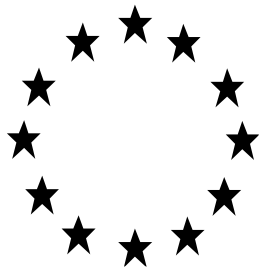
Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

PRODUCT ASSESSMENT REPORT OF A BIOCIDAL PRODUCT FOR NATIONAL AUTHORISATION APPLICATIONS



Biopren® 50 LML mosquito larvicide concentrate

Product type 18

S-methoprene

Case Number in R4BP: BC-SN019523-27

Evaluating Competent Authority: IT

Date: August 2019

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1 CONCLUSION

BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is a slow acting insecticide (PT18) containing the active substance S-methoprene XXXXXXXX (minimum purity: XXXXXX), that considerably reduces *Aedes* and *Culex spp.* mosquitoes population during the developmental stage.
The product can be used outdoor by Trained Professionals to treat small scale water holding features/aquatic areas not connected to natural aquatic compartment or STP (such as unused pools, ponds padded by geofoil, rainwater holding barrels), which are not used for drinking water storage, irrigation, bathing or for keeping (ornamental) fish, and which may be suitable, temporarily or permanently, for the breeding of mosquito larvae.

Based on the assessment, the IT-CA concludes that this product is sufficiently efficacious against the target organisms and can be safely used by Trained Professionals according to the use instructions of the SPC.

The conditions for granting an authorisation according to Article 19(1) of Regulation (EU) No. 528/2012 are fulfilled.

2 ASSESSMENT REPORT

2.1 Summary of the product assessment

2.1.1 Administrative information

2.1.1.1 Identifier of the product

Identifier	**Country (if relevant)**
BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE	IT

2.1.1.2 Authorisation holder

Name and address of the authorisation holder	**Name**	Babolna Bio Ltd
	Address	Szállás utca 6, 1107 Budapest, Hungary
Authorisation number		
Date of the authorisation		
Expiry date of the authorisation		

2.1.1.3 Manufacturer of the product

Name of manufacturer	Babolna Bio Ltd
Address of manufacturer	Szállás utca 6, 1107 Budapest, Hungary
Location of manufacturing sites	Dr Köves János út 1-3, 2943 Babolna, Hungary

2.1.1.4 Manufacturer of the active substance

Active substance	S-methoprene
Name of manufacturer	XXXXXXXXX
Address of manufacturer	XXXXXXXXXX
Location of manufacturing sites	XXXXXXXXX

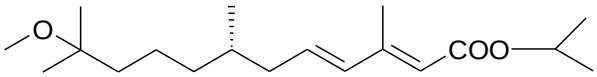
2.1.2 Product composition and formulation

NB: the full composition of the product according to Annex III Title 1 should be provided in the confidential annex.

Does the product have the same identity and composition as the product evaluated in connection with the approval for listing of the active substance(s) on the Union list of approved active substances under Regulation No. 528/2012?

Yes ☐
No ☒

2.1.2.1 Identity of the active substance

Main constituent	
ISO name	S-methoprene
IUPAC or EC name	Isopropyl-(2E,4E, 7S)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate
EC number	Not available List number: 613-834-0
CAS number	65733-16-6
Index number in Annex VI of CLP	
Minimum purity / content	XXXXX
Structural formula	

2.1.2.2 Candidate for substitution

S-methoprene is not a candidate for substitution.

2.1.2.3 Qualitative and quantitative information on the composition of the biocidal product XXXXXXX

2.1.2.4 Information on technical equivalence

The active substance used in BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is from the same source evaluated for the purpose of the approval, i.e. Babolna Bio Ltd. Therefore, no technical equivalence assessment is required.

2.1.2.5 Information on the substance(s) of concern

XXXXXXXXXXXXXXXXXX

Please, also refer to the confidential annex as regards the endocrine disrupting (ED) properties of the co-formulants.

2.1.2.6 Type of formulation

ZW (CS+EW)

2.1.3 Hazard and precautionary statements

Classification and labelling of the products of the family according to the Regulation (EC) 1272/2008

Classification	
Hazard category	Skin Sens. 1 Aquatic Chronic 2
Hazard statement	H317 May cause an allergic skin reaction. H411 Toxic to aquatic life with long lasting effects.
Labelling	
Signal words	Warning
Pictograms	GHS07; GHS09
Hazard statements	H317 May cause an allergic skin reaction. H411 Toxic to aquatic life with long lasting effects.
Precautionary statements	P261 Avoid breathing dust/fume/gas/mist/vapours/spray. P273 Avoid release to the environment. P280 Wear protective gloves/coveralls. P302+P352 IF ON SKIN: Wash with plenty of water/… P333+P313 If skin irritation or rash occurs: Get medical advice/attention. P391 Collect spillage. P501 Dispose of contents/container to ... in accordance with local/regional/national/international regulation (to be specified). The manufacturer/supplier must specify whether the disposal regulations apply to the product, the container or both.
Note	The label must contain the indication: Contains octadecanoic acid, 12-hydroxy-, polymer with. alpha.-hydro-.omega.-hydroxypoly(oxy-1,2-ethanediyl) and reaction mass of 5-chloro-2-methyl-2H-isothiazol-3-one and 2-methyl-2H-isothiazol-3-one (3:1)

2.1.4 Authorised use

2.1.4.1 Use description

Table 1. Use # 1 – Trained Professionals

Product Type	PT18 - Insecticides, acaricides and products to control other arthropods (Pest control)
Where relevant, an exact description of the authorised use	Slow acting insecticide that significantly reduces the number of *Aedes* and *Culex* spp. mosquitoes during the developmental stage
Target organism (including development stage)	*Culicidae:* *Aedes* spp. mosquitoes' larvae (L3-L4) *Culex* spp. mosquitoes' larvae (L3-L4)
Field of use	Outdoor The product is used to treat small scale water holding features/aquatic areas not connected to the natural aquatic compartment or the STP, such as: - unused pools - ponds padded by geofoil - rainwater holding barrels which are not used for drinking water storage, irrigation, bathing or for keeping (ornamental) fish, and which may be suitable, temporarily or permanently, for the breeding of mosquito larvae.
Application method	Spraying (direct application by knapsack or hand-held equipment)
Application rates and frequency	Dosage depends on the type of breeding site, quality and depth of water. Clean water: 220 mL product/hectare or 0.022 mL product/m^2 (water depth <30 cm) 290 mL product/hectare or 0.029 mL product/m^2 (water depth >30 cm) Slightly contaminated water: 290 mL product/hectare or 0.029 mL product/m^2 (water depth <30 cm) 360 mL product/hectare or 0.036 mL product/m^2 (water depth >30 cm) The given dosage should be diluted with a minimum volume of 5 L water per 0.1 ha or 1000 m^2. Frequency: Re-apply the product only after 10 days, if needed.
Category of user	Trained Professional
Pack sizes and packaging material	Bottle Coex PE/PA or HDPE (1 L up to 10 L) Can Coex PE/PA or HDPE (1 L up to 10 L)

2.1.4.2 Use-specific instructions for use[1]

NA

2.1.4.3 Use-specific risk mitigation measures

NA

2.1.4.4 Where specific to the use, the particulars of likely direct or indirect effects, first aid instructions and emergency measures to protect the environment

NA

2.1.4.5 Where specific to the use, the instructions for safe disposal of the product and its packaging

NA

2.1.4.6 Where specific to the use, the conditions of storage and shelf-life of the product under normal conditions of storage

NA

2.1.5 General directions for use

2.1.5.1 Instructions for use

Apply to treat small scale water holding features/aquatic areas not connected to the natural aquatic compartment or the STP (such as unused pools, ponds padded by geofoil, rainwater holding barrels), which are not used for drinking water storage, irrigation, bathing or for keeping (ornamental) fish, and which may be suitable, temporarily or permanently, for the breeding of mosquito larvae.

Dosage depends on the type of breeding site and depth of water.

Clean water:
220 mL product/hectare or 0.022 mL product/m^2 (water depth < 30 cm)
290 mL product/hectare or 0.029 mL product/m^2 (water depth > 30 cm)

Slightly contaminated water:
290 mL product/hectare or 0.029 mL product/m^2 (water depth < 30 cm)
360 mL product/hectare or 0.036 mL product/m^2 (water depth > 30 cm)

The given dosage should be diluted with a minimum volume of 5 L water per 0.1 ha or 1000 m^2.

Detailed description of Application:
SHAKE WELL BEFORE USING. BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE may separate on standing and must be thoroughly agitated prior to dilution. Rinse the empty container three times and add rinses to the spray tank.
Mixing: DO NOT mix with oil. Always use clean equipment. Partially fill spray-tank with water, then add the recommended amount of BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE, shake and complete filling. Where possible, use the mixture on the day of mixing. Mild agitation during application is desirable.
Mix BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE in sufficient water to deliver the application rate recommended on this label (220-360 mL product/ha or 0.022-0.036 mL product/m^2, depending on the type of breeding site, quality and depth of water). A minimum application volume of 5 L water per 0.1 ha or 1000 m^2 (i.e. 22 to 36 mL of product should be diluted into 5 L of water) should be used. For a different volume of the equipment container and a different size of the area to be treated, the trained professional will adjust the product dose for dilution accordingly.
Only coarse sprayers are recommended.

In general, the residuality of the product is 10 days. Re-apply the product only after 10 days, if needed. Please note that heavy rain can affect the efficacy of the product

Always read the label or leaflet before use and follow all the instructions provided.
Avoid continuous use of the product.
Take into account the life cycle and characteristics of target insects to adapt treatments. In particular, target the most susceptible stage of the pest, timing of applications and areas to be treated.
Adopt integrated pest management methods such as the combination of chemical, physical control methods and other public health measures, taking into account local specificities (climatic conditions, target species, conditions of use, etc).
Alternate products containing active substances with different mode of action, (to remove resistant individuals from the population).
Establish a baseline and monitor levels of effectiveness on populations in key areas (at least one survey per year) in order to detect any significant changes in susceptibility to active substance. Information from resistance monitoring programs allows early detection of problems and gives information for correct decision making.
The users should inform if the treatment is ineffective and report straightforward to the authorization holder.
Do not apply to water used for crops irrigation.
Do not use if food, feed or drinking water could be contaminated.

2.1.5.2 Risk mitigation measures

Repeated exposure may cause allergic disorders, therefore avoid contact with eyes and skin.
Wear protective chemical resistant gloves (glove material to be specified by the authorisation holder within the product information) and coveralls (coveralls norms specified by the authorisation holder within the product information) during product handling phase and cleaning of spray equipment.
Wear disposable gloves/coveralls during product handling phase and cleaning of spray equipment.
Wash hands after use.
The product cannot be used to treat swimming pool water.
Do not apply the product to water bodies that are in connection with natural/fresh water (e.g. brook, river, lake, etc.).
The water holding features to be treated must not be connected to STP.

2.1.5.3 Particulars of likely direct or indirect effects, first aid instructions and emergency measures to protect the environment

Likely direct or indirect adverse effects:
- Allergic skin reaction

First Aid Measures:
- Relocate the individual from the exposure source and remove any contaminated/spattered clothing articles.
- Eye exposure: ALWAYS check for and remove contact lenses, wash eyes with plenty of water with eye lids open for at least 15 minutes.
- Skin contact: wash affected area with plenty of water and soap, NO scrubbing.
- In case mouth contact or ingestion: Do NOT induce vomiting unless told to do so by poison control center operator or health care professional; rinse mouth, drink a few glasses of water.
- Keep the individual calm and at rest, conserve body temperature and control breathing. If necessary check for pulse and initiate artificial respiration.
- If necessary take the person to a healthcare center, bring packaging or label whenever possible.

NEVER LEAVE THE AFFECTED INDIVIDUAL UNATTENDED!

Advice for medical and healthcare personnel:
- Monitor vital signs and provide symptomatic and supportive treatment.

WHEN ASKING FOR MEDICAL ADVICE KEEP PACKAGING OR LABEL AT HAND AND CALL YOUR LOCAL POISON CONTROL CENTER ☎ [*INSERT LOCAL NUMBER HERE*].

Emergency measures:
- In case of skin contact, get medical attention if feel unwell or symptoms occur.

2.1.5.4 Instructions for safe disposal of the product and its packaging

The product and its container should be disposed of as hazardous waste. Collect spillage. Do not discharge unused product on the ground, into water courses, into pipes (sink, toilets…) nor down the drains.
Dispose of unused product, its packaging and all other waste, in accordance with local regulations.

2.1.5.5 Conditions of storage and shelf-life of the product under normal conditions of storage.

The available data support a shelf-life of **30 months**. Always store unused product in a dry, cool place, in well ventilated area, out of direct sunlight. Protect from frost: the product must not be stored under conditions of < 5°C. Keep out of reach of children and domestic animals.

2.1.6 Other information

None available.

2.1.7 Packaging of the biocidal product

Type of packaging	Size/volume of the packaging	Material of the packaging	Type and material of closure(s)	Intended user (e.g. professional, non-professional)	Compatibility of the product with the proposed packaging materials (Yes/No)
Bottle	up to 10 L	COEX PE/PA or HDPE	plastic closure cap	Trained professional	yes
Can	up to 10 L	COEX PE/PA or HDPE	plastic closure cap	Trained professional	yes

2.1.8 Documentation

2.1.8.1 Data submitted in relation to product application

Please, find the list of studies under '3.1 List of studies for the biocidal product' and also '3.3 New information on the active substance'.

2.1.8.2 Access to documentation

Babolna Bio Ltd is the owner of active substance dossier evaluated for the approval of S-methoprene under PT18 and also the sponsor of the studies prepared for the BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE authorisation process.

2.2 Assessment of the biocidal product

2.2.1 Intended use as applied for by the applicant

Table 2. Intended use # 1 – Trained Professionals

Product Type	PT18 - Insecticides, acaricides and products to control other arthropods (Pest control)
Where relevant, an exact description of the authorised use	Mosquito control
Target organisms (including development stage)	*Culicidae*: *Culex* mosquitoes Larvae *Aedes* mosquitoes Larvae
Field of use	Outdoor Possible breeding sites: swamps and marshes, stagnant water, ditches, drains, flooded remnants, woodland pools, and possible breeding sites for mosquitoes. Apply in all the artificial water cumulation such as puddles, pools, artificial basins and in all the close hydraulic systems etc.
Application methods	Spraying
Application rates and frequency	Dosage: Depends on the type of breeding site, quality and depth of water Clean water: 220 mL/hectare (water depth <30 cm) 290 mL/hectare (water depth > 30 cm) Slightly contaminated water (marshy, swampy area, rice land): 290 mL/hectare (water depth < 30 cm) 360 mL/hectare (water depth > 30 cm) Highly contaminated water (sewer treatment plant, infiltration pool): 360 mL/hectare (water depth < 30 cm) 400 mL/hectare (water depth > 30 cm) The given dosage should be diluted with water as the working solution volume is recommended to be 5-50 L/hectare. Pour 2-3 litres of water into the container of spraying equipment, add the suitable dosage of BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE and then fill up to the final volume. Frequency: Depends on the rate of infestation. In general, the residuality of the product is 7 - 14 days pending on conditions.
Category of user	Trained Professionals
Pack sizes and packaging material	Bottle Coex PE/PA or HDPE up to 10 L Drum***** Metal drum with epoxy resin inner layer up to 55 L Can

	Tin***** Coex PE/PA or HDPE up to 10 L

(*) **refMS (IT): Not supported by the applicant by means of storage stability data**

2.2.2 Physical, chemical and technical properties

XXXXXX

Conclusion on the physical, chemical and technical properties of the product

BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is a ZW formulation, i.e. a mixed formulation of CS and EW, intended for dilution into water prior to spray application. According to the description of the intended use as applied for by the applicant, the highest dilution is when 220 mL of the product (per hectare) is applied in 50 L working solution, which corresponds to ca. 220 g in 50 kg, i.e. 0.44% w/w. Whereas, the lowest dilution is when 400 mL of the product (per hectare) is applied in 5 L working solution, which corresponds to ca. 400 g in 5 kg, i.e. 8% w/w.
The overall a.s. content is 5.0% w/w as pure a.s. (minimum purity: 95% w/w): 1.25% w/w as free S-methoprene and 3.75% w/w as micro-encapsulated S-methoprene.

BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is an off-white, viscous aqueous liquid formulation, with a characteristic slightly-sweetish odour.
The pH of the product at 20°C is neutral. The pH of a 1% (w/v) dilution proved to be 6.5-6.7). D_4^{20} was determined to be 1.025.

Storage stability tests were conducted on the product in its original packaging (HDPE bottle). No significant change in the packaging was observed at the end of the storage (either accelerated and long term). Since BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is an aqueous formulation, results can be extrapolated to COEX PE/PA but cannot be extrapolated to metal containers, unless additional storage stability data are provided.

- Accelerated storage stability test: the product in its original packaging (HDPE bottle) was kept at 54°C for 2 weeks. No significant chemical change occurred (a.s. content variation: -1.3%); no significant change in the product appearance was observed, either. No data on the pH of the product after accelerated storage was provided; nonetheless, taking into account the product composition and neutral pH, the available data allow to expect the product is stable when occasionally subject to higher than normal temperatures.
- Long-term storage stability study: the **3-yr storage** stability study was on-going at dossier submission; both intermediate and final results have been made available during the evaluation of the product.
  After 3 years at 20±1 °C, the a.s. content proved to vary by -0.7%. No change in the product appearance was observed. No data on the pH of the product was provided in the 3-yr storage stability study report. So, the pH of an aged sample was requested by the refMS. Data was submitted by the applicant on the same batch investigated in the 3-yr storage stability study, showing the product remains neutral upon storage (6.8 and 7.2 at 20±1 °C, for the neat formulation and its 1% dilution, respectively, after overall storage of 3 years + 8 months).

Additionally, upon request of the refMS, results were presented for persistent foam (CIPAC MT 47), spontaneity of dispersion (CIPAC MT 160), suspensibility (CIPAC MT 184), pourability (CIPAC 148.1), and wet sieve test (CIPAC MT 185). The most relevant technical characteristics of the product proved to be still satisfactory after **storage for 30 months** (namely after ca. 32/33-month storage, see NOTE below the phys-chem properties table), thus ensuring that BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE remains suitable for use after transportation and storage. As for pourability, results after storage proved to be slightly out of the acceptable limits. To ensure that no excessive residues remain in the container, label contains: "Rinse the empty container three times and add rinses to the spray tank".
Taking into account the overall storage stability data (after **32/33 months** or **3 years**), in conclusion results can support a shelf-life of **30 months**.

Low temperature stability test was not conducted. Therefore, label contains: "Protect from frost: the product must not be stored under conditions of < 5°C".

Testing on the effect of light is not necessary for BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE. Though the a.s. is sensitive to light, opaque packaging ensures protection from direct sunlight. So, exposure to sunlight is negligible when the product is correctly stored in its original packaging (HDPE or COEX PA/PE) according to label instructions.

In the original IUCLID dossier the applicant indicated the product as a CS formulation, so the following technical characteristics were addressed for BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE (the ones indicated as relevant by the FAO manual for CS formulations), to ensure the product is easy to handle and offers good miscibility with water:
- persistent foam;
- spontaneity of dispersion;
- suspensibility;
- pourability.

