L/m^2 min max	g as/m^2 min max	(m)
Indoors	Northern and Southern EU	Biopren® Pharaoh`s Ant Colony Eliminator	Pharaoh`s ant	RB	5 g/kg	NA	1 – 2 per year	6 months	5 g/kg	NA	0.5g/m^2	2 baiting stations are applied per 20m^2.

(a) *e.g.* biting and suckling insects, fungi, molds; (b) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(c) GCPF Codes - GIFAP Technical Monograph No 2, 1989 ISBN 3-8263-3152-4); (d) All abbreviations used must be explained
(e) g/kg or g/l;(f) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench;
(g) Kind, *e.g.* overall, broadcast, aerial spraying, row, bait, crack and crevice equipment used must be indicated;
(h) Indicate the minimum and maximum number of application possible under practical conditions of use;
(i) Remarks may include: Extent of use/economic importance/restrictions

[3] adapted from: EU (1998a): European Commission: Guidelines and criteria for the preparation of complete dossiers and of summary dossiers for the inclusion of active substances in Annex I of Directive 91/414/EC (Article 5.3 and 8,2). Document 1663/VI/94 Rev 8, 22 April 1998

APPENDIX III: LIST OF STUDIES

Data protection is claimed by the applicant in accordance with Article 12.1(c) (i) and (ii) of Council Directive 98/8/EC for all study reports marked "Y" in the "Data Protection Claimed" column of the table below. It is assumed that the relevant studies are not already protected in any other Member State of the European Union under existing national rules relating to biocidal products. It was however not possible to confirm the accuracy of this information.

Section No / Reference No	**Author(s)**	**Year**	**Title** **Source (where different from company)** **Company** **Report No.** **GLP (where relevant)** **(Un)Published**	**Data Protection Claimed (Yes/No)**	**Owner**
IIIA, 3.1.1	Laky, V.	2006a	Determination of the Boiling Point of Ss-Methoprene. LAB International Research Centre Hungary Ltd., Report no. 05/112-324AN, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.1.2/1	Laky, V.	2006a	Determination of the Boiling Point of S-Methoprene. LAB International Research Centre Hungary Ltd., Report no. 05/112-324AN, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.1.2/2	Anderson, W.	1999	Product Chemistry: Technical Grade Product. Stillmeadow, Inc., Report no. 4755-98, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.1.3	Anderson, W.	1999	Product Chemistry: Technical Grade Product. Stillmeadow, Inc., Report no. 4755-98, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.2/1	Anderson, W.	1999	Product Chemistry: Technical Grade Product. Stillmeadow, Inc., Report no. 4755-98, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.2/2	Bates, M.	2007	S-Methoprene: Evaluation of Vapour Pressure	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.3	Anderson, W.	1999	Product Chemistry: Technical Grade Product. Stillmeadow, Inc., Report no. 4755-98, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.4/1	Anderson, W.	1999	Product Chemistry: Technical Grade Product Stillmeadow, Inc., Report no. 4755-98, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.

Section No / Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)Published	Data Protection Claimed (Yes/No)	Owner
IIIA, 3.4/2	-	2002	Infrared Spectra of S-Methoprene IR Laboratory of the Institute for Organic Chemistry, Report no. not documented, non GLP (unpublished).	No	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.4/3	Wooley, S. M. and Mullee, D. M.	2006	Nuclear Magnetic Resonance Spectra and Infrared Spectrum	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.4/4	-	1998	NMR Spectra of S-Methoprene NMR Laboratory of the Faculty of Chemical Engineering, Report no. not documented, non GLP (unpublished).	No	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.4/5	Wooley, S. M. and Mullee, D. M.	2006	Nuclear Magnetic Resonance Spectra and Infrared Spectrum	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.4/6	-	2002	MS Spectra of S-Methoprene MS Laboratory of the Department of Physical Chemistry, Report no. not documented, non GLP (unpublished).	No	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.4/7	Laky, V.	2006b	Determination of the Mass Spectrum of S-Methoprene	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.5	Anderson, W.	1999	Product Chemistry: Technical Grade Product Stillmeadow, Inc., Report no. 4755-98, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.7	Laky, V.	2006b	Determination of the Solubility of S-Methoprene in Organic Solvents. LAB International Research Centre Hungary Ltd., Report no. 05/112-358AN, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.9	Anderson, W.	1999	Product Chemistry: Technical Grade Product Stillmeadow, Inc., Report no. 4755-98, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.9	Rivendell International	2012	Calculating the n-octanol/water partition coefficient of S-Methoprene following OECD guidance No. 117, Ireland	Yes	Bábolna Bioenvironmental Centre Ltd.