The wet sieve test was also carried out, to ensure the sprayability of the diluted product.
As for suspensibility, the 4 g/L and 100 g/L testing solutions (corresponding to 0.4% and 10% dilutions, respectively) encompass the highest and lowest dilutions for the intended use as applied for by the applicant and are, therefore, acceptable. Indeed, the 10% dilution is slightly higher than actually requested, however satisfactory results were obtained (under worst-case conditions) which can be extended to the 8% dilution.
No further testing is deemed necessary for technical characteristics, though the product was eventually clarified by the applicant to be a ZW. Test results showed the satisfactory performance of BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE, in particular that the product is homogeneous on application, with no blockages of the spraying equipment.

BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is not intended to be used in combination with other products. The surface tension of the product (8% dilution) was found to be 31.8 mN/m at 20°C. Dynamic viscosity proved to be 143.7 mPa s and 116.0 mPa s at 20°C and 40°C, respectively.

2.2.3 Physical hazards and respective characteristics

Property	Guideline and Method	Purity of the test substance (pure AS, % w/w)	Results	Ref.
Explosives	Justification for the non-submission of data	--	Since neither the a.s. nor the co-formulants are officially classified or self-classified as explosives, the product is not expected to possess explosive properties	IUCLID TOC_4.1
Flammable gases	--	--	Not applicable, the product is liquid (ZW)	IUCLID TOC_4.2
Flammable aerosols	As above	--	Not applicable, the product is liquid (ZW)	IUCLID TOC_4.3
Oxidising gases	As above	--	Not applicable, the product is liquid (ZW)	IUCLID TOC_4.4
Gases under pressure	As above	--	Not applicable, the product is liquid (ZW)	IUCLID TOC_4.5
Flammable liquids	As above	--	Since neither the a.s. nor the co-formulants are officially classified or self-classified as flammable, the product is not expected to be a flammable liquid. Furthermore, the product is water-based (water is ca. 50% w/w)	IUCLID TOC_4.6
Flammable solids	As above	--	Not applicable, the product is liquid (ZW)	IUCLID TOC_4.7
Self-reactive substances and mixtures	As above	--	There are no chemical groups associated with explosive or self-reactive properties	IUCLID TOC_4.8
Pyrophoric liquids	As above	--	Based on the available information and experience in production and handling, the product does not ignite spontaneously on coming into contact with air at normal temperatures	IUCLID TOC_4.9
Pyrophoric solids	As above	--	Not applicable, the product is liquid (ZW)	IUCLID TOC_4.10
Self-heating substances and mixtures	As above	--	Not applicable, the product is liquid (ZW)	IUCLID TOC_4.11

Property	Guideline and Method	Purity of the test substance (pure AS, % w/w)	Results	Ref.
Substances and mixtures which in contact with water emit flammable gases	As above	--	Experience in handling and use shows that product does not emit flammable gases after contact with water	IUCLID TOC_4.12
Oxidising liquids	--	--	The ingredients contain oxygen, but this element is chemically bonded only to carbon or hydrogen. Since none of the ingredients are officially classified or self-classified as oxidising, the product is not expected to possess oxidising properties	IUCLID TOC_4.13
Oxidising solids	As above	--	Not applicable, the product is liquid (ZW)	IUCLID TOC_4.14
Organic peroxides	As above	--	No organic peroxides are present. The product should not be considered for classification in this class	IUCLID TOC_4.15
Corrosive to metals	As above	--	The product should not be considered for classification in this class (halogen-free, no strong base/acid, no chelating agents, pH of the neat formulation is neutral)	IUCLID TOC_4.16
Auto-ignition temperatures of products (liquids and gases)	EU method A.16	4.05% w/w batch No.: 128436	No self-ignition was observed up to 400°C	IUCLID TOC_4.17.1
Relative self-ignition temperature for solids	As above	--	Not applicable, the product is liquid (ZW)	IUCLID TOC_4.17.2
Dust explosion hazard	As above	--	Not applicable, the product is liquid (ZW)	IUCLID TOC_4.17.3

Conclusion on the physical hazards and respective characteristics of the product
Since neither the a.s. nor the co-formulants are officially classified or self-classified as explosive or oxidising, it can be anticipated that BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE has neither explosive nor oxidising properties.

Neither the a.s. nor the co-formulants are officially classified or self-classified as flammable, so BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is not expected to be a flammable liquid; besides, the product is an aqueous formulation (water is ca. 50% w/w). No self-ignition was observed up to 400°C. There are no chemical groups associated with self-reactive properties, either.

Experience in production and handling shows that BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE does not ignite spontaneously on coming into contact with air at normal temperatures. Experience in handling and use shows that the product does not emit flammable gases after contact with water, either.

BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE should not be considered for classification in the hazard classes of organic peroxide and corrosive to metals, based on considerations on the a.s. and the co-formulants.

On the basis of the available data/information, BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE does not pose any physical hazards. Therefore, the need for a risk characterisation for physical hazards is not envisaged.

2.2.4 Methods for detection and identification

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Analytical methods for residues

XXXXXXXXXXXXXXXXXXXXXXXXXX

Analytical methods for substances of concern

XXXXXXXXXXXX

2.2.5 Efficacy against target organisms

2.2.5.1 Function and field of use

BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is an insecticide that is effective against Mosquitoes' larvae (*Culex spp., Aedes spp.*), by considerably reducing their number. It is to be used outdoors by trained professionals.

BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE releases S-methoprene (Insect Growth Regulator) into water where mosquitoes breed. BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE prevents the emergence of adult mosquitoes from treated sites.

S-methoprene has no effect on mosquitoes which have reached the pupal or adult stage prior to treatment. Treated larvae continue to develop normally to the pupal stage, after which they fail to emerge and drown. BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE has sufficient activity to be effective against existing broods when applied to any larval stage at recommended rates. Third and fourth larval stages are more susceptible to the effects of S-methoprene than early stages.

2.2.5.2 Organisms to be controlled and products, organisms or objects to be protected

Culex spp. L3-L4
Aedes spp. L3-L4

2.2.5.3 Effects on target organisms, including unacceptable suffering

BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is an S-methoprene (juvenile hormone analogue) based insect growth regulator for prevention of the emergence of adult mosquitoes.

2.2.5.4 Mode of action, including time delay

Methoprene is an invertebrate metabolic inhibitor that does not seem to cause direct toxic effects in mammals. (IPCS INCHEM / WHO, No 47, Methoprene).
It modulates ecdysteroid signalling during insect development and metamorphosis.
S-methoprene is an analogue to a unique insect-growth regulating hormone, which does not resemble any known mammalian hormones. Applied at very low rates, while insect populations are still in the egg or larval stage of their life cycle, S-methoprene prevents development to the adult reproductive stages so that insects die in arrested immaturity. S-methoprene is not toxic when applied to adult stages of the target insect.
Since it interferes with the normal life cycle of insects and is not directly toxic to the pest, S-methoprene is considered to be a biochemical pesticide (EXTOXNET 2001).

2.2.5.5 Efficacy data

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organisms**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
For the control of mosquitoes	By trained professional users	Biopren 50 LML mosquito larvicide concentrate Batch No.: 100613/ Manufactured: 2014.07.22.	Mosquito: *Aedes aegypti (Culicidae)*	WHO Guidelines for Laboratory and Field Testing of Mosquito Larvicides (WHO/CDS/WHOPES/GCDPP/2005.13)	**Laboratory test (dose-finding study):** 3 test doses, 17 L capacity plastic containers, room temperature: 23-26ºC, relative humidity: 40-50%. Observations: 1-9 days: every 24 hours On the 10th day: the end of the exposition period, live larvae and pupae into a smaller container. Residual hatching inhibition: every 10 days a new batch of mosquito larvae were placed into the same test container	0.01 ppm (equivalent to 360 mL/ha) dose: Acceptable inhibition until 10 days (90.51%) 0.03 ppm (equivalent to 3X360 mL/ha) dose: Acceptable inhibition until 20 days (97.12%) 0.05 ppm (equivalent to 5X360 mL/ha) dose: Acceptable inhibition until 30 days (91.11%)	Biological laboratory efficacy trial of Biopren 50 LML on *Aedes aegypti* József Schmidt (2015) Code No: 154.007.-010, 154.019-022., 154.029.-032., 154.033-035., 154.039-040.
For the control of mosquitoes	By trained professional users	Biopren liquid (50 g/L S-methoprene)	*Aedes vigilax*	No guideline available	**Laboratory trial:** Dose: 220 mL/ha	Under the detailed laboratory	Laboratory evaluation of the efficacy of Biopren

					Ae. vigilax larvae were collected from salt marsh and transported to the laboratory in 20 litre buckets. Temperature of 23ºC, and a 12:12 h light:dark cycle. Third-instar larvae were exposed in test water with a salinity of 33 g/litre. Container: glass aquaria holding 10 litres of test concentration. Three untreated control aquaria holding 50 test larvae each. The test larvae were not fed during testing to minimize variability caused by nutritional and metabolic condition.	conditions the untreated larvae took from 1-8 days to pupate. By comparison, larvae treated with the various IGR formulations took 8-13 days to pupate. In terms of control efficacy, the Biopren concentrated formulation object of the present application caused 100% mortality of treated *Ae. vigilax*	sand granule (0.4% S-methoprene) and Biopren liquid (5% S-methoprene) for applications against *Ae. vigilax* Australia's premier salt marsh arbovirus vector D. Thomas 2006. GB06-01 (support study)
For the control of mosquitoes	By trained professional users	Biopren liquid (50 g/L S-methoprene)	*Aedes vigilax*	No guideline available	**Small plot study:** Dose: 220 mL/ha Temperature: 23ºC, and a 12:12 h light:dark cycle.	The Biopren concentrated formulation object of the present application was found to be effective,	Small plot field evaluation of the efficacy of Biopren liquid and Biopren sand for applications against the salt marsh mosquito

					Five replicated treatments (1 treatment per saltmarsh pool x 4-5 replicate pools per treatment), small (3-5 m^2) pools. 50 third-instar larvae were included in each replicate. Observations: Larval and pupal mortality every 24 hours until all immature stages had emerged or were dead.	killing 96%-100% of treated larvae at the lower label rate	vector *Aedes vigilax* D. Thomas, C. Perel 2006. GB06-02 (support study)
For the control of mosquitoes	By trained professional users	Biopren liquid (50 g/L S-methoprene)	*Culex. annulirostris larvae*	No guideline available	**Field bioassay:** Dose: 220 mL/ha Temperature: 23ºC, and a 12:12 h light:dark cycle. 40 liter plastic containers, with 2 kg of washed sand, and filled with tap water. Lucerne was then added to each container, as it is a well known oviposition attractant, 0.02 g of fish food was also added as a food source. Placed under trees	At rate of 220 mL/ha, 100% *Cx. annulirostris* mortality was recorded for 7 days, with control efficacy decreasing to 43% at 9 days post-treatment.	Field Bioassay Evaluation of Biopren Liquid and Biopren Sand for Control of Australia's Premier Freshwater Mosquito Vector *Culex annulirostris* D. Thomas 2006. GB06-03 (support study)

					approximately 50 meters from a freshwater pond known to produce *Cx. annulirostris*. The containers were then monitored daily for *Cx. annulirostris* colonization, which occurred within 24 h. The containers were then treated when the first cohort of larvae had reached the third-instar stage. 10 days post-treatment, all pupae were collected. Pupal mortality was then scored		
For the control of mosquitoes	By trained professional users	Biopren 50 LML mosquito larvicide concentrate 50 g/kg S-methoprene lot 100613 Manufacturing date: 22.07.2014	*Aedes aegypti* *Aedes albopictus* *Culex pipiens*	CA-Dec12-Doc.6.2.a-Final Manual for the Authorization of Pesticides - EU part – Biocides - Chapter 7 Efficacy - version 1.1; January 2013 and guideline WHO/CDS/WHOPES/GCDPP/2005.13	**Semi-field trial:** Dose: dilution in water at a rate of 290 mL/ha (0.29 mL/10 m²). Actual amount of product applied = 28 µL on 0.96 m². Colony breeding conditions: 28+/-1°C, 75+/-10% HR, light 700 lux 16 h + darkness 8 h.	The product BIOPREN 50 LML MOSQUITO LARVICIDE CONCENTRATE, applied at a dose of 290 mL/ha gave 100% reduction of emergence throughout the 3 week	Laboratory measurement of the effectiveness of an IGR-insecticide speciality intended for the control of mosquitoes larvae Bruno Serrano 2015 Report No: 1931b/0515R

					25 larvae of 3rd instar in each water tank (replicate) of 300 L of water. Acclimatization: 48 h. The complete duration of the observation was 3 weeks (it was the time for the 80% of the larvae to become adults in the Untreated Control series)	observation period.	
For the control of mosquitoes	By trained professional users	5% S-methoprene Batch No: 100613 Manufacturing date: 22/07/2014	L_3 stage *Culex pipiens larvae*	No guideline available Babolna Bio's method was followed	**Laboratory trial:** Dose: 0.005 ppm Total exposure duration: 20 days During the trials, 3 parallel and control test were applied. 50 larvae were put into the containers and stayed there for a maximum of a 10 days period. The test containers were examined every day and dead larvae and pupae were removed, their number recorded. Living larvae and pupae	Immediate inhibition emergence (0 to 10 days) was 94.77%, At the 10-20 days exposition period the inhibition decreased to 21.58%	Efficacy Study Of Biopren 50 LML Mosquito Larvicide Concentrate In Laboratory On *Culex pipiens species* József Schmidt 2015 154.082.-083., 154.097.-098

					were then transferred into a biocide-free environment to check hatching inhibition efficacy. Observation was prolonged until the hatching inhibition of the product fell under 90%. Control mortality was 7.3-10.7%		
For the control of mosquitoes	By trained professional users	Biopren 50LML larvicide concentrate – Batch no. 132737	*C. pipiens* and *Aedes albopictus*	CA-Dec12-Doc.6.2.a-Final Manual for the Authorization of Pesticides - EU part – Biocides - Chapter 7 Efficacy - version 1.1; January 2013 and guideline WHO/CDS/WHOPES/GCDPP/2005.13	**Field study:** 10 treated road drains + 10 control road drains located in a commercial area in north Italy (Bologna province – 44°40'55" N – 11°29'13" E). Dimension of each drain was40X40X60 cm. Inhibition of emergence was recorded and assigned to each species after identification. Due to heavy rains, no sufficient data could be recorded after 2	At day 2 post-treatment, the inhibition of adult production (%IE) for *Cx. pipiens* was 80.8% (AIE=98.6%) for the dose of 0.2 mL/drain and 92.5% (AIE=99.1%) for the dose of 0.006 mL/drain whereas for *Ae. albopictus* is IE=60 % for the dose of 0.2 mL/drain and IE=100% for the dose of 0.006 mL/drain. At day 7 and 13 post-	Analysis of larvicide effect and residual activity of Biopren 50L ML (active ingredient S-methoprene) in road drains in urban areas against *Culex pipiens* and *Aedes albopictus.* RF_EZS_18_Report Efficacy Biopren 2018_Report 1_BBIO

					days post-treatment.	treatment, the density of larvae L3-4 and Pupae of either species decreased even in the control drains, therefore it was not possible to calculate %IE.	
For the control of mosquitoes	By trained professional users	Biopren LML (5% S-methoprene) Batch No.: 46758 DOM: 04.09.06	*Aedes vigilax* (early 3rd/late 4th larval instar)	No guidelines available	**Field study:** 10 containers measuring each 35x25x10 cm, were filled with 10 kg of sand and 2 litres of seawater. In each container were put 30. For the negative control were set up 4 containers holding each 30 larvae too. The larvae fed with 0.04 g of K9 fish food. Treatment was applied at a dosage 5 L mix/ha (corresponding to 290 mL/ha of concentrate) by helicopter, at a height of 2 meters and a flying speed of 75 knots.	The aerial application of the product, at a dose of 290 mL/ha gave the following results: -2% of adult mosquitoes emergence (compared with 92% of the negative control); - 65%±11% of pupation rate at 3 days post treatment and 77%±11% at 4 days post treatment. The negative controls gave a percentage of pupation equal to 98%±2% at 3 and 4 days post treatment.	Field bioassay evaluation of an aerial application of Biopren Liquid Mosquito Larvicide against the saltmarsh arbovirus vector Aedes vigilax. Perel C., 2016_Report No. 4.

					The aerial bioassay was conducted at the following environmental conditions: temperature of 26.5 °C and 82% RH. Treated and untreated containers were monitored for 8 days post-treatment.		

Conclusion on the efficacy of the product

BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is used to control the larvae of different mosquito species thus considerably reducing the number of mosquitoes during their development stages. The product was tested in semi-field and laboratory trials for the species of interest, providing information on the efficacy for *Culex* as well as *Aedes* spp., with a residual efficacy of 10 days. Upon request, the Applicant sponsored a field study which, however, could not be completed due to adverse weather conditions. The partial data obtained (2 days after treatment) indicated sufficient reduction (above 99%) for *C. pipiens* and *A. albopictus* IE at product concentration of 360 mL/ha in medium polluted water. According to the BPR guidance, field studies are mandatory to authorize a biocidal product for professional use however, in some cases, field studies may be efficiently substituted by lab studies. In the present case the field study could not be completed. Nevertheless, as the authorized product application is only to treat small holding water bodies, not connected to surface water or STP, a situation that may efficiently be mimicked in the lab, we deemed the data provided sufficient to demonstrate the efficacy of the product, though only for those small scale applications specified in section 2.1.4 (Authorised use). The partially completed field study was considered as supportive of the efficacy of the product.

A general activity of the BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE against mosquitoes is also supported by additional field studies provided that examined, as test species, *Culex annulirostris* and *Aedex vigilax*. As neither species is present in Europe, such studies were considered only as supporting evidences. The field study carried out on *A. vigilax* (whose natural breeding site is salt marsh water) confirms that using the product in salt water does not affect efficacy.

2.2.5.6 Occurrence of resistance and resistance management

To prevent the development of resistance it is advised to use insecticides with different mode of action as well in the pest control program. Resistance to S-methoprene has been reported for populations of *Aedes* mosquitoes in the United States (Marcombe *et al.*, 2017), in Malaysia (Lau *et al.*, 2015) and in Cyprus for populations of Culex mosquitoes (Vasquez *et al.*, 2009).
According to Marcombe *et al.* (2017), Monooxygenases (cytochrome P-450s) enzyme systems could be involved an IGR resistance. In the case of BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE it is advised to use adulticide product after a few application of the larvicide product.
To avoid the occurrence of resistance, avoid continuous use of the product and alternate products containing active substances with different mode of action (to remove resistant individuals from the population). The life cycle and characteristics of target insects should be taken into account to adapt treatments. In particular, target the most susceptible stage of the pest, timing of applications and areas to be treated. Adopt integrated pest management methods such as the combination of chemical, physical control methods and other public health measures, taking into account local specificities (climatic conditions, target species, conditions of use, etc). Levels of effectiveness on population in key areas should be monitored and the users should inform if the treatment is ineffective and report straightforward to the authorisation holder.

2.2.5.7 Known limitations

None is known.

2.2.5.8 Evaluation of the label claims

BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE has been shown to have sufficient activity to considerably reduce the number of *Aedes* and *Culex* spp. mosquitoes during the developmental stage when applied to small water-holding bodies (not connected to surface water of STP) at the concentration of 0.022 to 0.036 mL/m^2, depending on the water depth and quality of the water, with residual effect up to 10 days.

2.2.5.9 Relevant information if the product is intended to be authorised for use with other biocidal product(s)

The product is not intended to be used with other biocidal products.

2.2.6 Risk assessment for human health

2.2.6.1 Assessment of effects on Human Health

Skin corrosion and irritation

In vitro studies were not performed with the product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE.
No dermal irritation study was performed with BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE.
No human data are available on skin corrosion/irritation.

Conclusion used in Risk Assessment – Skin corrosion and irritation	
Value/conclusion	No specific skin irritation/corrosion study with the product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is available. Data waiving is acceptable. In the absence of a specific study, the skin irritation/corrosion potential of the biocidal product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE has to be estimated by considering the available data on each of the components.
Justification for the value/conclusion	No specific skin irritation/corrosion study with the product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is available. The a.s. S-methoprene is not skin irritant. Other co-formulants are not classified as corrosive or irritating to skin either.
Classification of the product according to CLP and DSD	No classification of the product according to CLP.

Data waiving	
Information requirement	Testing on the product/mixture does not need to be conducted if there are valid data available on each of the components in the mixture sufficient to allow classification of the mixture according to the rules laid down in Regulation (EC) No 1272/2008 (CLP), and synergistic effects between any of the components are not expected.
Justification	On the basis of the above mentioned reasoning, following the Guidance on information requirements (2014) and regulation 1272/2008/EC, for animal welfare reasons, the IT CA agrees that a specific skin irritation study is not required. Data are available on the active substance and other co-formulants and based on regulation 1272/2008/EC it can be concluded that no classification is necessary for skin irritation/corrosion.

Eye irritation

No *in vitro* studies are available with the product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE.
No eye irritation study was performed with BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE.
No human eye irritation data are available.

Conclusion used in Risk Assessment – Eye irritation	
Value/conclusion	No specific eye irritation/corrosion study is available. Data waiving is acceptable. In the absence of a specific study, the eye irritation/corrosion potential of the biocidal product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE has to be estimated by calculation on the basis of the available data on each of the components.
Justification for the value/conclusion	Neither the a.s. nor all the co-formulants are classified for eye irritation/corrosion. In the absence of a specific study, the eye irritation of the biocidal product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE has to be estimated by evaluating data on all the component of the b.p.
Classification of the product according to CLP and DSD	No classification of the product according to CLP.

Data waiving	
Information requirement	Testing on the product does not need to be conducted if there are valid data available on each of the components in the mixture sufficient to allow classification of the mixture according to the rules laid down in Regulation (EC) No 1272/2008 (CLP), and synergistic effects between any of the components are not expected”
Justification	The study with the product is scientifically not justified. Data are available on the active substance and other co-formulants and based on regulation 1272/2008/EC, the eye irritation of the biocidal product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE has to be estimated by calculation.

Respiratory tract irritation

No animal studies or human data are available on respiratory tract irritation.

Conclusion used in the Risk Assessment – Respiratory tract irritation	
Justification for the conclusion	There are currently no standard tests and no OECD TG available for respiratory irritation and there is no testing requirement for respiratory irritation under the Biocides Regulation. As the Guidance on information requirements (2014) stated: "the data on local dermal or ocular corrosion/irritation might contain information that is relevant for the respiratory endpoint and this should be considered……. with regard to the exposure conditions." None of the components, including the active substance, are classified as skin/eye irritants and are not expected to have the potential to cause respiratory tract irritation. The product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is not expected to be irritating to the respiratory tract. None of the components, including the active substance, are classified as skin or eye irritants and are not expected to have the potential to cause respiratory tract irritation.
Classification of the product according to CLP and DSD	No classification of the product according to CLP.

Data waiving	
Information requirement	There are currently no standard tests and no OECD TG available for respiratory irritation and there is no testing requirement for respiratory irritation under the Biocides Regulation.
Justification	Data waiving is acceptable, based on the product intrinsic properties and its uses. In the formulation of the product none of the components are classified for skin or eye irritation and are not expected to have the potential to cause respiratory tract irritation.

Skin sensitization

No skin sensitization study was performed with Biopren® 50 LML mosquito larvicide concentrate.
No human skin sensitization data are available.

Conclusion used in Risk Assessment – Skin sensitisation	
Value/conclusion	No specific skin sensitization study is available. Data waiving is acceptable. The product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is classified as a skin sensitizer.
Justification for the value/conclusion	The active substance is not sensitizing on skin. The product contains a co-formulant, which is classified as Skin Sens. 1, H317 (may cause an allergic skin reaction). Based on the concentration limits of regulation 1272/2008, BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE also requires the same classification. Other sensitizing components are not present in BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE.
Classification of the product according to CLP and DSD	The product is classified as Skin Sens. 1, H317 (may cause an allergic skin reaction) according to CLP.

Data waiving	
Information requirement	Testing on the product does not need to be conducted if there are valid data available on each of the components in the mixture sufficient to allow classification of the mixture.
Justification	The study with the product is scientifically not justified. Data are available on the active substance and other co-formulants and based on regulation 1272/2008/EC, the sensitization potential of the biocidal product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE has to be estimated by calculation.

Respiratory sensitization (ADS)

No animal respiratory sensitization study and no human respiratory sensitization data are available.

Conclusion used in Risk Assessment – Respiratory sensitisation	
Value/conclusion	No specific respiratory sensitization study is available. Data waiving is acceptable.
Justification for the value/conclusion	None of the components in BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE are classified as respiratory sensitizers. One of the co-formulant is classified as skin sensitizer. Based on the a.s. intrinsic properties and the intended uses of the biocidal product, the Applicant requested the waiving of the respiratory sensitization study and stated that the exposure of humans via inhalation it is unlikely. Moreover, the active substance is of low vapour pressure (0.623×10^{-3} Pa at 20°C).
Classification of the product according to CLP and DSD	No classification of the product according to CLP.

Data waiving	
Information requirement	No study is available. There are currently no standard tests and no OECD test guidelines available for respiratory sensitisation.
Justification	Data waiving is acceptable. No standard tests or guidelines exist for this endpoint. None of the components in BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE are classified as respiratory sensitizers, only one of the components is classified as skin sensitizer and therefore based on the concentration limits of regulation 1272/2008, also the biocidal product requires the same classification for the skin sensitization. However, based on the a.s. intrinsic properties and the intended uses of the biocidal product, the Applicant stated that the exposure of humans via inhalation it is unlikely. In the absence of a specific study, data on the active substance and other co-formulants have to be taken into account for the classification.

Acute toxicity

Acute toxicity by oral route

No acute oral toxicity study was performed with BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE.
No human acute oral toxicity data are available.

Value used in the Risk Assessment – Acute oral toxicity	
Value	No specific acute oral toxicity study on the product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is available. Data waiving is acceptable.
Justification for the selected value	The available data on the components of the b.p. shows that none of them are classified as Acute Tox. by oral route. Classification can be estimated by considering the available data on all the components of the b.p..
Classification of the product according to CLP and DSD	No classification of the product according to CLP.

Data waiving	
Information requirement	Testing on the product does not need to be conducted if there are valid data available on each of the components in the mixture sufficient to allow classification of the mixture.
Justification	The study with the product is scientifically not justified. Data are available on the active substance and other co-formulants (none of the components are classified for this endpoint) and based on regulation 1272/2008/EC, the acute oral toxicity of the biocidal product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE has to be estimated by calculation considering the information on all the components in the product.

Acute toxicity by inhalation

No acute inhalation toxicity study was performed with BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE.
No human acute inhalation toxicity data are available.

Value used in the Risk Assessment – Acute inhalation toxicity	
Value	No study is available. Data waiving is acceptable. In the absence of a specific study, the acute inhalation toxicity of the biocidal product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE has to be estimated by calculation.
Justification for the selected value	None of the components of the b.p. are classified for this endpoint. Moreover, considering that testing by the inhalation route is appropriate only if exposure of humans via inhalation is likely, taking into account: • the vapour pressure of the a.s. (> 1 x 10^{-2} Pa at 20 °C) and/or • the active substance is included in products that are powders or are applied in a manner that generates exposure to aerosols, particles or droplets of an inhalable size (MMAD <50 micrometers), data waiving for BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE can be considered acceptable.
Classification of the product according to CLP and DSD	No classification of the product according to CLP.

Data waiving	
Information requirement	Testing by the inhalation route can be waived considering both the intrinsic properties of the active substance and the co-formulants and the intended use of the product.
Justification	The study with the product is scientifically not justified. Data are available on the active substance and other co-formulants (none of the components are classified for this endpoint) and based on regulation 1272/2008/EC, the acute inhalation toxicity of the biocidal product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE has to be estimated by calculation considering the information on all the components in the product. Furthermore, the Applicant stated that an inhalation exposure is not expected, the intended use requires that large droplets are being formed during application and therefore an inhalable fraction of droplets is not expected to appear.

Acute toxicity by dermal route

No acute dermal toxicity study was performed with BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE.
No human acute dermal toxicity data are available.

Value used in the Risk Assessment – Acute dermal toxicity	
Value	No specific acute dermal toxicity study on the product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is available. Data waiving is acceptable. In the absence of a specific study, the acute dermal toxicity of the biocidal product has to be estimated by calculation. With this regard, neither the a.s. nor the co-formulants are classified for this endpoint.
Justification for the selected value	Data on each of the components in the mixture are available and sufficient to allow classification of the mixture according to the rules laid down in Regulation (EC) No 1272/2008 (CLP). The active substance has no acute toxicity via the dermal route. There are no co-formulants classified for this endpoint in the product.
Classification of the product according to CLP and DSD	No classification of the product according to CLP.

Data waiving	
Information requirement	Testing on the product does not need to be conducted if there are valid data available on each of the components in the mixture sufficient to allow classification of the mixture.
Justification	The study with the product is scientifically not justified. Data are available on the active substance and other co-formulants (none of the components are classified for this endpoint) and based on regulation 1272/2008/EC, the acute dermal toxicity of the biocidal product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE can be estimated by calculation.

Information on dermal absorption

No dermal absorption study was performed with the product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE.

Value(s) used in the Risk Assessment – Dermal absorption	
Substance	S-methoprene
Value(s)*	75%
Justification for the selected value(s)	The Applicant required the data waiving and referred to a study available from the S-methoprene dossier in which the representative product (Biopren® Pharaoh's Ant Colony Eliminator) was tested. On the basis of the results obtained in the above mentioned study, the Applicant proposed a value of 3.5 %. IT CA do not agree with this conclusion and in the following is reported all the reasoning because this value has been considered not applicable for the present formulation: - a clear comparison between the two products (test and current) has not been provided and therefore it is not possible to evaluate the real comparability of the two products also for the type of formulation; - despite the total S-methoprene pure concentration of the a.s. in the biocidal product is higher with respect to the test item, in the justification provided by the Applicant is reported that "*the microencapsulated form, ensures that S-methoprene is released continuously at a slow rate over a longer period*"; this conditions could make easier the dermal penetration of the a.s.; - the presence in the current product of high percentage of surfactants (one at 11.58%, skin sensitizer and another one at 4%) does not allow to exclude and to quantify possible enhancement in the rate of the absorbed amount of the a.s. by dermal route; - the two formulations (test and current) do not have the same sensitizing potential, based on classification. Indeed, on the basis of the presence of a sensitizer surfactant present at concentration above the concentration limits for classification, also the product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE has to be classified as skin sensitizer. Moreover, the skin sensitising potential is not taken into account during testing for dermal absorption. Regarding dermal absorption, the guidance on the BPR: Volume III Assessment & Evaluation (Parts B+C) version 2.1 February 2017 establishes the following: "The establishment of a value for dermal absorption may be performed by use of a tiered approach from a worst case to a more refined estimate". According to this, in the first tier, depending on phys. / chem. information, a default value for dermal absorption could be used. Default dermal absorption values can be calculated following the approach described in the EFSA Guidance Document for dermal absorption (EFSA, 2012). According to the EFSA guidance and considering the a.s. content (<5% w/w) a default dermal absorption value of 75% has to be used for the exposure estimation.
Data waiving	

Information requirement	No specific dermal absorption study with BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE has been performed and therefore provided. According to the guidance on the BPR: The establishment of a value for dermal absorption may be performed by use of a tiered approach from a worst case to a more refined estimate. If no experimental data are available, studies with similar formulations should be looked for or further information used that may give at least a rough estimate. But in this case strict and transparent rules should be followed as to when another formulation or product can be considered similar.
Justification	No specific dermal absorption study with BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE has been performed and therefore provided. The Applicant required the data waiving and referred to a study available from the S-methoprene dossier applied for the representative product (Biopren® Pharaoh's Ant Colony Eliminator). According to the EFSA guidance in absence of similar formulations (in terms of concentration and surfactants content) , the bridging cannot be accepted and therefore for BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE, a default dermal absorption value of 75% has to be considered on the basis of the a.s. content (<5%w/w) in the product.

Available toxicological data relating to non active substance(s) (i.e. substance(s) of concern)

There is only one substance of concern present in the product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE: **octadecanoic acid, 12-hydroxy-, polymer with .alpha.-hydro-.omega.- hydroxypoly(oxy-1,2-ethanediyl)** (CAS No. 70142-34-6, referred to in the MSDS as Kolliphor HS 15 or Solutol HS 15 – Kolliphor HS 15 is the new name, the manufacturer and identity are the same), present in a concentration >1% (for the exact concentration see confidential composition statement).

The following toxicological information is available on octadecanoic acid, 12-hydroxy-, polymer with .alpha.-hydro-.omega.-hydroxypoly(oxy-1,2-ethanediyl) (based on MSDS):

Classification: Skin Sens. 1
Hazard Statement: H317 May cause an allergic skin reaction.

Acute toxicity
Virtually nontoxic after a single ingestion.
LD50 rat (oral): > 20.600 mg/kg

Irritation
Not irritating to the skin. Not irritating to the eyes.
Skin corrosion/irritation rabbit: non-irritant (OECD Guideline 404)
Serious eye damage/irritation rabbit: non-irritant (OECD Guideline 405)

Respiratory/Skin sensitization
May cause sensitization by skin contact.
Guinea pig maximization test guinea pig: skin sensitizing (OECD Guideline 406)

Germ cell mutagenicity
The substance was not mutagenic in bacteria. No mutagenic effect was found in various tests with mammalian cell culture and mammals.

Reproductive toxicity
The results of animal studies gave no indication of a fertility impairing effect.

Developmental toxicity
In animal studies the substance did not cause malformations.

Repeated dose toxicity and Specific target organ toxicity (repeated exposure)
No adverse effects were observed after repeated exposure in animal studies.

Aspiration hazard
No data available.

Besides octadecanoic acid, 12-hydroxy-, polymer with .alpha.-hydro-.omega.-hydroxypoly(oxy-1,2-ethanediyl), no other substances of concern are present in the product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE. All other co-formulants are non-hazardous from a toxicological point of view. For the exact composition of the product, see separate confidential annex.

Available toxicological data relating to a mixture

There is only one substance of concern present in the product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE: octadecanoic acid, 12-hydroxy-, polymer with .alpha.-hydro-.omega.-hydroxypoly(oxy-1,2-ethanediyl). For the relevant details see previous point. No other substances of concern are present in the product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE. Testing on the product/mixture does not need to be conducted if there are valid data available on each of the components in the mixture sufficient to allow classification of the mixture according to the rules laid down in Regulation (EC) No 1272/2008 (CLP), and synergistic effects between any of the components are not expected.

Other

Not applicable.

2.2.6.2 Exposure assessment

Identification of main paths of human exposure towards active substance(s) and substances of concern from its use in biocidal product

Summary table: relevant paths of human exposure							
Exposure path	**Primary (direct) exposure**			**Secondary (indirect) exposure**			
	Industrial use	**Professional use**	**Non-professional use**	**Industrial use**	**Professional use**	**General public**	**Via food**
Inhalation	n.a.	yes	n.a.	n.a.	no	yes	no
Dermal	n.a.	yes	n.a.	n.a.	no	yes	no
Oral	n.a.	no	n.a.	n.a.	no	no	no

List of scenarios

Summary table: scenarios			
Scenario number	**Scenario** (e.g. mixing/ loading)	**Primary or secondary exposure Description of scenario**	**Exposed group** (e.g. professionals, non-professionals, bystanders)
1.	PHED Scenario Mixing / Loading Liquids	Primary exposure Mixing of the product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE. PPE used.	Professionals
2.	PHED Scenario Applicator, Open Cab Groundboom	Primary exposure Application of BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE, groundboom / open cab. PPE used.	Professionals
3.	PHED Scenario Groundboom / Open Cab Mixing&Loading + Application	Primary exposure Mixing and application of BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE, groundboom / open cab. PPE used.	Professionals
4.	PHED Scenario Manually pressurized handwand scenario	Primary exposure Mixing&loading and application of BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE, manually-pressurized handwand	Professionals
5.	PHED Scenario Backpack sprayer scenario	Primary exposure Mixing&loading and application of BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE, backpack sprayer	Professionals
6.	Cleaning of equipment	Primary exposure Post-application step, cleaning of spray equipment	Professionals
7.	Indirect exposure of bystander children	Secondary exposure Children aged 1-3 years old (*toddlers*)	Bystanders
8.	Indirect exposure of bystander adults	Secondary exposure	Bystanders
9.	Indirect exposure of resident children	Secondary exposure Children aged 1-3 years old (*toddlers*)	Residents
10.	Indirect exposure of resident adults	Secondary exposure	Residents

Industrial exposure

Industrial use of BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is not intended.

Professional exposure

Professional exposure refers to professional users such as Trained Professionals. In general, the trained professional user is subject to national worker protection legislation and has residual risk controlled through control measures, which may include the use of personal protection equipment if required.

The active substance S-methoprene and the product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE are manufactured and formulated in Hungary. No human health exposure scenarios have been assessed for the manufacturing of the active substance or for the formulation of the product.

Potential exposure to S-methoprene from BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE will occur through use of the product. Exposure assessment for use of this product is undertaken below. In addition, there is negligible indirect exposure to BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE expected via the environment.

Although the 'Field of use' of the product as originally intended by the applicant has been eventually revised, the following considerations and calculations related to Scenarios *[1]* to *[3]* (created for modelling the treatment of larger water bodies) are maintained in this PAR, as follows.

The application of BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is the following: the preparation has to be spread as a ground application at a dose of 220-360 mL/ha. It has a residual efficacy of 10 days and the frequency of application varies. Treatment against mosquitoes has to be repeated when 4th stage larvae appear, however for worst case calculations treatment after 3 weeks is taken into account.