Section No / Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)Published	Data Protection Claimed (Yes/No)	Owner
IIIA, 3.10/1	Anderson, W.	1999	Product Chemistry: Technical Grade Product Stillmeadow, Inc., Report no. 4755-98, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.10/2	Szabó, E.,	2005	Storage Stability Tests of S-Methoprene Technical Bábolna Környezetbiológiai Központ Kft., Report no. Edition 1, Non-GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.11	Laky, V.	2006c	Determination of the Auto-ignition Temperature of S-Methoprene. LAB International Research Centre Hungary Ltd., Report no. 05/112-355AN, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.12	Laky, V.	2006d	Determination of the Flash Point of S-Methoprene. LAB International Research Centre Hungary Ltd., Report no. 05/112-352AN, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.13	Laky, V.	2006e	Determination of the Surface Tension of S-Methoprene. LAB International Research Centre Hungary Ltd., Report no. 05/112-326AN, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.14	Laky, V.	2006f	Determination of the Viscosity of S-Methoprene. LAB International Research Centre Hungary Ltd., Report no. 05/112-359AN, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.17/1	Anderson, W.	1999	Product Chemistry: Technical Grade Product. Stillmeadow, Inc., Report no. 4755-98, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 3.17/2	Anderson, W.	2003	Storage Stability with Corrosion Characteristics (OPPTS Series 830 Sections 6317 and 6320). Stillmeadow, Inc., Report no. 4817-98, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.

Section No / Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)Published	Data Protection Claimed (Yes/No)	Owner
IIIA, 4.2(c)	Geffke, T.	2007	S-Methoprene Technical Residue Analytical Method for Determination in Tap Water, Surface Water and Ground Water. Dr. U. Noack-Laboratorien, Report No: CRA119111, GLP (unpublished)	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 6.1.1	Kuhn, J. O.	1999a	Acute Oral Toxicity Study In Rats. STILLMEADOW, Inc., Report No.: 4749-98, GLP (unpublished)	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 6.1.2	Kuhn, J. O.	1999b	Acute Dermal Toxicity Study In Rabbits. STILLMEADOW, Inc., Report no.: 4750-98, GLP (unpublished)	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 6.1.3	Leeper, L.	1999	Acute Inhalation Toxicity Study In Rats. STILLMEADOW, Inc., Report no.: 4751-98, GLP (unpublished)	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 6.1.4/1	Kuhn, J. O.	1999c	Primary Dermal Irritation Study In Rabbits. STILLMEADOW, Inc., Report no.: 4753-98, GLP (unpublished)	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 6.1.4/2	Kuhn, J. O.	1999d	Primary Eye Irritation Study In Rabbits. STILLMEADOW, Inc., Report no.: 4752-98, GLP (unpublished)	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 6.1.5	Kuhn, J. O.	1999e	Dermal Sensitization Study In Guinea Pigs. STILLMEADOW, Inc., Report no.: 4754-98, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 6.2/1	Ford, G.	2010	[14C] – S – Methoprene: Toxicokinetic Study in the Rat Quotient Bioresearch (Rushden) Ltd., Report no., LIH/02 (Unpublished)	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 6.2/2	Bond, P.	2010	Summary Statement: [14C] – S – Methoprene: Metabolite Identification by GC-MS/MS (LIH02) Quotient Bioresearch (Rushden) Ltd.	Yes	Bábolna Bioenvironmental Centre Ltd.

Section No / Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)Published	Data Protection Claimed (Yes/No)	Owner
IIIA, 6.3.1/1	Wazeter, F. X. and Goldenthal, E. I.	1973	Twenty-eight Day Tolerance Study in Mice. International Research and Development Corporation, Report no. 322-002, non-GLP (unpublished)	Yes	Wellmark International[4]
IIIA, 6.3.1/2	Nelson, R.	1972	Two-Week Pilot Toxicity Study with ZR-515 Technical in Beagle Dogs. Industrial Bio-test Laboratories, Inc., IBT No. C1646, non-GLP (unpublished)	Yes	Wellmark International[5]
IIIA, 6.4.1/1	Szakonyi, I.P.,	2002	90-day Repeated Dose Oral Toxicity Study of S-Methoprene Technical in Rats. Toxicological Research Centre Ltd., Hungary, Report no.: 01/616-101P GLP (unpublished)	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 6.4.1/2	Török, T.	2007	90-Day Oral Toxicity Study of Test Item S-Methoprene Technical in Beagle Dogs. LAB International Research Centre Hungary Ltd., Hungary, Report no.: 06/188-101K, GLP (unpublished)	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 6.4.1/3	Jorgenson, T. A. and Sasmore, D. P.	1972	Toxicity Studies of Altosid™ Technical (1) Ninety-day Subacute in Rats (2) Ninety-day Subacute in Dogs. Stanford Research Institute, SRI Project LSC-1833 Report No. 2, non-GLP (unpublished)	Yes	Wellmark International1
IIIA, 6.5/2	Wazeter, F. X., Goldenthal, E. I., Geil, R.G., Benson, B.W., Keller, W.F. and Blanchard, G.L.	1975	Two Year Oral Toxicity Study in Rats. International Research and Development Corporation, Report no. 322-001, non-GLP (unpublished)	Yes	Wellmark International[5]