S-methoprene is not volatile, evaporation of the active substance will be so small that the **inhalation exposure** is considered to be negligible. However, as a spray application the risk of inhalation exposure to S-methoprene for trained professional users during use is calculated and proved to be negligible. Similarly, for non-users, the risk of inhalation exposure to residues during or after application via the environment is considered to be negligible.

The main route of exposure is **dermal exposure** of users during loading and application, however trained professional users are expected to wear protective clothes and gloves which reduce the exposure and risk to a negligible level. After application, non-users are not likely to come into contact with BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE used in mosquito treatment. However, as a worst case, secondary exposure calculations are also included.

BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is not likely to directly reach the mouth of the trained professional users. Therefore, the risk during use is considered to be negligible. Similarly, for non-users, risk of **oral exposure** to residues during or after application is considered to be negligible.

Exposure assessments have been prepared using both the default values from the Technical Notes for Guidance (TNsG) on Human Exposure to Biocidal Products (2007), and

ECHA Guidance for Human Health Risk Assessment (2013) and US EPA PHED Surrogate Exposure Guide.

Since an appropriate harmonised model for biocides is currently not available for the foreseen use as an alternative, the US EPA Occupational Pesticide Handler Unit Exposure Reference Table is used. This model is based on a number of sources, including the Pesticide Handler Exposure Database (PHED), the Outdoor Residential Exposure Task Force (ORETF) the Agricultural Handler Exposure Task Force (AHETF), or other available registrant-submitted exposure monitoring studies.

The exposure values present in the PHED guidance in µg/lb ai are converted in mg/kg.

The trained professional user is expected to use gloves and coveralls, therefore only defaults where the worker has protective clothes and gloves were used.

The product is recommended to be used 1 time per 3 weeks. Nevertheless, as a worst-case approach, the long-term AEL value (0.076 mg/kg bw/day) is used for the risk assessment.

During the product life cycle the human exposure may occur at time of loading of the product.
Trained professional users are assumed to wear protective gloves when handling the products. Gloves are assumed to reduce the exposure of hands by 90%.

It is assumed that 100% of inhalation exposure is absorbed. For dermal absorption, the 75% from the EFSA guidance is used in the calculations. Operator body weight is assumed to be 60 kg.

Scenario [1]

Description of Scenario [1]		
PHED scenario Mixing / Loading Liquids, Single layer, Gloves Professional user, mixing and loading Outdoor use, treating mosquito breeding sites Dose: 360 mL/ha product Treated area (worst case): 50 ha PPE used		
	Parameters	Value
Tier 1	Concentration of active substance in product	5% w/w
	User body weight	60 kg
	Dermal absorption of S-methoprene	75%
	Inhalation absorption of S-methoprene	100%
	Default dermal exposure value from PHED guidance	0.0829 mg a.i./kg a.i.
	Default inhalation exposure value from PHED guidance	0.00048 mg a.i./kg a.i.
Tier 2	n.a.	
Tier 3	n.a.	

Scenario [2]

Description of Scenario [2]		
PHED scenario Applicator, Open cab, Groundboom, Single layer, Gloves Professional user Outdoor use, treating mosquito breeding sites Dose: 360 mL/ha product Treated area (worst case): 50 ha PPE used		
	Parameters	Value
Tier 1	Concentration of active substance in product	5% w/w
	User body weight	60 kg
	Dermal absorption of S-methoprene	75%
	Inhalation absorption of S-methoprene	100%
	Default dermal exposure value from PHED guidance	0.0355 mg a.i./kg a.i.
	Default inhalation exposure value from PHED guidance	0.00075 mg a.i./kg a.i.
Tier 2	n.a.	
Tier 3	n.a.	

Scenario [3]

Description of Scenario [3]		
PHED Groundboom / Open cab, Single layer, Gloves, mixing&loading and application combined scenario Professional user Outdoor use, treating mosquito breeding sites Dose: 360 mL/ha product Treated area (worst case): 50 ha PPE used		
	Parameters	Value
Tier 1	Concentration of active substance in product	5% w/w
	User body weight	60 kg
	Dermal absorption of S-methoprene	75%
	Inhalation absorption of S-methoprene	100%
	Default dermal exposure value from PHED guidance	0.118 mg a.i./kg a.i.
	Default inhalation exposure value from PHED guidance	0.00123 mg a.i./kg a.i.
Tier 2	n.a.	
Tier 3	n.a.	

Owing to the revision of the 'Field of use', new exposure calculations were performed. Scenarios *[4]* to *[5]* were created for modelling the use of BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE for the treatment of small scale water holding features/aquatic areas not connected to natural aquatic compartment or the STP.

The following approach is presented. An appropriate harmonised model for biocides is currently not available for the foreseen use, thus another relevant scenario has to be selected.

The presented model is based on the guidance of the US EPA Occupational Pesticide Handler Unit Exposure Surrogate Reference Table (June 2018). This table provides pesticide exposure information for risk assessment based on exposure scenarios, exposure routes and applicable personal protective equipment. It presents the current recommended unit exposures for standard EPA occupational pesticide handler exposure scenarios. These values are derived from a number of sources, including the Pesticide Handler Exposure Database (PHED), the Outdoor Residential Exposure Task Force (ORETF) the Agricultural Handler Exposure Task Force (AHETF), or other available registrant-submitted exposure monitoring studies. The guide contains several specific use scenarios for broadcast spraying treatments, also for aquatic areas. The implemented values thus have a solid, well-founded background that is valid and relevant for the intended use.

The product may be applied by different types of knapsack or hand-held sprayers. Several scenarios are presented in this guide which could be relevant for BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE. These scenarios include "Mixer / Loader / Applicator, Manually-pressurized handwand"; "Mixer / Loader / Applicator, Backpack Sprayer" and "Mixer / Loader / Applicator, Mechanically-pressurized Handgun Sprayer". A common aspect in these scenarios is that they all include the task for mixing&loading as well as the application phase.

From these scenarios the exposure scenario "Mixer / Loader / Applicator, Manually-pressurized handwand" is the one that has the highest set exposure values **without gloves** and the "Mixer / Loader / Applicator, Backpack Sprayer" is the one that has the highest set exposure value **with gloves**. Calculations are presented for both models to provide the best possible overview and to represent a worst case approach which covers all application types. For the activity type within the scenarios the use for treatment in aquatic areas was selected.

As a Tier 1 approach, the values without protective gloves or respirator are presented. Tier 2 refinement is presented with gloves and without respirator. It is expected that the professional user will always wear gloves during use.

For BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE, no dermal absorption study was performed. In the Tier 1 calculations thus the EFSA default of 75% is implemented. Since the risk is acceptable even with this value, no further refinement is proposed.

Scenario [4]

Description of Scenario [4]		
US EPA Occupational Pesticide Handler Unit Exposure Surrogate Reference Table (June 2018): **Mixer / Loader / Applicator, Manually-pressurized Handwand; treatment of aquatic areas** Professional user Outdoor use, treating mosquito breeding sites in areas not connected to surface water or STP		
	Parameters	Value
Tier 1	Concentration of active substance in product	5% w/w
	Dose	360 mL/ha product
	Treated area (worst case):	4 ha
	User body weight	60 kg
	Dermal absorption of S-methoprene	No study available. 75% default EFSA value as Tier 1 approach
	Inhalation absorption of S-methoprene	100%
	Default dermal exposure value from guidance (single layer clothes, no gloves)	100000 µg a.i./lb a.i. = 220.46 mg a.i./kg a.i.
	Default inhalation exposure value from guidance (no respirator)	30 µg a.i./lb a.i. = 0.066 mg a.i./kg a.i.
Tier 2 (gloves)	Default dermal exposure value from guidance (single layer clothes, no gloves)	430 µg a.i./lb a.i. = 0.948 mg a.i./kg a.i.
	Default inhalation exposure value from guidance (no respirator)	same as in Tier 1
Tier 3	n.a.	

Scenario [5]

Description of Scenario [5]		
US EPA Occupational Pesticide Handler Unit Exposure Surrogate Reference Table (June 2018): **Mixer / Loader / Applicator, Backpack sprayer; general broadcast, treatment of aquatic areas** Professional user Outdoor use, treating mosquito breeding sites in areas not connected to surface water or STP		
	Parameters	Value
Tier 1	Concentration of active substance in product	5% w/w
	Dose	360 mL/ha product
	Treated area (worst case):	4 ha
	User body weight	60 kg
	Dermal absorption of S-methoprene	No study available. 75% default EFSA value as Tier 1 approach
	Inhalation absorption of S-methoprene	100%
	Default dermal exposure value from guidance (single layer clothes, no gloves)	8260 µg a.i./lb a.i. = 18.21 mg a.i./kg a.i.
	Default inhalation exposure value from guidance (no respirator)	2.58 µg a.i./lb a.i. = 0.0057 mg a.i./kg a.i.
Tier 2 (gloves)	Default dermal exposure value from guidance (single layer clothes, with gloves)	8260 µg a.i./lb a.i. = 18.21 mg a.i./kg a.i. (the same value is specified within the guide as for Tier1)
	Default inhalation exposure value from guidance (no respirator)	same as in Tier 1
Tier 3	n.a.	

Calculations for Scenarios [1-5]

Summary table: estimated exposure from professional uses					
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake**	**Estimated dermal uptake**	**Estimated oral uptake**	**Estimated total uptake**
Scenario [1]	2/with PPE	0.000007 mg/kg bw/day	0.000956 mg/kg bw/day	n.a.	0.000963 mg/kg bw/day
Scenario [2]	2/with PPE	0.000012 mg/kg bw/day	0.00041 mg/kg bw/day	n.a.	0.00042 mg/kg bw/day
Scenario [3]	2/with PPE	0.000019 mg/kg bw/day	0.00137 mg/kg bw/day	n.a.	0.00138 mg/kg bw/day
Scenario [4]	1/no gloves	8.135×10^{-5} mg/kg bw/day	0.2034 mg/kg bw/day	n.a.	0.2035 mg/kg bw/day
	2/with gloves	8.135×10^{-5} mg/kg bw/day	0.0008745 mg/kg bw/day	n.a.	0.0009558 mg/kg bw/day
Scenario [5]	1/no gloves	6.996×10^{-6} mg/kg bw/day	0.0168 mg/kg bw/day	n.a.	0.0168 mg/kg bw/day
	2/with gloves	6.996×10^{-6} mg/kg bw/day	0.0168 mg/kg bw/day	n.a.	0.0168 mg/kg bw/day

See the calculation tables in Annex 3.2.

Further information and considerations on scenarios [1-5]

With regard to the post-application phase, compared to the mixing and loading performed with the concentrate and the application task, the cleaning of the equipment which contains only the residues from the dilution remaining after application can be considered as negligible. However, an assessment is reported (p. 60 of this document).

For the assessment of local effects, see section on risk characterisation for human health – local effects (p. 78 of this document).

Combined scenarios

Separate mixing & loading and application scenarios exist in the PHED guidance, which are presented in Scenarios 1 and 2, respectively. Scenario 3 corresponds to the added values of the mixing & loading and application phases presented in Scenarios 1 and 2. This could be considered as a combined scenario.

As the selected scenario of the US EPA Occupational Pesticide Handler Unit Exposure Surrogate Reference Table already incorporates the mixing, loading and application steps, the presented values for Scenarios 4 and 5 already show the combined exposure to the product.

Moreover, combined exposure is assumed for Scenarios 3, 4 and 5 with Scenario 6, as described as follows.

An additional assessment of post-application exposure by the BEAT model was added to the PAR, following the request of a commenting cMS in the MRP process.

The BEAT model contains one scenario for the cleaning of the spray equipment. This scenario is based on the cleaning of spray equipment performed in car body repair shops. According to this scenario, "usually, the spray gun is cleaned with water and later the parts that still remain dirty are rubbed with paper, rag or brush, using water or any cleaning solution." This scenario comprised several different activities. The main body regions exposed during the cleaning of the spray gun are the hands, though there might be splashes to other parts of the body".

The indicative (75th percentile) exposure values are 19.28 µL/min for body exposure and 35.87 µL/min for hand exposure. This scenario is also discussed in Recommendation no. 4 of the BPC Ad hoc Working Group on Human Exposure (HEAdhoc) where the BEAT model was compared to the RISKOFDERM model and the former one was found more relevant for the task of cleaning of spray equipment. A default value of 20 min was adopted in this recommendation as the duration for the cleaning task. It should be noted that this may be considered as an absolute worst case for the current product as the BEAT model and HEAdhoc Recommendation 4 concerns the cleaning of spray equipment in antifouling use (paint spray equipment). The working solution of BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is not a viscous solution, it may be cleaned very easily; thus the total time required for the cleaning of the equipment should not take more than 10 minutes. Nevertheless, the default value suggested in the Recommendation was used in the calculations as an absolute worst case, which may be considered as an overestimation of actual expected exposure.

In case a duration of 20 minutes is applied, the exposure will be 19.28 x 20 = 385.6 µL/day for body exposure and 35.87 x 20 = 717.4 µL/day for hand exposure (cleaning is only performed once at the end of the day or after the last treatment). The overall exposure is to 1103 µL dilution/day according to the scenario. When the dilution is prepared, as a worst case 36 mL concentrate is added to prepare 5L of solution. With an active substance content of 5% w/w in the concentrate and a product density of 1.025, 1103 µL of solution will contain 0.407 mg S-methoprene.

When the worst-case default EFSA value of 75% dermal absorption and a body weight of 60 kg are applied, the **systemic exposure is 0.0051 mg/kg bw/day**.

The values presented above represent **Tier 1** values where no PPE is used. However **Tier 2** calculations have already been performed in the human health exposure and risk assessment and it is evident that the professional user will perform the cleaning of the equipment with the use of protective gloves/coveralls. Therefore Tier 2 results are also calculated:

According to the Biocides Human Health Exposure Methodology the default protection factor by protective gloves for challenges by a liquid is 90%. For body exposure a protection factor of 80% is applied for the use of coated coveralls where a challenge is light, which is relevant in this case. As a result, the body exposure will be reduced to 77.12 µL/day and the hand exposure will be 71.74 µL/day when PPE is used (task duration is kept as 20 min). The overall exposure is thus to 148.86 µL dilution/day. This amount of dilution contains **0.0549 mg/kg bw/day S-methoprene.**

With the worst-case dermal absorption of 75% and a default body weight of 60 kg, the **internal systemic exposure in Tier 2 is 0.00069 mg/kg bw/day**.
Inhalation and oral exposure will be negligible for the cleaning task.

To summarize, the following input values were used:

Scenario [6]

Description of Scenario [6]: Post-application step, cleaning of spray equipment – Estimated on the basis of BEAT / HEAdhoc Recommendation no. 4.		
Professional user cleaning the spray equipment which contains any remaining dilution. This step is performed once daily at the end of the working day. 36 ml product is diluted to 5 L working solution. Active substance content in concentrate: 5%, density: 1.025. Dilution density may be considered as 1.		
	Parameters	Value
Tier 1 (no PPE)	body exposure (BEAT/HEAdhoc 4)	19.28 µL/min
	hand exposure (BEAT/HEAdhoc 4)	35.87 µL/min
	duration of cleaning (HEAdhoc 4)	20 min
	dermal absorption (EFSA)	75%
	user body weight (Biocides Human Health Exposure Methodology)	60 kg
Tier 2 (with PPE – gloves and coated coverall)	Glove protection factor for challenges by liquid (Biocides Human Health Exposure Methodology)	90%
	Coated coverall protection factor for light challenge (Biocides Human Health Exposure Methodology)	80%

When combined exposure is assessed, the exposure values calculated for the cleaning of spraying equipment (0.0051 mg/kg bw/day and 0.00069 mg/kg bw/day) may be used for Tier 1 and Tier 2, respectively, to be added to the exposure from the mixing&loading and application phases.
The following are the scenarios for which combined exposure should be assessed:

Scenario [1]: mixing & loading step
Scenario [2]: application
Scenario [3]: a combination of the two previous scenarios and, thus, already a combined scenario
Scenario [4]: manually pressurized handwand scenario
Scenario [5]: backpack sprayer scenario
Scenario [6]: cleaning of equipment

For the calculation of a combined exposure with cleaning, only Scenarios [3], [4] and [5] are relevant (since Scenario [3] = Scenarios [1]+[2]).
The combined exposure values are reported in the following table.

Summary table: estimated combined exposure from professional uses					
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake**	**Estimated dermal uptake**	**Estimated oral uptake**	**Estimated total uptake**
Scenarios [3] + [6]	2/with PPE	0.000019 mg/kg bw/day	0.00137 + 0.00069 = 0.00206 mg/kg bw/day	n.a.	0.00208 mg/kg bw/day
Scenarios [4] + [6]	1/no PPE	8.135×10^{-5} mg/kg bw/day	0.2034 + 0.0051 = 0.2085 mg/kg bw/day	n.a.	0.2086 mg/kg bw/day
	2/with PPE	8.135×10^{-5} mg/kg bw/day	0.0008745 + 0.00069 = 0.00156 mg/kg bw/day	n.a.	0.00165 mg/kg bw/day
Scenarios [5] + [6]	1/no PPE	6.996×10^{-6} mg/kg bw/day	0.0168 + 0.0051 = 0.0219 mg/kg bw/day	n.a.	0.0219 mg/kg bw/day
	2/with PPE	6.996×10^{-6} mg/kg bw/day	0.0168 + 0.00069 = 0.0175 mg/kg bw/day	n.a.	0.0175 mg/kg bw/day

Non-professional exposure

Non-professional use of BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is not intended.

Exposure of the general public

The product is eventually authorized to treat small scale water holding features/aquatic areas which are not used for drinking water storage, irrigation, bathing or for keeping (ornamental) fish, and which may be suitable, temporarily or permanently, for the breeding of mosquito larvae.
The treatment of swimming pools is not intended. Indeed, mosquitoes are not expected to breed in swimming pools, which are treated with active chlorine or other disinfectants. At any rate, though the water holding features intended for treatment are usually not suitable for swimming purposes, a sentence is added to the label that swimming in treated water is not allowed.
With regard to 'dipping of arms and hands', the need for an additional risk assessment is not justified, in consideration of the revised 'Field of use'. In any case, the a.s. concentration in the treated water would be extremely low due to dilution (worst-case concentration: 3.708×10^{-3} µg/L). Dipping of arms and hands into treated water would only occur occasionally and only for a short time, further the contact surface would be very limited. Therefore, it can be anticipated that the risk from such a scenario would be negligible.

Indirect exposure can occur in case of drifting and bystanders or general public entering the treated, drift zone.
For the calculation of exposure the EFSA guidance (2014)* on exposure of operators, workers, bystanders and residence were used. The aim of exposure assessment in this context is to consider realistic and high exposure scenarios arising from the proposed Good Agricultural Practice for non-dietary systemic exposure that can be compared with appropriate toxicological reference values. As the EFSA guidance uses different defaults and parameters than the PAR templates, see results presented below in separate tables.

*: GUIDANCE OF EFSA: Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. EFSA Journal 2014;12(10):3874, (approved on 17 October 2014)
Calculator: Latest version: 30 Mar 2015 - Version produced to support guidance document published 23/10/2014

Definitions of exposed groups:

- **Bystanders are:** persons who could be located within or directly adjacent to the area where PPP application or treatment is in process or has recently been completed; whose presence is quite incidental and unrelated to work involving PPPs, but whose position might lead them to be exposed during a short period of time (acute exposure); and who take no action to avoid or control exposure.

- **Residents are:** persons who live, work or attend school or any other institution adjacent to an area that is or has been treated with a PPP; whose presence is quite incidental and unrelated to work involving PPPs but whose position might lead them to be exposed; who take no action to avoid or control exposure; and who might be in the location for up to 24 hours per day (longer term exposure).

Default values:

Bodyweight:
In all calculations, it should be assumed, as a default, that adults have a body weight (bw) of 60 kg and that default body weight for children less than three years old (*toddlers*) is 10 kg.

Exposure durations:
Resident and bystander (for acutely toxic active substances (a.s.) only): 2 hours (default for resident on lawn; dermal, surface deposits), 0.25 hours (dermal, entry into treated crops) and 24 hours (inhalation from vapour).

The following defaults and inputs were used:

Substance name	S-methoprene	
Product name	Biopren 50 LML mosquito larvicide concentrate	

Reference value non-acutely toxic active substance (RVNAS)	0.076	mg/kg bw/day
Reference value acutely toxic active substance (RVAAS)	0.35	mg/kg bw/day

Crop type	Cereals	
Substance properties		
Formulation type	soluble concentrates, emulsifiable concentrate, etc.	
Minimum volume water for application (liquids)	5	L/ha
Maximum application rate of active substance	**0.01845**	**kg a.s. /ha**
50% Dissipation Time DT50	30	days
Initial Dislodgeable Foliar Residue	3	µg/cm^2 of foliage/kg a.s. applied/ha
Dermal absorption of product	75%	
Dermal absorption of in-use dilution	75%	
Oral absorption of active substance	35.00%	
Inhalation absorption of active substance	100.00%	
Vapour pressure of active substance	low volatile substances having a vapour pressure of <5*10^{-3}Pa	

Scenario		
Indoor or Outdoor application	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Buffer strip	2-3	m
Number of applications	8	
Interval between multiple applications	21	days
Season (upward spraying orchards only)	not relevant	

Bystanders:

In this section the exposure of persons were calculated who could be located within or directly adjacent to the area where PPP application or treatment is in process or has recently been completed. These persons typically exposed during a short period of time (acute exposure) and take no action to avoid or control exposure.

Defaults and parameters used:

Crop type	Cereals	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Application rate of the product	0.01845	kg a.s./ha
Buffer strip	2-3	m
Concentration of active substance (in-use dilution for liquid applications)	3.69	g a.s./l
Dermal absorption of product	75.00%	
Dermal absorption of in-use dilution	75.00%	
Oral absorption	35.00%	
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.05535	µg a.s./cm^2
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa
Concentration in air	0.001	mg/m^3
Bystander dermal spray drift exposure - adult	1.21	ml spray dilution/person
Bystander dermal spray drift exposure - child	0.74	ml spray dilution/person
Bystander inhal. spray drift exposure - adult	0.00050	ml spray dilution/person
Bystander inhal. spray drift exposure - child	0.00112	ml spray dilution/person
Exposure duration	2	hours
Exposure duration entry into treated crops	0.25	hours
Light clothing adjustment factor	18.0%	
Breathing rate adult	0.23	m^3/kg bw/day
Breathing rate child (1-3 years old)	1.07	m^3/kg bw/day
Drift percentage on surface (90th percentile)	8.50%	
Turf transferable residues percentage	5.00%	
Transfer coeff. of surface deposits-adult	14500	cm^2/hour
Transfer coeff. of surface deposits-child (1-3 years old)	5200	cm^2/hour
Saliva extraction percentage	50.00%	
Surface area of hands mouthed	20	cm^2

Frequency of hand to mouth activity	20	events/hour
Ingestion rate for mouthing of grass per day	25	cm^2
Dislodgeable residues percentage transferability for object to mouth	20.00%	
Transfer coefficient for entry into treated crops - adult	7500	cm^2/h
Transfer coefficient for entry into treated crops - child	2250	cm^2/h

Results:

Results of exposure by spray drift, vapour and surface deposits.

Total

1-3 years old child (*toddler*)

	Spray drift	Vapour	Surface deposits
Total systemic exposure (mg a.s./day)	**1.6834518**	**0.0107000**	**0.0159314**
Total systemic exposure per kg body weight (mg/kg bw/day)	**0.1683452**	**0.0010700**	**0.0015931**
% of RVAAS	**48.10%**	**0.31%**	**0.46%**

Adult

	Spray drift	Vapour	Surface deposits
Total systemic exposure (mg a.s./day)	**2.7477585**	**0.0138000**	**0.0434492**
Total systemic exposure per kg body weight (mg/kg bw/day)	**0.0457960**	**0.0002300**	**0.0007242**
% of RVAAS	**13.08%**	**0.07%**	**0.21%**

Residents:

In this section, the exposure of persons was calculated who live, work or attend school or any other institution adjacent to an area that is or has been treated with a PPP.
These persons typically take no action to avoid or control exposure; and who might be in the location for up to 24 hours per day (longer term exposure).

Defaults and parameters used:

Croptype	Cereals	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Buffer strip	2-3	m
Application rate of the product	0.01845	kg a.s./ha
Concentration of active substance (in-use dilution for liquid applications)	3.69	g a.s./l
Dermal absorption of product	75.00%	
Dermal absorption of in-use dilution	75.00%	
Oral absorption	35.00%	
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.05535	µg a.s./cm^2
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa
Concentration in air	0.001	mg/m^3
Resident dermal spray drift exposure 75th percentile - adult	0.47	ml spray dilution/person
Resident dermal spray drift exposure 75th percentile - child	0.327	ml spray dilution/person
Resident inhal. spray drift exposure 75th percentile - adult	0.00010	ml spray dilution/person
Resident inhal. spray drift exposure 75th percentile - child	0.00022	ml spray dilution/person
Resident dermal spray drift exposure mean - adult	0.22318	ml spray dilution/person
Resident dermal spray drift exposure mean - child	0.18	ml spray dilution/person
Resident inhal. spray drift exposure mean - adult	0.00009	ml spray dilution/person
Resident inhal. spray drift exposure mean - child	0.00017	ml spray dilution/person
Exposure duration dermal	2	hours
Exposure duration inhalation	24	hours
Exposure duration entry into treated crops	0.25	hours
Light clothing adjustment factor	18.0%	
Breathing rate adult	0.23	m^3/day/kg
Breathing rate child (1-3 years old)	1.07	m^3/day/kg
Drift percentage on surface (75th percentile)	5.60%	
Drift percentage on surface (mean)	4.10%	
Turf transferable residues percentage	5.00%	
Transfer coeff. of surface deposits-adult	7300	cm^2/hour
Transfer coeff. of surface deposits-child (1-3 years old)	2600	cm^2/hour

Saliva extraction percentage	50.00%	
Surface area of hands mouthed	20	cm^2
Frequency of hand to mouth activity	9.5	events/hour
Ingestion rate for mouthing of grass per day	25	cm^2
Dislodgeable residues percentage transferability for object to mouth	20.00%	
Transfer coefficient for entry into treated crops (75th percentile) - adult	7500	cm^2/h
Transfer coefficient for entry into treated crops (75th percentile) - child	2250	cm^2/h
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm^2/h
Transfer coefficient for entry into treated crops (mean) - child	1794	cm^2/h

Results:

Results of exposure by spray drift, vapour and surface deposits.

Total

1-3 years old child (*toddler*)

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)
Total systemic exposure (mg a.s./day)	**0.7428893**	**0.0107000**	**0.0052664**
Total systemic exposure per kg body weight (mg/kg bw/day)	**0.0742889**	**0.0010700**	**0.0005266**
% of RVNAS	**21.23%**	**0.31%**	**0.15%**

Adult

	Spray drift	Vapour	Surface deposits
Total systemic exposure (mg a.s./day)	**1.0669635**	**0.0138000**	**0.0144114**
Total systemic exposure per kg body weight (mg/kg bw/day)	**0.0177827**	**0.0002300**	**0.0002402**
% of RVNAS	**5.08%**	**0.07%**	**0.07%**

Combined scenarios

Combined secondary exposure to BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is not considered relevant. See detailed tables above.

Monitoring data

No monitoring data are available with BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE.

Dietary exposure

Dietary exposure to BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is not considered to be relevant, thus no calculations have been performed.

List of scenarios

Not considered to be relevant for BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE.

Information of non-biocidal use of the active substance

Not considered relevant for BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE. No non-biocidal use is intended.

Estimating Livestock Exposure to Active Substances used in Biocidal Products

Not considered relevant for BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE.

Estimating transfer of biocidal active substances into foods as a result of professional and/or industrial application(s)

Not considered relevant for BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE.

Estimating transfer of biocidal active substances into foods as a result of non-professional use

Not considered relevant for BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE.

Exposure associated with production, formulation and disposal of the biocidal product

The active substance, S-methoprene and the product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE are manufactured and formulated in Hungary. No human health exposure scenarios have been assessed for the manufacturing of the active substance or for the formulation of the product.

The active substance S-methoprene is manufactured in a closed system which is described in the confidential annex of the dossier supporting inclusion decision of S-methoprene. Full PPE is required (Gloves, coverall, face-shield and respirator) during filling and maintenance. No cleaning of the apparatus occurs since only S-methoprene is produced in the system. The only operator contact with the active ingredient is during sampling for quality.

Exposure during formulation of the product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is expected to be minimal due to operating in a closed system. Measurement and mixing of components is automated and controlled by computer. During the production every worker must wear protective glasses, plastic gloves, mask and overall. Therefore, no hazard identified during manufacturing, and no risk assessment is needed.

Aggregated exposure

Aggregated exposure is not considered relevant for BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE.

Summary of exposure assessment

Scenarios and values to be used in risk assessment			
Scenario number	**Exposed group (e.g. professionals, non-professionals, bystanders)**	**Tier/PPE**	**Estimated total uptake**
1.	Professionals	2/with PPE	0.000963 mg/kg bw/day
2.	Professionals	2/with PPE	0.00042 mg/kg bw/day
3.	Professionals	2/with PPE	0.00138 mg/kg bw/day combined 3. + 6.: 0.00208 mg/kg bw/day
4.	Professionals	1/no gloves	0.2035 mg/kg bw/day combined 4. + 6.: 0. 2086 mg/kg bw/day
		2/with gloves	0.0009558 mg/kg bw/day combined 4. + 6.: 0.00165 mg/kg bw/day
5.	Professionals	1/no gloves	0.0168 mg/kg bw/day combined 5. + 6.: 0.0219 mg/kg bw/day
		2/with gloves	0.0168 mg/kg bw/day combined 5. + 6.: 0.0175 mg/kg bw/day
6.	Professionals	1/no gloves	0.0051 mg/kg bw/day
		2/with gloves	0.00069 mg/kg bw/day
7.	Bystander children (1-3 years old, *toddlers)*	1/no PPE	0.17 mg/kg bw/day
8.	Bystander adults	1/no PPE	0.047 mg/kg bw/day
9.	Resident children (1-3 years old, *toddler*)	1/no PPE	0.076 mg/kg bw/day
10.	Resident adults	1/no PPE	0.018 mg/kg bw/day

2.2.6.3 Risk characterisation for human health

Reference values to be used in Risk Characterisation

Reference	Study	NOAEL (LOAEL)	AF[1]	Correction for oral absorption	Value
AELshort-term	Rabbit developmental study	100 mg/kg bw/day	100	oral absorption: 35%	0.35 mg/kg bw/day
AELmedium-term	90-day dog study	100 mg/kg bw/day	100	oral absorption: 35%	0.35 mg/g bw/day
AELlong-term	2-year rat study	21.7 mg/kg bw /day	100	oral absorption: 35%	0.076 mg/g bw/day
ARfD	n.a.	n.a.	n.a.	n.a.	n.a.
ADI	n.a.	n.a.	n.a.	n.a.	n.a.

[1] Background and reason for assessment factor: AF 10 for interspecies differences (for toxicokinetic differences multiplied by the toxicodynamic differences) and AF 10 for intraspecies differences (covers the most sensitive individual; for toxicokinetic differences multiplied by the toxicodynamic differences)

Maximum residue limits or equivalent

In the Inclusion Directive of S-methoprene PT18 (in force on 1-9-2015), it is described that 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 of the European Parliament and of the Council or Regulation (EC) No 396/2005 of the European Parliament and of the Council shall be verified, and any appropriate risk mitigation measures shall be taken to ensure that the applicable MRLs are not exceeded.
As there is no accepted final guidance on the Biocide MRL establishment procedure, MRLs (due to biocide use) from other Regulations should be considered. As S-methoprene is not approved under PPP regulation, default MRL exists and should not be exceeded.

Based on the intended use of BIOPREN® MOSQUITO LARVICIDE GRANULE, it can be concluded that the use of the product will not result in the appearance of residues in food or feed. The product is not used in the vicinity of food and feed, food processing or on any food contact material. The water treated with the product cannot be used for watering of plants. Therefore, no MRL exceedance is expected.

Specific reference value for groundwater

As specific reference value for groundwater, we accept the permissible concentration laid down by Directive 98/83/EC.

Risk for industrial users

Industrial use of BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is not intended.

Risk for professional users

Systemic effects

Task/ Scenario	Tier	Systemic NOAEL mg/kg bw/d	AEL mg/kg bw/d	Estimated uptake mg/kg bw/d	Estimated uptake/ AEL (%)	Acceptable (yes/no)
PHED scenario mixing&loading/ [1]	2	100	0.076	0.000963	1.27%	**yes**
PHED scenario application/ [2]	2	100	0.076	0.00042	0.55%	**yes**
PHED scenario mixing&loading +application/ [3]	2	100	0.076	0.00138	1.82%	**yes**
Mixer/ Loader/ Applicator, Manually-pressurized Handwand; treatment of aquatic areas/ [4]	1	100	0.076	0.2035 mg/kg bw/day	267.7%	**no**
Mixer/ Loader/ Applicator, Manually-pressurized Handwand; treatment of aquatic areas/ [4]	2	100	0.076	0.000956 mg/kg bw/day	1.26%	**yes**
Mixer/ Loader/ Applicator, Backpack sprayer; treatment of aquatic areas/ [5]	1	100	0.076	0.0168 mg/kg bw/day	22.11	**yes**
Mixer/ Loader/ Applicator, Backpack sprayer; treatment of aquatic areas/ [5]	2	100	0.076	0.0168 mg/kg bw/day	22.11	**yes**

In Tier 1 without the use of gloves, one scenario shows an unacceptable risk whereas the other ones are acceptable even without PPE. Trained professional users will never apply the product without gloves; therefore the Tier 1 estimation will not be relevant during actual use. When gloves are worn, the risk is acceptable for all scenarios. It should also be considered that the calculations were based on the absolute worst case EFSA dermal absorption value (75%) which evidently overestimates the absorption and thus the calculated risk is also a high overestimation of actual values. Nevertheless, the risk is shown to be acceptable under use conditions even with these parameters.

Combined scenarios

Separate mixing & loading and application scenarios exist in the PHED guidance, which are presented in Scenarios 1 and 2, respectively. Scenario 3 corresponds to the added values of

the mixing & loading and application phases presented in Scenarios 1 and 2. This could be considered as a combined scenario.
As the selected scenario of the US EPA Occupational Pesticide Handler Unit Exposure Surrogate Reference Table already incorporates the mixing, loading and application steps, the presented values for Scenarios 4 and 5 already show the combined exposure to the product.

Moreover, combined exposure is assumed for Scenarios 3, 4 and 5 with Scenario 6:

Task/ Scenario	**Tier**	**Systemic NOAEL mg/kg bw/d**	**AEL mg/kg bw/d**	**Estimated uptake mg/kg bw/d**	**Estimated uptake/ AEL (%)**	**Acceptable (yes/no)**
Scenarios [3] + [6]	2/with PPE	100	0.076	0.00208 mg/kg bw/day	2.74	**yes**
Scenarios [4] + [6]	1/no PPE	100	0.076	0.2086 mg/kg bw/day	274.46	**no**
	2/with PPE	100	0.076	0.00165 mg/kg bw/day	2.16	**yes**
Scenarios [5] + [6]	1/no PPE	100	0.076	0.0219 mg/kg bw/day	28.80	**yes**
	2/with PPE	100	0.076	0.0175 mg/kg bw/day	23.01	**yes**

As remarked above, in Tier 1 without the use of gloves, Scenarios [4] + [6] show an unacceptable risk. However, trained professional users will never apply the product without gloves, therefore the Tier 1 estimation will not be relevant during actual use.

In conclusion, **the exposure as a result of a cleaning step does not impact on the outcome of the HH Risk Assessment: the addition of a cleaning step to the previous calculations still results in acceptable risks.**

Local effects

There is a co-formulant in the product classified as Skin sens. 1: octadecanoic acid, 12-hydroxy-, polymer with .alpha.-hydro-.omega.- hydroxypoly(oxy-1,2-ethanediyl), CAS No. 70142-34-6 (referred to in the MSDS as Kolliphor HS 15 or Solutol HS 15 – Kolliphor HS 15 is the new name, the manufacturer and identity are the same), which is present in a concentration >1%. Based on the classification and concentration of this component, the product also has to be classified as Skin Sens. 1, H317 - May cause an allergic skin reaction. Thus, local effects of the product also have to be discussed.

The ECHA guidance suggests a qualitative approach for local sensitizing effects. For this assessment, the following elements are considered:

No skin sensitization studies are available with the product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE.

The active substance S-methoprene does not produce local effects, neither after single nor repeated exposure. However, as stated above, one co-formulant is present in the product which is classified as Skin Sens. 1 and is present at > 1% w/w (namely at 11.58% w/w). Due to this co-formulant, the product is classified as Skin Sens. 1 (H317) and thus a risk characterisation for local effects is relevant.

The trained professional user only encounters the concentrate when filling the spraying device. If 360 mL concentrate is used, it contains 360 mL x 1.025 g/mL x 11.58% w/w = 42.73 g of the co-formulant which is Soc. In 5 litre (approx. 5000 g) working solution, it means that it will be present at 42.73 g x 100 / 5000 g = 0.85% w/w. At this concentration, the dilution is not expected to be a sensitizer. Based on the guidance on the BPR Volume III Human Health - Assessment & Evaluation (Parts B+C), local effects that need to be considered for risk characterisation include sensitizing effects that lead to classification with H334 or H317. Consequently, local assessment is relevant for the mixing & loading step.

A qualitative assessment is presented: during the loading step, the user pours the concentrate into the spraying equipment, while care should be taken to prevent any splashes. Nevertheless, the use of protective gloves and coveralls is mandatory and can be expected from trained professional users which will prevent the product from reaching the skin of the person performing the application. Gloves/coveralls should also be used during the application of the product which prevents any contact with the dilution as well, thus eliminating any local risks.