[4] Bábolna Bioenvironmental Centre Ltd. have obtained a letter of access to the Wellmark International studies. Please refer to the confidential folder for these references.

Section No / Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)Published	Data Protection Claimed (Yes/No)	Owner
IIIA, 6.6.1	Hernádi, D.	2002	For the Testing of S-Methoprene Technical with Bacteria Reverse Mutation Assay. Toxicological Research Centre Ltd., Report no.: 01/616-007M, GLP (unpublished)	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 6.6.2	Béres, E.	2002	In vitro Mammalian Chromosomal Aberration Study of Test Item S-Methoprene Technical. Toxicological Research Centre Ltd., Hungary, Report no.: 01/616-020C, GLP (unpublished)	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 6.6.3	Béres, E.	2002	Mutagenic Evaluation of Test Item S-Methoprene Technical in CHO/HPRT Assay. Toxicological Research Centre Ltd., Hungary, Report no.: 01/616-015C, GLP (unpublished)	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIA, 7.1.1.1.1/01	Laky, V.	2002a	Hydrolysis of S-Methoprene as a function of pH. Toxicological Research Centre Ltd, Report No. 01/616-336AN, GLP (unpublished).	Y	Bábolna Bioenvironmental Centre Ltd.
IIIA 7.1.1.1.2/01	McCorquodale, G.	2009	McCorquodale, G. (2009), Photodegradation of [^{14}C]-S Methoprene, Charles River, Tranent, Edinburgh, EH33 2NE, UK. GLP. Unpublished report no: 807299.	Y	Bábolna Bioenvironmental Centre Ltd.
IIIA, 7.1.1.2.1/01	Gáty, S.	2002a	Determination of biodegradability of S-Methoprene Technical test item with closed bottle test. Toxicological Research Centre Ltd., Report No. 01/616-322AN, GLP (unpublished).	Y	Bábolna Bioenvironmental Centre Ltd.
IIIA, 7.1.2.1.1/01	Gáty, S.	2002b	Activated sludge, respiration inhibition test with S-Methoprene technical test item. Toxicological Research Centre Ltd., Report No. 01/616-027AS, GLP (unpublished).	Y	Bábolna Bioenvironmental Centre Ltd.

Section No / Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)Published	Data Protection Claimed (Yes/No)	Owner
IIIA, 7.1.2.2.2/01	Schooley, D. A. et al	1975	Environmental degradation of the insect growth regulator Methoprene (Isopropyl (2E, 4E)-11-Methoxy-3,7,11-trimethyl-2,4-dodecadienoate). II Metabolism by aquatic microorganisms. J. Agr. Food Chem., 23 (2): 393-298	N	Public literature
IIIA, 7.1.2.2.2/02	Schaefer, Ch. H. and Dupras, E. F.	1973	Insect developmental inhibitors. 4. Persistence of ZR-515 in water. Journal of Economic Entomology 66 (4): 923- 925	N	Public literature
IIIA, 7.2.3.1/01	Laky, V.	2002b	Adsorption/desorption test of S-Methoprene technical. Toxicological Research Centre Ltd., Report No. 01/616-331TL, GLP (unpublished).	Y	Bábolna Bioenvironmental Centre Ltd.
IIIA, 7.3.2/01	McManus, K.	2006	Environmental distribution of S-Methoprene (Mackay Level I fugacity model). Rivendell Consulting Limited, Report no.: RI2006/04/04, Non-GLP (unpublished).	Y	Bábolna Bioenvironmental Centre Ltd.
IIIA, 7.4.1.1/01	Gáty, S.	2002c	Fish acute toxicity study S-Methoprene technical test item on Zebrafish, Toxicological Research Centre Ltd., Report No. 01/616-009H, GLP (unpublished).	Y	Bábolna Bioenvironmental Centre Ltd.
IIIA, 7.4.1.2/01	Gáty, S.	2002d	Acute immobilisation test with S-Methoprene technical in Daphnia magna, Toxicological Research Centre Ltd., Report No. 01/616-023DA, GLP (unpublished).	Y	Bábolna Bioenvironmental Centre Ltd.
IIIA, 7.4.1.2/02	Istvan, A.	2012	Acute Toxicity of S-methoprene on *Daphnia magna* in a 48-hour Acute Immobilisation Test, TOXI-COOP ZRT., 8230 Balatonfüred, Arácsi út 97 , Hungary, report no.: 484.441.3614 (unpublished)	Y	Bábolna Bioenvironmental Centre Ltd.
IIIA, 7.4.1.3/01	Hernádi, D.	2002	Algal growth inhibition test with S-Methoprene technical. Toxicological Research Centre Ltd., Report No. 01/616-022AL, GLP (unpublished).	Y	Bábolna Bioenvironmental Centre Ltd.