Hazard:
Hazard Category: medium
[NOTE by refMS-IT: according to the applicant, a skin sensitization study has been performed recently with Biopren 50 LML mosquito larvicide concentrate, which has shown that the product is a weak skin sensitizer. However, since it was not part of the dossier nor submitted at some point of the evaluation at a later stage, the study has never been evaluated by the refMS-IT]
Effects in terms of C&L: Skin sens.1, H317
Additional relevant hazard information: sensitising property due to one co-formulant present in the product

Exposure:
PT: 18

Who is exposed: Trained professional users
Tasks, uses, processes: Mixing & loading step – filling the spraying device
Potential exposure route: splashes to skin
Frequency and duration of potential exposure: Low frequency (max. 1/day), duration: few minutes.
Potential degree of exposure: please see detailed exposure calculation results in PAR section 2.2.6.2, Scenario 1.
Relevant RMM & PPE: labelling for skin sensitization, instructions for use, packaging reducing risk for exposure by splashes, use of appropriate gloves is recommended for loading, washing of hands after use.

Risk:
Conclusion on risk: Acceptable (appropriate RMM, PPE recommended, no significant exposure expected, trained professionals following instructions for use).

Conclusion
It is assumed that the trained professional user is wearing protective gloves and coveralls in the above scenarios.
From the above risk characterization, it can be concluded that the BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE has a negligible human risk based on the evaluated scenarios.

Risk for non-professional users

Non-professional use of BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is not intended.

Risk for the general public

Systemic effects

Task/ Scenario	Tier	Systemic NOAEL mg/kg bw/d	AEL mg/kg bw/d	Estimated uptake mg/kgbw/d	Estimated uptake/ AEL * (%)	Acceptable (yes/no)
Indirect exposure of bystander children (1-3 years old, *toddlers*)/[7]	1	100	0.35	0.17	48.5%	**yes**
Indirect exposure of bystander adults/[8]	1	100	0.35	0.047	13.4%	**yes**
Indirect exposure of resident children (1-3 years old, *toddlers*)/[9]	1	100	0.35	0.076	21.7%	**yes**
Indirect exposure of resident adults/[10]	1	100	0.35	0.018	5.1%	**yes**

Note: (*): Named as % of RVAAS (Reference value non-acutely toxic active substance) in the calculation.

Combined scenarios

Combined secondary exposure to BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is not considered relevant. See detailed tables above.

Local effects

Non-users are not likely to come into contact with BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE. The calculations presented above show that exposure is negligible. The product as a concentrate is classified as a skin sensitizer, however application is already performed with the diluted product. The product will become further diluted in the environment and the extremely small amount that might come into contact with bystanders or residents is not expected to elicit any local effects at all.

Conclusion

Indirect exposure can occur in case of drifting and bystanders or general public entering the treated area.

For the calculation of exposure the EFSA guidance (2014)* on exposure of operators, workers, bystanders and residence were used.

*: GUIDANCE OF EFSA: Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. EFSA Journal 2014;12(10):3874, (approved on 17 October 2014) Calculator: Latest version: 30 Mar 2015 - Version produced to support guidance document published 23/10/2014

The aim of exposure assessment in this context is to consider realistic and high exposure scenarios arising from the proposed Good Agricultural Practice for non-dietary systemic exposure that can be compared with appropriate toxicological reference values.

For bystanders, the exposure of persons was calculated who could be located within or directly adjacent to the area where PPP application or treatment is in process or has recently been completed. These persons typically exposed during a short period of time (acute exposure) and take no action to avoid or control exposure. Based on the calculations it can be concluded that the risk for bystanders (*toddlers* and adults) is negligible.

For residents, the exposure of persons was calculated who live, work or attend school or any other institution adjacent to an area that is or has been treated with a PPP. These persons typically take no action to avoid or control exposure; and who might be in the location for up to 24 hours per day. Based on the calculations it can be concluded that the risk for residents (*toddlers* and adults) is negligible.

Risk for consumers via residues in food

Exposure to BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE via residues in food is not considered to be relevant.

Risk characterisation from combined exposure to several active substances or substances of concern within a biocidal product

BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE only contains one active substance, S-methoprene. Consequently, combined exposure of several active substances is not considered relevant.
Only one substance of concern is present in the product: octadecanoic acid, 12-hydroxy-, polymer with .alpha.-hydro-.omega.-hydroxypoly(oxy-1,2-ethanediyl), which is sensitizing and due to its concentration (>1% w/w), the product is also classified as Skin Sens. 1. Adequate PPE (protective gloves and coveralls) is sufficient to address this local effect (see above), combined exposure of substances of concern is not relevant for the product.

2.2.7 Risk assessment for animal health

The product is not expected to pose any unacceptable effect on non-target animals. For the assessment of risks regarding non-target organisms see evaluation below in the risk assessment for the environment section. No further studies are considered relevant for the product.

2.2.8 Risk assessment for the environment

The environmental exposure of S-methoprene, formulated as ZW, mixed formulation of CS (capsule suspension) and EW (emulsion, oil in water), is assessed. The product contains 5% w/w S-methoprene: 3.75% microencapsulated S-methoprene + 1.25% 'free' S-methoprene. The insecticide function of the product is the control of mosquitoes through disruption of the development and metamorphosis of the larvae, and ultimately to prevent egg production. The trade name for the S-methoprene product is BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE. The preparation is proposed as a spray application for outdoor use by trained professional users.

BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is an S-methoprene based insect growth regulator, a juvenile hormone analogue. BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE prevents the emergence of adult mosquitoes, but has no effect on mosquitoes which have reached the pupal or adult stage prior to treatment.

The environmental exposure of S-methoprene was assessed in accordance with the Guidance on the Biocidal Products Regulation Volume IV Environment - Assessment and Evaluation (Parts B + C) Version 2.0 October 2017.

The preparation has to be sprayed onto water surfaces, according to the following dosing: 220-360 mL/ha. For presenting the risk assessment of 5% w/w S-methoprene on the environment, all representative use scenarios were selected for the exposure (and hazard) assessment.

2.2.8.1 Effects assessment on the environment

PNEC determination on S-methoprene active ingredient:

Details of PNEC determinations are provided in the S-methoprene Assessment Report. PNECs relevant to risk characterisation in the affected compartments are as follows:

The maximum permissible concentration according to European Drinking Water Directive (DWD) 98/83/EC is 1 x 10^{-4} mg/L (i.e. 0.1 µg/L).

Limit value = 1 x 10^{-4} mg/L = 0.1 µg/L

Freshwater invertebrates are representative of one of the more sensitive groups. The 21-day NOEC value on *Daphnia magna* was used (0.019 mg/L). Assessment factor of 100 was used.
PNECaquatic (SW) = 0.00019 mg/L

PNECsediment = 0.00038 mg/kg wwt

The value of PNECsoil was decided and accepted in the Assessment Report of S-methoprene (PNECsoil = 0.0003 mg/kg). It shall be noted that new terrestrial studies have been submitted at the time of the BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE product dossier submission. The 28 days study result on *Folsomia candida* (Collembola) was a $NOEC_{reproduction}$ of 47 mg/kg soil dry weight, a $EC_{50,reproduction}$ of 79.85 mg/kg soil dry weight and a $EC_{10,reproduction}$ of 24.75 mg/kg soil dry weight; on Earthworm the $NOEC_{reproduction}$ was 106 mg/kg soil dry weight (56 day) and NOEC mortality was 213 mg/kg soil dry weight (28 day). The $EC_{10,\ reproduction}$ value of 24.75 mg/kg soil dry weight for Collembola should be used in the PNEC derivation.
The new terrestrial studies were evaluated and incorporated in the revised version of the AR & LoEPs of S-methoprene drafted by the eCA-IE in November 2018, which was presented by eCA-IE at BPC-28 in December 2018 (please, refer to BPC-28 minutes). Therefore, the following updated PNECsoil (peer-reviewed and agreed) will be used for the risk assessment:

PNECsoil = 0.168 mg/kg dwt (= 0.148 mg/kg wwt)

PNEC derivation in Sewage Treatment Plants (STP): The assessment factor is 1.
$PNEC_{STP}$ = 6.85 mg/L

Information relating to the ecotoxicity of the biocidal product which is sufficient to enable a decision to be made concerning the classification of the product is required

According to the aquatic acute toxicity studies, the most sensitive species is the *Daphnia magna* with result of EC50 of 0.22 mg/L.
A summary of the aquatic ecotoxicological data presented indicates the following key endpoints:

Fish toxicity:	96 h LC50 in Zebrafish (*Brachydanio rerio*) = 4.26 mg/L
Invertebrate toxicity:	48 h LC50 in Cladoceran (*Daphnia magna*) = 0.22 mg/L
Algal toxicity:	72 h ErC50 in *Selenastrum capricornutum* (Prinz-Starr) = 2.264 mg/L

Based on the above acute toxicity results a chronic study was also commissioned on *Daphnia magna*.

Invertebrate chronic toxicity:	21 d NOEC in Cladoceran (*Daphnia magna*) = 0.019 mg/L

The above ecotoxicity studies together with the biodegradation studies are sufficient for classification of S-methoprene.

Further Ecotoxicological studies

Further ecotoxicological studies were commissioned for risk assessment purposes.

Summary table - Further ecotoxicological studies

Summary table of further ecotoxicological studies									
Method, Guideline, GLP status, Reliability	**Species/ Inoculum**	**End point**	**Exposure**		**Results**			**Remarks**	**Ref.**
			Design	Dura-tion	EC_{10}	EC_{50}	EC_{100}		
OECD 209, GLP, Reliability: 2	Microorganisms (Activated sewage sludge)	EC50 (3h)	Respiration Inhibition Test	3 h		6.85 (AR)			IUCLID section 9.2.1.5
OECD 222, ISO No.:11268-2 GLP, Reliability: 1	Earthworm (*Eisenia fetida*)	$NOEC_{reproduction}$ (56 d) $NOEC_{mortality}$ (28 d)	Reproduc-tion test	56 d 28 d		Rep: 241 Mort: 405 mg/kg dry soil		$NOEC_{reproduct}$ = 106 mg/kg dry soil $NOEC_{mortality}$ = 213 mg/kg dry soil	IUCLID section 9.2.5
OECD 232, ISO No.:11267-2 GLP, Reliability: 1	Collembola (*Folsomia candida*)	$NOEC_{reproduction}$(56 d)	Reproduc-tion test	28 d	24.75 mg/kg dwt (26 d) (corrected to 16.83 mg/kg dwt)	79.85		$NOEC_{reproduct}$ (56 d) = 47 mg/kg dry soil	IUCLID section 9.2.3.1

Conclusion used in Risk Assessment – Further ecotoxicological studies	
Value/conclusion	PNECsoil = 0.168 mg/kg dwt (= 0.148 mg/kg wwt) Peer-reviewed and agreed at BPC-28
Justification for the value/conclusion	New terrestrial studies were evaluated and incorporated in the revised version of the AR & LoEPs of S-methoprene drafted by eCA-IE in November 2018, which was presented by eCA-IE at BPC-28 in December 2018 (please, refer to BPC-28 minutes).

	The $EC_{10,\ reproduction}$ value of 24.75 mg/kg soil dry weight for Collembola was used in the PNECsoil derivation. The study has been conducted with a high content of organic material in the artificial soil (i.e. 5% peat). The resulting endpoints had to be corrected for differences between the organic matter content of the test soil and that of the standard soil defined for biocides. For the latter, the standard average organic matter content of 3.4% was used to convert the endpoint to a standard soil for biocides, resulting in an $EC_{10,\ reproduction}$ value of 16.83 mg/kg soil dwt. As additional data on a least two arthropod species are needed to reduce the AF from 100 to 50, for these kind of compounds an AF of 100 has been applied.

Effects on any other specific, non-target organisms (flora and fauna) believed to be at risk (ADS)

Data waiving	
Information requirement	Toxicity to plants
Justification	In the scientific literature effects on plants have not been reported.

Data waiving	
Information requirement	Toxicity to terrestrial macro-organisms
Justification	Please see above the new ecotoxicological studies with S-methoprene on terrestrial organisms. Further studies are not considered relevant. The exposure and risk to the soil is expected to be negligible. Moreover, S-methoprene will degrade rapidly in the environment.

Supervised trials to assess risks to non-target organisms under field conditions

Data waiving	
Information requirement	Supervised trials under field conditions
Justification	Not applicable. The product is not applied directly on plants or soil.

Studies on acceptance by ingestion of the biocidal product by any non-target organisms thought to be at risk

Data waiving	
Information requirement	Studies on acceptance by ingestion of the biocidal product by any non-target organisms

Justification	The product is not a bait formulation therefore it is not attractive for non-target organisms for ingestion. The product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is sprayed on areas covered with water. Moreover S-methoprene will degrade rapidly in the aquatic environment.

Secondary ecological effect e.g. when a large proportion of a specific habitat type is treated (ADS)

Not relevant. The product is used against mosquito's larvae. The product is directly applied to these areas. Secondary exposure is not expected. Moreover S-methoprene will degrade rapidly in the aquatic environment.

Foreseeable routes of entry into the environment on the basis of the use envisaged

The Level 1 Fugacity Calculator based on Subsurface Contamination Reference Guide. Prepared by the EPA Office of Emergency and Remedial Response, October 1990.EPA/540/2-90/01 was used to simulate the equilibrium distribution for evaluating equilibrium chemical distribution between environmental phases (air, water, soil.) of S-methoprene in an environment at equilibrium. No degrading reactions, advective processes or intermedia transport processes (e.g. wet deposition or sedimentation) were considered.

Physical-chemical properties and partition coefficient data were input values used by the model to derive environmental properties. Various default values were used in the model which used the typical value found in a system such as volume in air, water and soil etc. These parameters were then used to quantify S-methoprene behaviour in an evaluative environment. Please refer to the "Environmental properties" section for input parameters and environmental properties generated by the model.

The Organic carbon-water partition coefficient (L/kg) value was obtained from laboratory work. (Laky, V. (2002b), Adsorption/desorption test of S-methoprene technical) Three values were calculated which were 684, 537, 1407. The mean was calculated to be 876 L/kg.

Distribution was simulated for the following homogenous environmental media (or compartments): air, water, soil.

The Level 1 Fugacity Calculator ver1.2 by Karl Nieman was used to predict the environmental distribution or partitioning of S-methoprene in the environment in a closed environment at equilibrium. The physical-chemical properties, partition coefficient data and user-defined volumes and densities were used to quantify the behaviour of S-methoprene for the following homogenous environmental compartments: air, water, soil. S-methoprene was predicted to partition predominantly to soil. Negligible amounts in water and no partitioning in air and non-aqueous phase liquid. S-methoprene distribution result: partitioned to soil (95.43%), to water (4.28%) to air (0.0%), and non-aqueous phase liquid (NAPL) (0.0%)

Further studies on fate and behaviour in the environment (ADS)

Summary table on further studies on fate and behaviour in the environment							
Method, Guideline, GLP status, Reliability	**Compartment**	**pH**	**Temp [°C]**	**Initial TS concentra-tion, C0 [mol/L]**	**Half-life, DT50 [d]**	**Remarks**	**Reference**
OECD 301D, GLP, Reliability 2	Act. Sludge (Ready biodegradability)		20 ± 1 °C	2 & 8 mg/L	--	Degradation: 2 mg/L: 49.45; 8 mg/L: 20.99	CAR IIIA 7.1.1.2.1
OECD 302C GLP, Reliability 1	Act. Sludge (Inherent biodegradability)	7.0-7.77	25 ± 2 °C			Biodeg-radation: Thod: 24.5% (14 d) 85.8% (28 d)	Dr. Vértesi, A. (2014); Inherent Biodeg-radability
OECD 111 GLP, Reliability 2	Water, Hydrolysis	4, 7, 9, 1.2	25, 37 & 50 37 °C		>1 m 17 h		CAR IIIA 7.1.1.1.1
OECD Draft Guideline: Phototransformation GLP, Reliability 2	Water, Photolysis	7	22 ± 2 ºC	0.436 µg/g	4.8 h		CAR IIIA 7.1.1.1.2-1

Conclusion used in Risk Assessment – Further studies on fate and behaviour in the environment	
Value/conclusion	Ready biodegradability – Not readily biodegradable
Justification for the value/conclusion	This closed bottle test concluded that S-methoprene is not readily biodegradable. At the higher test concentration of 8 mg/L less degradation took place relative to tests performed at 2 mg/L. This suggests a concentration effect. The study does not report the concentration of test item used in the toxicity test. If the test was performed at a low concentration of test item, negligible inhibition may take place resulting in the observed result in the tox control. 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 EC20 values) obtained in toxicity testing)". For S-methoprene the EC50 for activated sludge is reported as >100 mg/L (3 hr). The test concentrations used in the experiment were 2 mg/L and 8 mg/L. The higher test concentration of 8 mg/L lies above the water solubility. The results at 2 mg/L may be more reliable than the results at 8 mg/L. The validity criteria for the test were fulfilled.

Conclusion used in Risk Assessment – Further studies on fate and behaviour in the environment	
Value/conclusion	Inherent biodegradability – Inherently biodegradable however specific inherent biodegradability criteria were not met
Justification for the value/conclusion	The modified MITI (II) test showed >70% degradation within 28 days. This represents inherent biodegradability (as specified in TGD). The failure to reach 70% within 14 days means that the specific inherent biodegradability criteria were not met and therefore that extrapolation of the results for use in STP models is not possible.

Conclusion used in Risk Assessment – Further studies on fate and behaviour in the environment	
Value/conclusion	Hydrolysis - hydrolytically stable at pH 4, 7 and 9 at all temperatures examined.
Justification for the value/conclusion	S-methoprene technical was found to be hydrolytically stable at pH 4, 7 and 9 at all temperatures examined. (25, 37 and 50). At pH 1.2 hydrolysis of the test material was rapid with a DT50 value of 17 hours.

Conclusion used in Risk Assessment – Further studies on fate and behaviour in the environment	
Value/conclusion	Aqueous photolysis - fast photodegradation, DT50 = 4.8 hour
Justification for the value/conclusion	S-methoprene was shown to be readily degradable in water by simulated sunlight indicating that S-methoprene would not be expected to persist in upper layers of natural surface waters.

Leaching behaviour (ADS)

For product type 18 Insecticides leaching study is not relevant. Furthermore, S-methoprene has a very low solubility.

Testing for distribution and dissipation in soil (ADS)

Distribution

Summary table of the adsorption/desorption in soil									
Method, Guideline, GLP status, Reliability	Soil	Adsorbed AS [%]	K_a	K_{aOC}	K_d	Kf	l/n	Remarks	Reference
OECD 106, GLP, Reliability 1	Soil 1 Soil 2 Soil 3 average	53 45 47		537 684 1 407 876	7.9 6.5 5.5		---		Laky, V. (2002b), Adsorption/ desorption test of S-Methoprene technical CAR IIIA 7.2.3.1

K_a = Adsorption coefficient

K_{aOC} = Adsorption coefficient based on organic carbon content

K_d = Desorption coefficient

K_{dOC} = Desorption coefficient based on organic carbon content

K_a/ K_d = Adsorption / Desorption distribution coefficient

S-methoprene is readily adsorbed to and desorbed from the soil. With Koc values of 537, 684 and 1407 in three soil types and an average of 876, S-methoprene is classified as being of low mobility according to the McCall and UK Soil Survey and Land Research Centre Pesticide Mobility classification systems.

No further studies were submitted due to the use pattern proposed for S-methoprene and the indication that based on the above study that S-methoprene exhibits low mobility in soil.

Dissipation

Summary table on half lives in soil					
Process	DT_{50} measured in test	DT_{50} at 12°C	Rate constant at 12°C	Remarks	Reference[1]
Biodegradation					
Aerobic *Soil 1* *Soil 2* *Soil 3* *Soil 4*	 0.93 0.78 0.79 0.83	 1.76 1.48 1.50 1.57	 0.393 0.469 0.463 0.440		IUCLID section 10.2

Conclusion used in Risk Assessment –Distribution and dissipation in soil	
Value/conclusion	Persistence – Not persistent
Justification for the value/conclusion	The DT50 values at 12 °C are well below the trigger value of 120 days, therefore S-methoprene is not persistent.

Testing for distribution and dissipation in water and sediment (ADS)

Distribution

No data submitted.

Dissipation

Summary table on half lives in water and sediments					
Compartment /process	DT_{50} measured in test	DT_{50} at 12°C	Rate constant at 12°C	Remarks	Reference
Freshwater					
Aerobic biodegradation *River system* *Pond system*	 0.78 d 0.54 d	 1.48 1.02	 0.469 0.677		IUCLID Section 10.2
Freshwater sediment					
Aerobic biodegradation *River system* *Pond system*	 3.74 6.75	 7.09 12.74	 0.098 0.054		IUCLID Section 10.2

Summary table of identified metabolites /transformation- or reaction products in water and sediments				
Compartment	Metabolite/ transformation- or reaction product	[%] of active substance	Remarks	Reference
Freshwater				
Aerobic biodegradation *River system* *Pond system*	 River system M2* M3* M4* Pond system M2* M3* M4*	 7.8 10.2 2.1 6.2 5.8 5.6		IUCLID Section 10.2
Freshwater sediment				
Aerobic biodegradation *River system* *Pond system*	 River system M2* M3* Pond system M2* M3*	 1.6 2.0 1.9 1.9		IUCLID Section 10.2

Note:
M2: Isopropyl (2E,4E)-11-hydroxy-3,7,11-trimethyldodeca-2,4-dienoate
M3: (2E,4E)-11-Methoxy-3,7,11-trimethyldodeca-2,4-dienoic acid
M4: (2E,4E)-11-hydroxy-3,7,11-trimethyldodeca-2,4-dienoic acid

Conclusion used in Risk Assessment –distribution and dissipation in water and sediment	
Value/conclusion	S-methoprene and its metabolites degraded fast in the water-sediment system.
Justification for the value/conclusion	The primary route of degradation was mineralization (54.9-67.5%). Significant formation of bound residues was observed (36.9-41.0%). Acidic harsh extraction under reflux followed by organic matter fraction was conducted on the non-extracted residues from the Day 7 only released 1.6% or less of the total radioactivity. Overall, parent S-methoprene as well as the two major metabolites M2 and M3 showed rapid dissipation from the total system. Neither S-methoprene nor the metabolites appear to be persistent in the water-sediment system.

Testing for distribution and dissipation in air (ADS)

Summary table on half lives in air			
	Value	Unit	Remarks
Molecular weight	310.48		
Melting point	---	°C	
Boiling point	279.9	°C	
Vapour pressure at 20°C	1.08	mPa	At 25 °C
Henry's Law Constant (20 °C)	0.0306	Pa/m3/mol	At 20 °C

Summary table of half lives identified relevant metabolites and transformation products in air

Data to address the fate of S-methoprene in air was not submitted as the exposure of the air expected to be negligible. The physiochemical properties of S-methoprene do not suggest that this substance will pose a risk to the atmospheric environment.

Exposure of the atmospheric compartment to S-methoprene is not expected. The nature of the formulation BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE, sprayed onto the water surface is unlikely to generate significant levels of particulates to the air. Furthermore, S-methoprene exhibits a medium to low volatility and sensitive to light. Thus an accumulation of S-methoprene in air and long range transport of the product is unlikely. Therefore no risk assessment is performed for the atmosphere.

Dissipation

Conclusion used in Risk Assessment –distribution and dissipation in air	
Value/conclusion	No accumulation of S-methoprene and its long-range transport is expected
Justification for the value/conclusion	The physiochemical properties of S-methoprene do not suggest that this substance will pose a risk to the atmospheric environment. S-methoprene exhibits a medium to low volatility and sensitive to light. Thus an accumulation of S-methoprene in air and long range transport of the product is unlikely therefore no distribution and dissipation study was made.

Data waiving	
Information requirement	Study on distribution and dissipation in air
Justification	No accumulation of S-methoprene and its long-range transport is expected. The physiochemical properties of S-methoprene do not suggest that this substance will pose a risk to the atmospheric environment. S-methoprene exhibits a medium to low volatility and sensitive to light. Thus an accumulation of S-methoprene in air and long range transport of the product is unlikely therefore no distribution and dissipation study was made.

If the biocidal product is to be sprayed near to surface waters then an overspray study may be required to assess risks to aquatic organisms or plants under field conditions (ADS)

Not applicable.

Acute aquatic toxicity

Summary table for acute aquatic toxicity									
Guideline/ Test method/ GLP status/ reliability	**Species**	**End point**	**Exposure**		**Results**			**Remarks**	**Ref.**
			Design	Duration	LC/EC_0	LC/EC_{50}	LC/EC_{100}		
Fish									
OECD 203/ GLP/ Reliability: 2	Zebrafish (*Brachydanio rerio*)	96 hr LC50		96 hr		4.26 mg/L			CAR, IIIA7.4.1.1/01.
Invertebrates									
OECD 202; EC 440/2008; EPA 712-C-96-114 / GLP /	*Daphnia magna*	48 hr EC_{50} 24 hr EC_{100}		48 24		0.22 mg/L	0.66 mg/L	Most sensitive short-term endpoint	CAR, IIIA7.4.1.2/02.
Algae (growth inhibition)					NOE_rC/ ErC_{10}	E_bC_{50}	E_rC_{50}		
OECD 201 / GLP / Reliability 2	Green alga, *Selenastrum capricornutum* (Prinz-Starr)	72 hr E_rC_{50}		72 hr			2.264 mg/L		CAR III, 7.4.1.3/01.

Conclusion used in Risk Assessment – Acute aquatic toxicity	
Value/conclusion	EC50 = 0.22 mg/L (*Daphnia*)
Justification for the value/conclusion	Acute toxicity studies indicated that *Daphnia* is the most sensitive indicator of toxicity to S-methoprene.

Chronic aquatic toxicity

Summary table for chronic aquatic toxicity							
Guideline/ Test method/ GLP status/ reliability	**Species**	**End point/ Type of test**	**Exposure**		**Results**	**Remarks**	**Reference**
			Design	Duration	LOEC/ NOEC/ EC_{10}		
Invertebrates							
OECD 211/ GLP / Reliability 1	*Daphnia magna*	21 d NOEC	Reproduction Test	21d	0.019 mg/L	Most sensitive long-term endpoint	CAR, IIIA7.4.3.4/01.

Conclusion used in Risk Assessment- Chronic Aquatic toxicity	
Value/conclusion	PNECaquatic established as 0.00019 mg/L
Justification for the value/conclusion	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.

Measured aquatic bioconcentration

Study on aquatic bioconcentration was waived as the result of QSAR calculation was accepted by RMS evaluating S-methoprene.

Estimated aquatic bioconcentration

Summary table – Estimated aquatic bioconcentration					
Basis for estimation	**Log K_{ow} (measured)**	**Estimated BCF for fish (freshwater)**	**Estimated BCF for fish eating bird/predator**	**Remarks**	**Reference**
BCFBAF QSAR model	6.34	516	Not applicable		IIIA, 7.4.2.1

Conclusion used in Risk Assessment –Aquatic bioconcentration	
Value/conclusion	PBT assessment: S-methoprene is not bioaccumulative
Justification for the value/conclusion	For S-methoprene (CAS: 65733-16-6) calculations using BCFBAF, the CAS number is provided to the software and the SMILES structure are generated automatically. Also the partition coefficient value is also provided, i.e. Log Kow 6.34. For this model other physical-chemical properties are not necessary as they are not part of this specific model calculation. 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 CLP Regulation (EC) No. 1272/2008 the bioconcentration factor (BCF) threshold limit for classification purposes is 500. From the calculation the BCF of S-methoprene is 516, therefore, based on these results, S-methoprene has a bioaccumulation potential according to the CLP criteria. However according to the criteria for the PBT assessment for Annex XIII to Regulation (EC) 1907/2006 S-methoprene does not meet the B criterion (>2000).

If the biocidal product is to be sprayed outside or if potential for large scale formation of dust is given then data on overspray behaviour may be required to assess risks to bees and non-target arthropods under field conditions (ADS)

BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is a product only intended for trained professionals. It is expected that professionals follow good application practices, which ensures that only the intended water surfaces will be treated with the product. With the use of a spraying equipment, a targeted application is possible limiting exposure to other areas, e.g. soil. For BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE, only coarse sprayers producing big droplets are recommended. Large droplets settle quickly after application, thus drifting to non-target surfaces will not occur.

2.2.8.2 Exposure assessment

Emission estimation

Scenario [1]: ditches of rainwater drainage system and road drains.

The uses ditches of rainwater drainage system and road rains could be covered by the assessment of direct emission to surface water in urban areas (PT 6.2/6.3 and 7-10)[2].

The application dose of BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE in ditches and road drains is 360 mL/ha water, that correspond to 0.01845 kg/ha of a.s. (product density: 1.025 g/mL; a.s. % w/w in the product: 5% w/w). In case we take an average drain of 50 L, this would mean that 6.15 mg product should be applied to this drain that correspond to 0.3235 mg/ditches of rainwater drainage system of S-methoprene (5.26% technical material).

According to the ESD for PT14, 300 cesspools are considered for a mixed sewer system per 10000 inhabitants. Calculated with the value of 300 catch basins and the effluent value from the above-mentioned recommendation, the Elocal,water is 9.23 x 10^{-5} kg/d if we consider as a worst case that all 300 drains are treated at the same time and the emitted water contains all the product used for treatment without degradation. The concentration of S-methoprene in the water entering the STP (Clocal $_{infl}$) is calculated by considering the volume of water entering the STP.

Surface water and STP

Direct rainwater discharge

Input parameters for calculating the local emission		
Input	**Value**	**Unit**
$Elocal_{wastewater}$	0.0000923	kg/d
$EFFLUENT_{wastewater}$	0.6 x 10^{6}	L/d
Clocal $_{eff}$ = $Elocal_{wastewater}$ / $EFFLUENT_{wastewater}$	1.62 x 10^{-10}	kg/L

Calculations:

According to the equation 45 of the Guidance on the Biocidal Products Regulation Volume IV Environment - Part B Risk Assessment (active substances) Version 1.0 April 2015 the $Clocal_{water}$ is calculated as follow:

2 https://echa.europa.eu/documents/10162/16908203/pt_6_7_8_9_10_assessment_of_direct_emission_surface_water_urban_areas_en.pdf/56073606-24c6-4b77-89ea-bfeec98d5943

Input parameters for calculating the local emission		
Input	**Value**	**Unit**
Kp_{susp} solid-water partitioning coefficient of suspended matter	87.6	L/kg
$SUSP_{water}$ concentration of suspended matter in the river	15	mg/L
DILUTION dilution factor	10	-
$Clocal_{water}$ local concentration in surface water $Clocal_{water} = Clocal_{eff} /((1+Kp_{susp} \times SUSP_{water} \times 10^{-6}) \times DILUTION$		mg/L

PECsw = $Clocal_{water}$ = 1.62×10^{-11} kg/L = 1.62×10^{-5} mg/L

Sediment

PEClocal for sediment can be compared to the calculated PNEC for sediment dwelling organisms. The concentration of S-methoprene can be derived from the corresponding water body concentration, assuming a thermodynamic partitioning equilibrium. In accordance with Guidance on the Biocidal Products Regulation Volume IV Environment - Part B Risk Assessment (active substances) Version 1.0 April 2015 the concentration of S-methoprene in sediment is estimated in the following way:

$$PEClocal_{sed} = \frac{K_{susp\text{-}water}}{RHO_{susp}} * PEClocal_{water} * 1{,}000 \quad \text{Eq. 50}$$

Where:
$PEClocal_{sed}$ = predicted environmental concentration in sediment (mg/kg)
$K_{susp\text{-}water}$ = suspended matter-water partition coefficient (m^3/m^3)
RHO_{susp} = bulk density of suspended matter (kg/m^3)
$PEClocal_{water}$ = concentration in surface water during emission episode (mg/l)

$$RHO_{susp} = Fsolid_{susp} * RHO_{solid} + Fwater_{susp} * RHO_{water} + Fair_{susp} * RHO_{air} \quad \text{Eq. 18}$$

Where:
Fx_{comp} fraction of phase x in compartment comp (m^3/m^3)
RHOx density of phase x (kg/m^3)
RHO_{comp} wet bulk density of compartment comp (kg/m^3)

$$K_{susp\text{-}water} = F_{air} * K_{air\text{-}water} + Fwater_{susp} + Fsolid_{susp} * \frac{Kp_{susp}}{1000} * RHOsolid \quad \text{Eq. 24}$$

As $Fair_{susp} = 0$ the $F_{air} * K_{air\text{-}water}$ part = 0.

Where:
$K_{susp\text{-}water}$ = suspended matter-water partitioning coefficient (m^3/m^3)
$K_{air\text{-}water}$ =air-water partitioning coefficient
$Fwater_{susp}$ = Fraction water in suspended matter compartment (m^3/m^3)
$Fsolid_{susp}$ = Fraction solid in suspended matter compartment (m^3/m^3)
Kp_{susp} = Solids-water partition coefficient in suspended matter compartment (L/kg)
RHOsolid = Density of the solid phase (kg/m^3)

$$Kp_{susp} = Foc_{susp} * Koc \quad \text{Eq. 23}$$

Where:
Kp_{susp} = partition coefficient solid-water in suspended matter (L/kg)
Foc_{susp} = weight fraction of organic carbon in suspended matter (kgoc/kgsolid)
Koc= partition coefficient organic carbon – water (L/kg)

Calculations:

RHO_{susp} = 0.1 * 2,500 + 0.9 * 1,000 + 0 * 1.3= 1,150 kg/m^3

$K_{susp\text{-}water}$ = 0 + 0.9 + 0.1 * 87.6/1,000*2,500
$K_{susp\text{-}water}$ = 22.8
Kp_{susp} = 0.1 * 876 = 87.6 L/kg

$PECloca l_{sed}$ = 0.00032 mg/kg

Scenario [2]: puddles, pools, artificial basins and in all the closed hydraulic systems

The exposure assessment has been performed considering a treated area of 50 ha as worst-case for direct exposure of surface water and indirect exposure of surrounding soil of treated area. The application rate is 360 mL/ha water (depth >30 cm) that correspond to 0.01845 $kg_{a.s.}$/ha.

Direct exposure of surface water <u>without degradation</u>

The direct exposure of surface water has been calculated taking into account a treated area of 50 ha and a depth of 50 cm. The application rate of the product is 0.01845 kg a.s./ha that means 0.927 kg of a.s. for 50 ha. The total volume of treated area will be 250000 m^3 (50 ha x 0.5 m). If no degradation is considered, the concentration of a.s. in the product during emission episode will be 3.708 x 10^{-3} mg/L (0.927 kg / 250000 m^3 = 3.708 x 10^{-6} kg/ m^3).

PECsw = 3.708 x 10^{-3} mg/L

$$PECloca l_{sed} = \frac{K_{susp\text{-}water}}{RHO_{susp}} * PECloca l_{water} * 1000$$

RHOsusp = 1150 kg/m^3

Ksusp-water = 22.8

PECsed = 7.35 x 10^{-2} mg/kg

Refinement: *Direct exposure of surface water <u>with degradation</u>*

The exposure assessment has been refined taking into account the fast degradation of the active substance. In the simulated water sediment biodegradation study the DT_{50} value is 1.02 days for paddy water at 12°C.
Calculation:

k_{deg} = ln 2 / DT_{50} = 0.67956 d^{-1}

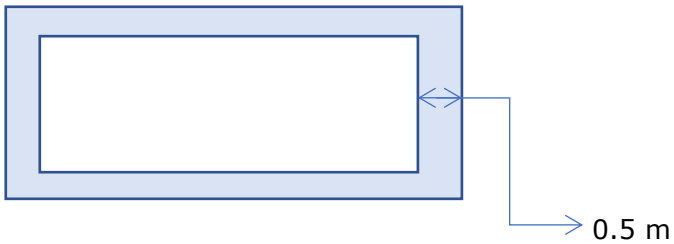
$E_{local.\ T} = E_{local.\ T0} * e^{-T*kdeg}$

The following table shows the PECs value for surface water and sediment after application considering degradation of a.s.:

Day	PECsw	PECsed
0	0.00371	0.07352
1	0.00188	0.03726
2	0.00095	0.01889
3	0.00048	0.00957
4	0.00024	0.00485
5	**0.00012**	0.00246
6	0.00006	0.00125
7	0.00003	0.00063
8	0.00002	**0.00032**
9	0.00001	0.00016
10	0.000004	0.00008

Indirect exposure of surrounding soil

The indirect exposure of surrounding soil will occur via drift or overspray, considering a treated area of 50 ha (500 x 1000 = 500000 m^2) and 0.5 m for soil depth and 0.5 m for the distance from the treated area. has been performed.



The surrounding soil area and volume potentially contaminated (in blue in the figure) will be about 1500 [(501x1001)-(500x1000)=1501 m^2) and 750 m^3 (1500x0.5=750 m^3). According to the Emission Scenario Document for insecticides, acaricides and products to control other arthropods for household and professional uses 2008 (PT 18), the emission factor due to deposition is 0.1.
The local emission from spray application due to deposition on soil is calculated as follows:

Variable/parameter (units)		Symbol	Unit
Input:			
Quantity of a.s. in the product applied	1.845×10^{-6}	Q_{prod}	kg/m^2
Area soil	1500	$AREA_{soil}$	m^2
Fraction emitted to soil during application due to deposition	0.1	$F_{spray.\ deposition}$	-
Soil volume around treated artificial basin	750	$V_{spray.soil}$	m^3
Bulk density of wet soil	1700	*RHOsoil*	kg_{wwt}/m^3
Output:			
Local emission from spray application due to deposition on soil $Elocal_{spray} = Q_{prod} \times AREA_{soil} \times F_{spray.\ deposition}$	2.768×10^{-4}	$Elocal_{spray}$	kg/d
Local concentration of active ingredient in soil adjacent to the artificial basin application $C_{spay\ appl.soil} = \frac{\text{Elocal } spray}{Vspray\ x\ RHOsoil}$	2.17×10^{-10}	$C_{spray.appl.soil}$	kg/kg_{wwt}

The local concentration of active ingredient in surrounding soil after application is 2.17 x 10^{-4} mg/kg_{wwt}.