Section No / Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)Published	Data Protection Claimed (Yes/No)	Owner
IIIA, 7.4.1.4/01	Gáty, S.	2002b	Activated sludge, respiration inhibition test with S-Methoprene technical test item. Toxicological Research Centre Ltd., Report No. 01/616-027AS, GLP (unpublished).	Y	Bábolna Bioenvironmental Centre Ltd.
IIIA, 7.4.2/01	Quistad, G. B. et al	1975	Environmental degradation of the insect growth regulator Methoprene (Isopropyl (2E, 4E)-11-Methoxy-3,7,11-trimethyl-2,4-dodecadienoate). III. Photodecomposition. J. Agr. Food Chem., 23 (2): 299-303	N	Public literature
IIIA, 7.4.2/02	Schooley, D. A. et al	1975	Environmental degradation of the insect growth regulator Methoprene (Isopropyl (2E, 4E)-11-Methoxy-3,7,11-trimethyl-2,4-dodecadienoate). II Metabolism by aquatic microorganisms. J. Agr. Food Chem., 23 (2): 393-298	N	Public literature
IIIA, 7.4.2/03	Schaefer, Ch. H. and Dupras, E. F.	1973	Insect developmental inhibitors. 4. Persistence of ZR-515 in water. Journal of Economic Entomology 66 (4): 923- 925	N	Public literature
IIIA, 7.4.2.1	Rivendell International.	2012	Calculating the Bio-concentration factor of S-Methoprene following US EPA EPI suite. Ireland. report no: RIV-IE-2012-12-07-01 (unpublished)		Bábolna Bioenvironmental Centre Ltd.
IIIA, 7.4.3.4/01	Istvan, A.	2012	Chronic Toxicity of S-methoprene to *Daphnia magna* in a 21-day Reproduction Test, TOXI-COOP ZRT., 8230 Balatonfüred, Arácsi út 97 , Hungary report no.: 484.447.3615 (unpublished)	Y	Bábolna Bioenvironmental Centre Ltd.
IIIA, 7.4.3.5.1/01	Craggs R, Golding L, Clearwater S, Susarla L, Donovan W.	2005	Control of chironomid midge larvae in wastewater stabilisation ponds: comparison of five compounds. Water Sci Technol., 51(12): 191-9	N	Public literature
IIIA, 7.4.3.5.1/02	Lothrop BB, Mulla MS.	1998	Field evaluation of controlled release pellet formulation of methoprene against chironomid midges in man-made lakes. J Am Mosq Control Assoc., 14(3): 335-9	N	Public literature

Section No / Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)Published	Data Protection Claimed (Yes/No)	Owner
IIIA, 7.4.3.5.1/03	Ali A.	1991	Activity of new formulations of methoprene against midges (Diptera: Chironomidae) in experimental ponds. J Am Mosq Control Assoc., 7(4): 616-20.	N	Public literature
IIIA, 7.4.3.5.1/04	Breaud, T.P., Farlow, J.E., Steelman, C.D. and Schilling, P.E.	1977	Effects of the insect growth regulator methoprene on natural populations of aquatic organisms in Louisiana intermediate marsh habitats. Mosquito News 37: 704-712	N	Public literature
IIIA, 7.5.3.1.1/01	US EPA	1991	Reregistration Eligibility Document (RED) Methoprene, United States Environmental Protection Agency, Office of Pesticide Programs, March 1991	N	Public literature
IIIA, 7.5.3.1.2/01	US EPA	1991	Reregistration Eligibility Document (RED) Methoprene, United States Environmental Protection Agency, Office of Pesticide Programs, March 1991	N	Public literature
IIIA, 7.5.3.1.3/01	US EPA	1991	Reregistration Eligibility Document (RED) Methoprene, United States Environmental Protection Agency, Office of Pesticide Programs, March 1991	N	Public literature
IIIB, 3.1	Anderson, W.	1999	Product Chemistry End-Use Product. OPPTS Series 830 Sections 6302, 6303, 6304, 6314, 6315, 6316, 6321, 7000 and 7300. Stillmeadow, Inc., Report no. 4816-98, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIB, 3.1.1	Laky, V.	2006a	Determination of the Physical State, Colour and Odour of Biopren Pharaoh's Ant Colony Eliminator. LAB International Research Centre Hungary Ltd., Report no. 06/228-357AN, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.

Section No / Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)Published	Data Protection Claimed (Yes/No)	Owner
IIIB, 3.1.2	Laky, V.	2006a	Determination of the Physical State, Colour and Odour of Biopren Pharaoh's Ant Colony Eliminator. LAB International Research Centre Hungary Ltd., Report no. 06/228-357AN, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIB, 3.1.3	Laky, V.	2006a	Determination of the Physical State, Colour and Odour of Biopren Pharaoh's Ant Colony Eliminator. LAB International Research Centre Hungary Ltd., Report no. 06/228-357AN, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIB, 3.2	Anderson, W.	1999	Product Chemistry End-Use Product. OPPTS Series 830 Sections 6302, 6303, 6304, 6314, 6315, 6316, 6321, 7000 and 7300. Stillmeadow, Inc., Report no. 4816-98, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIB, 3.3	Anderson, W.	1999	Product Chemistry End-Use Product. OPPTS Series 830 Sections 6302, 6303, 6304, 6314, 6315, 6316, 6321, 7000 and 7300. Stillmeadow, Inc., Report no. 4816-98, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIB, 3.4/1	Laky, V.	2006b	Determination of the Relative Self-Ignition Temperature of the Relative Self-Ignition Temperature of Biopren Pharaoh's Ant Colony Eliminator. LAB International Research Centre Hungary Ltd., Report no. 06/228-355AN, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIB, 3.4/2	Laky, V.	2006c	Determination of the Flammability of Biopren Pharaoh's Ant Colony Eliminator. LAB International Research Centre Hungary Ltd., Report no. 06/228-356AN, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIB, 3.5/1	Anderson, W.	1999	Product Chemistry End-Use Product. OPPTS Series 830 Sections 6302, 6303, 6304, 6314, 6315, 6316, 6321, 7000 and 7300. Stillmeadow, Inc., Report no. 4816-98, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.

Section No / Reference No	Author(s)	Year	Title Source (where different from company) Company Report No. GLP (where relevant) (Un)Published	Data Protection Claimed (Yes/No)	Owner
IIIB, 3.5/2	Laky, V.	2006d	Determination of the pH value of Biopren Pharaoh's Ant Colony Eliminator. LAB International Research Centre Hungary Ltd., Report no. 06/228-338AN, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIB, 3.5/3	Laky, V.	2006e	Determination of the Free Acidity or Alkalinity of Biopren Pharaoh's Ant Colony Eliminator. LAB International Research Centre Hungary Ltd., Report no. 06/228-361AN, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIB, 3.6/1	Anderson, W.	1999	Product Chemistry End-Use Product. OPPTS Series 830 Sections 6302, 6303, 6304, 6314, 6315, 6316, 6321, 7000 and 7300. Stillmeadow, Inc., Report no. 4816-98, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIB, 3.6/2	Laky, V.	2006f	Determination of the Bulk Density of Biopren Pharaoh's Ant Colony Eliminator. LAB International Research Centre Hungary Ltd., Report no. 06/228-325AN, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIB, 3.7/1	Anderson, W.	2003	Storage Stability with Corrosion Characteristics (OPPTS Series 830 Sections 6317 and 6320). Stillmeadow, Inc., Report no. 4817-98, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIB, 3.7/2	Laky, V.	2006g	Determination of the Flowability of Biopren Pharaoh's Ant Colony Eliminator After Heat Test. LAB International Research Centre Hungary Ltd., Report no. 06/228-360AN, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.
IIIB, 3.8	Laky, V.	2006g	Determination of the Flowability of Biopren Pharaoh's Ant Colony Eliminator After Heat Test. LAB International Research Centre Hungary Ltd., Report no. 06/228-360AN, GLP (unpublished).	Yes	Bábolna Bioenvironmental Centre Ltd.

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