Groundwater

PECgw = $PECloca l_{agr.soil,porew}$
Where:
$PECloca l_{grw}$ = predicted environmental concentration in groundwater (mg/L)
$PECloca l_{agr.soil,porew}$ = predicted environmental concentration in pore water (mg/L)

$$PECloca l_{agr.soil,porew} = \frac{PECloca l_{soil} * RHO_{soil}}{K_{soil-water} * 1000}$$

Where:
$PECloca l_{agr.soil,porew}$ = predicted environmental concentration in pore water (mg/L)
$PECloca l_{soil}$ = predicted environmental concentration in soil (mg/kg)
RHO_{soil} = bulk density of wet soil (2500 kg/m^3)
$K_{soil-water}$ = soil-water partitioning coefficient (26.480 m^3/m^3)
PECgw = 2.05 x 10^{-5} mg/L = 0.02 µg/L

Fate and distribution in exposed environmental compartments

Identification of relevant receiving compartments based on the exposure pathway									
	Fresh-water	Freshwater sediment	Sea-water	Seawater sediment	STP	Air	Soil	Ground-water	Other
Scenario 1	Yes	Yes	Not relevant	Not relevant	Not relevant	Not relevant	Not relevant	Not relevant	
Scenario 2	Yes	Yes	Not relevant	Not relevant	Not relevant	Not relevant	Yes	Yes	

Calculated PEC values

DT_{50} values derived from these studies can be used for the PEC calculations.

PEC calculations are considered as follows:
(PECpw, PECsoil, PECpgw) → flooded aerobic soil degradation.
(PECsw, PECsed) → aerobic aquatic water / sediment study.

Summary table on calculated PEC values						
	PEC_{STP}	**PEC_{water}**	**PEC_{sed}**	**PEC_{soil}**	**PEC_{GW}**	**PEC_{air}**
	[mg/m^3]	[mg/L]	[mg/kg_{wwt}]	[µg/kg_{wwt}]	[µg/L]	[mg/m^3]
Scenario 1 ditches of rainwater drainage system and road drains	n.a.	1.62 x 10^{-5}	0.00032	n.a.	n.a.	n.a.
Scenario 2 not connected to STP or aquatic compartment	n.a.	0.00012 (with degradation)	0.00032 (with degradation)	2.17 x 10^{-4}	0.02	n.a.

Primary and secondary poisoning

Primary poisoning

For the evaluated use scenarios, no primary poisoning is expected. The S-methoprene degrades very fast in aquatic environment: in the water-sediment biodegradation study in the pond system the DT_{50} was 0.54 day in the water phase, 6.72 days in the sediment phase and 0.87 days in the total system. In the soil degradation study the degradation of S-methoprene was also very fast: the average DT_{50} was 0.83 days.

Secondary poisoning

The product use excludes water holding features connected with surface water. From the CAR (December 2013): "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 S-methoprene would not be persistent in either soil or aquatic systems". The above suggests that the transport to natural waters would be negligible.
The above considered, the risk of secondary poisoning via ingestion of potentially contaminated food (e.g. earthworms or fish) by birds or mammals was not identified, either.

Bees
The worst-case concentration of S-methoprene in treated water is now calculated to be 3.708×10^{-3} µg/L. In the scientific literature, there are publications which show relationships of adverse effects on honeybees due to S-methoprene, but the exposure type is topically applied on bee abdomen. The exposure type adopted in the following studies is different from we expect but it appears of relevance that the topic application, when the chemical of concern has a short half-life and does not bioaccumulate (e.g. S-methoprene), appears to be the best to ensure a virtual 100% absorption.

Robinson, G.E., 1985. Effects of a juvenile hormone analogue on honeybee foraging behavior and alarm pheromone production. Journal of Insect Physiology 31, 277–282.

In this work, worker honeybees treated with 250 µg/bee of the juvenile hormone analogue methoprene shifted from the broodnest to the food storage region prematurely and displayed precocious foraging behaviour. Treatments with 25 and 2.5 µg did not cause significant effects. Methoprene did not influence individual foraging performance as measured by mean number of foraging trips/h, mean amount of time spent foraging/h or mean duration of the total foraging period. Methoprene also induced premature production of two alarm pheromones, 2-heptanone and isopentyl acetate. These results support the hypothesis that juvenile hormone regulates temporal division of labour in the honeybee colony.

G. Bloch, J.P. Sullivan, G.E. Robinson 2002. Juvenile hormone and circadian locomotor activity in the honeybee Apis mellifera. Journal of Insect Physiology 48 (2002) 1123–1131.

In this work, newly emerged bees were treated with 200 µg methoprene/bee, topically applied to the abdomen. The authors conclude "However, our results are not consistent with the hypothesis that JH influences circadian locomotor activity. A dose of methoprene that can induce precocious onset of foraging in other studies did not influence the onset of rhythmic locomotor activity, the clock's free-running period, or overall activity level".

Sullivan, J.P., Jassim, O., Fahrbach, S.E., Robinson, G.E., 2000. Juvenile hormone paces behavioral development in the adult worker honeybee. Hormones and Behavior 37, 1–14.

Two hundreds µg of methoprene were applied to the dorsal abdomen of an experimental group of bees. This dose of methoprene consistently causes precocious behavioural development in honeybees (Robinson, 1985, 1987a; Robinson et al., 1989; Withers, Fahrbach, and Robinson, 1995). The authors conclude that JH influences the pace of behavioral development in honey bees, but is not essential for either foraging or altering behavioural development in response to changes in conditions The principal significance of these results is that they demonstrate that JH influences the pace of behavioural development in adult worker honey bees, but is not necessary for behavioural development to occur.

Other publications adopt the same exposure type because probably is the most reliable. In addition, across the research papers consulted and the ones cited from them, an effect threshold appears to range 200-250 µg/bee although on the outcomes there is not a general agreement across the publications.

As a consequence of the chemical distribution in water, we can speculate the existence of a bee instant uptake/exposure to the chemical of concern by drinking or by contact of bee thorax/paws. Considering the above-mentioned predicted water concentration (3.708×10^{-3} µg/L), the previously mentioned thresholds result three magnitude orders higher than it. For the sake of simplicity, we considered an instant exposure by contact in a "clean" water body but the S-methoprene half-life is short and the product for its nature does not appear to ensure a constant exposure over a short time period. However, the exposure through the drinking way is still open but, in absence of experimental data, we believe that the above-mentioned figures are really far from the PEC value.

Considering the product use pattern and that the active substance disappears quickly from soil (DT_{50} = 1.55 days at 12°C), secondary exposure of bees through pollen is expected to be negligible. By restricting the use of BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE only to small water holdings and considering the revised calculation under the Risk characterization section which indicate a worst-case concentration of S-methoprene in treated water of 3.708×10^{-3} µg/L, the exposure of bees and other non-target arthropods through the drinking of treated waters is expected to be negligible, either.

2.2.8.3 Risk characterisation

Atmosphere

PNECs were not calculated for the air compartment. The physico-chemical properties of S-methoprene do not suggest that this substance will pose a risk to the atmospheric environment. The use pattern of the biocidal product BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is unlikely to generate significant levels of particulates to the air. Furthermore, S-methoprene exhibits a low volatility and is sensitive to light. Thus an accumulation of S-methoprene in air and long range transport of the product is unlikely. Therefore, no risk assessment is performed for the atmosphere.

Conclusion: Risk via the air compartment will not occur.

Sewage treatment plant (STP)

$PNEC_{STP}$ = 6.85 mg/L

Summary table on calculated PEC/PNEC values	
	$PEC/PNEC_{STP}$
Scenario 1	Not relevant
Scenario 2	Not relevant

The product is used outdoor, the Sewage Treatment Plant (STP) is not affected.

Conclusion:
STP compartment is not relevant.

Aquatic compartment

$PNEC_{sw}$ = 0.00019 mg/L
$PNEC_{sed}$ = 0.00038 mg/kg

Summary table on calculated PEC/PNEC values		
	$PEC/PNEC_{water}$	**$PEC/PNEC_{sed}$**
Scenario 1 ditches of rainwater drainage system and road drains	0.085	0.84

Conclusion: No unacceptable risk was identified in surface water and sediment, for ditches of rainwater drainage system and road rains.

Summary table on calculated PEC/PNEC values		
Without degradation		
	$PEC/PNEC_{sw}$	**$PEC/PNEC_{sed}$**
Scenario 2	0.003708/0.00019 = **19.5**	0.0735/0.00038 = **193**
With degradation		
	$PEC/PNEC_{sw}$	**$PEC/PNEC_{sed}$**
Scenario 2	0.00012/0.00019 = 0.63 (after 5 d)	0.00032/0.00038 = 0.84 (after 8 d)

Conclusion: As for Scenario 2, an unacceptable risk was identified in surface water and sediment when no degradation is considered. When degradation is taken into account the risk is acceptable 5 days after treatment for surface water and 8 days for sediment. However further reapplications of b.p. might lead to accumulation of a.s. in surface water and sediment. Therefore the proposed field of use cannot be authorized.
The following 'Field of use' is now proposed:

The product is used to treat small scale water holding features/aquatic areas, not connected to natural aquatic compartment or the STP, such as:

- unused pools
- ponds padded by geofoil
- rainwater holding barrels

which are not used for drinking water storage, irrigation, bathing or for keeping (ornamental) fish, and which may be suitable, temporarily or permanently, for the breeding of mosquito larvae.

Terrestrial compartment

$PNEC_{soil}$ = 0.168 mg/kg_{dwt} (= 0.148 mg/kg_{wwt})

Summary table on calculated PEC/PNEC value	
	$PEC/PNEC_{soil}$
Scenario 2	2.17 x 10^{-4} / 0.148 = 0.0015

Conclusion: An acceptable risk was identified in soil.

Groundwater

Limit value = 0.1 µg/L

Summary table on calculated PEC/Limit value	
	PEC/limit value
Scenario 2	0.02 / 0.1 = 0.2

Conclusion: An acceptable risk was identified in groundwater.

Primary and secondary poisoning

Conclusion: S-methoprene is intended for use outdoors, however exposure of aquatic or terrestrial organisms to S-methoprene is considered to be negligible. No risk assessment for the primary and secondary poisoning is considered necessary.
No risk assessment for bees is considered necessary, either.

Mixture toxicity

Screening step

Screening Step 1: Identification of the concerned environmental compartments

The environmental compartments that are likely to be exposed are the soil, ground water, surface water and sediment compartments.

Screening Step 2: Identification of relevant substances

There is no relevant component of the mixture (in respect to the environment) other than the active ingredient therefore the toxicity and the risk assessment of the active ingredient discussed in the previous paragraphs will cover the toxicity to the environment and risk assessment of the mixture as well.

Summary of relative toxic units		
	Relevant component 1 (active substance)	Relevant Component n
Content in the product [w/w %]	5	n.a.
Concerned environmental compartment 1 *(Aquatic compartment)*		
Organism 1 *(Acute fish)*	100	n.a.
Organism 2 *(Acute daphnia)*	100	n.a.
Organism 3 *(Acute algae)*	100	n.a.
Organism 4 *(Chronic daphnia)*	100	n.a.
Concerned environmental compartment n *(soil)*		
Organism 1 *(earthworm)*	100	n.a.
Organism 1 *(Collembola)*		

Screening Step 3: Screen on synergistic interactions

Screening step	
	Significant exposure of environmental compartments? Y
	Number of relevant substances 1
	Indication for synergistic effects for the product or its constituents in the literature? N

There is no more relevant component except the active ingredient, therefore no synergistic effect would occur. Furthermore the active ingredient S-methoprene is an Insect Growth Regulator (IGR), a Juvenile Hormone Analog. None of the component has the same mode of action and none of them expected to have synergistic effect.

Tiered approach

No relevant component except the active ingredient that has environmental toxicity was identified, therefore mixture risk assessment is covered by the risk assessment of the active ingredient S-methoprene. As all calculated risks of the product are acceptable, no need for tired approach.

Conclusion:
As all calculated risks of the product are negligible or acceptable, no need for tired approach.

Aggregated exposure (combined for relevant emission sources)

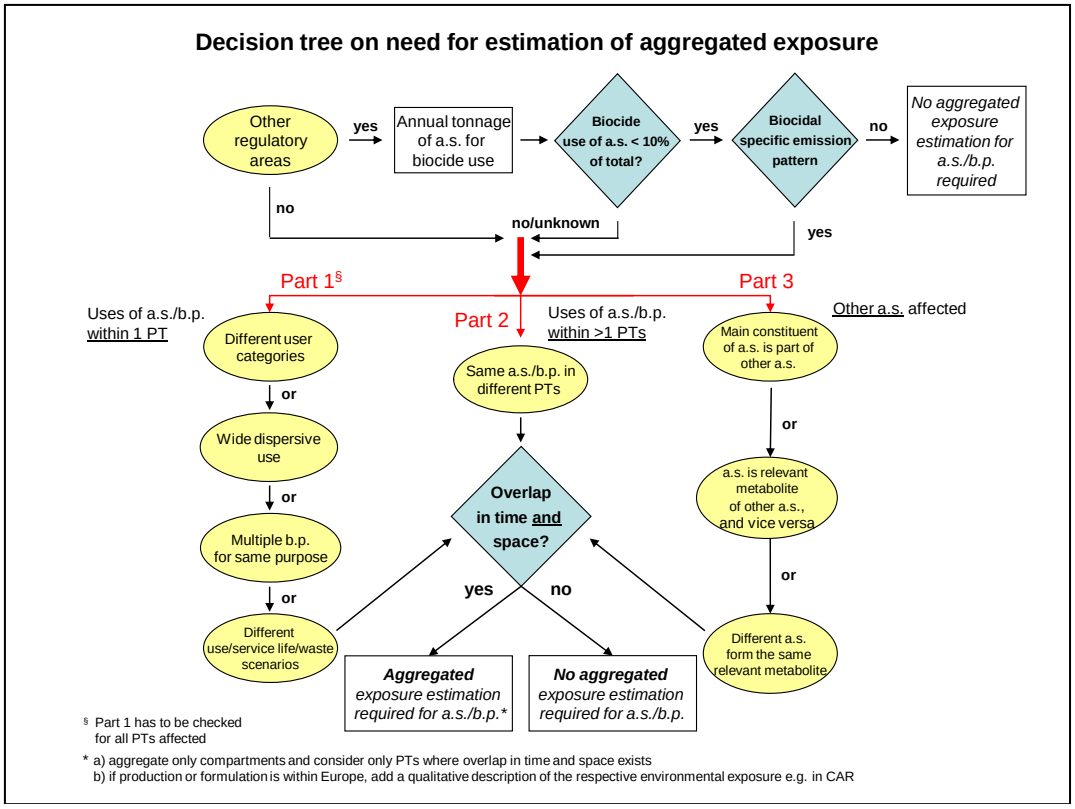


Figure 1: Decision tree on the need for estimation of aggregated exposure

Description:
S-methoprene is also authorized according to the veterinary regulation however S-methoprene mainly used in biocide products in the EU. These products are used in different areas, therefore there is no overlapping use of the products.

Decision steps:

Other regulatory areas?:	Yes
Biocide use of a.s. < 10 %?	No
Different user categories?:	Yes
Overlap in time and space?:	No
Conclusion:	**No aggregated exposure estimation required**

Conclusion: No aggregated exposure estimation required based on the decision tree analysis.

Overall conclusion on the risk assessment for the environment of the product
When used in accordance with the label instructions for Use, BIOPREN BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE complies with the environmental standards and will not cause unacceptable effects to the environment. The uses that can be authorised are those without any release to the aquatic compartment (indirect via the STP or direct).

2.2.9 Measures to protect man, animals and the environment

Detailed instructions are given on the product label.

Statement of risks arising and recommended methods and precautions concerning handling, storage, transport or fire:

Methods and precautions concerning placing on the market
BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is recommended for use by trained professional users.
Methods and precautions concerning handling and use
Eye protection: Not necessary Respiratory protection: Not necessary Other protective equipment: Wear disposable coveralls/gloves during application of the biocidal product. The usual precautionary measures for handling chemicals should be observed.
Methods and precautions concerning storage
Store at room temperature in a dry, cool place, in well ventilated area. Store away from heat, ignition sources and sunlight. Read and follow all precautions and instructions on the product label.
Methods and precautions concerning transport
BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is NOT classified as "Dangerous goods for transport". Proper shipping name: NON HAZARDOUS - not restricted
Methods and precautions concerning fire
Extinguishing media: Water, carbon dioxide Fire fighting procedures: In case of fire no special measures are needed for fire fighting.

Detailed procedures for the use and emergency measures in case of an accident:

Specific treatment in case of an accident, e.g. first-aid measures, antidotes, medical treatment if available		
Eyes	ALWAYS check for and remove contact lenses, wash eyes with plenty of water with eye lids open for at least 15 minutes	
Skin	May cause an allergic skin reaction. Wash affected area with plenty of water and soap, NO scrubbing.	Wash affe water.
Inhalation	Aqueous preparation, vapours are not harmful	
Ingestion	No known adverse effects	Rinse mou
Emergency measures to protect the environment		
Soak up the spilled material with an absorbent, place in a lockup container and handle as hazardous waste. Prevent from reaching surface waters or other water supplies. Avoid contact with skin and clothing.		

Procedures for the destruction or decontamination of the biocidal product and its packaging:

Procedures for waste management of the biocidal product and its packaging and where relevant, treated waste material for industry, professional users and the general public (non-professional users), e.g. possibility of reuse or recycling, neutralisation, conditions for controlled discharge, and incineration	
Disposal:	The product and its container should be disposed of as hazardous waste. Collect spillage. Prevent contamination of environment by wastes. Do not contaminate water, food or feed.
Uncleaned packaging:	Disposal in compliance with official regulations.
RCA/CERCLA hazardous waste:	Not listed.
No preliminary treatment of waste is necessary prior to disposal. Recycling is not an option.	

Possibility of neutralisation:

Possibility of destruction or decontamination following release in the air
The product is intended for trained professionals for outdoor use. It is expected that trained professionals follow good application practices. Only coarse sprayers producing big droplets are recommended. Large droplets settle quickly after application. Further, S-methoprene is non-volatile and is sensitive to light; thus, an accumulation of S-methoprene in air and long-range transport of the product is unlikely.
Possibility of destruction or decontamination following release in water, including drinking water
The product is applied outdoor in controlled way. In the case of accidental exposure, prevent spillages from reaching surface waters or other water supplies. Contain the spill, sweep spillage and transfer into waste containers for disposal. The product contains water and the active ingredient S-methoprene is rapidly degrading in water.
Possibility of destruction or decontamination following release in or on soil
Direct application on soil of the product is not expected. Release to soil is via spray drifting. In the case of accidental exposure, prevent spillages from reaching surface waters or other water supplies. Contain the spill, sweep spillage and transfer into waste containers for disposal. The product contains water ingredients and the active ingredient S-methoprene is rapidly degrading in water.

Controlled incineration

Not applicable.

Measures to protect animals

The product is used against mosquito larvae, therefore pets and wild animals are not expected to get in contact with the product. In addition, S-methoprene has fast photodegradation and biodegradation Therefore no risk mitigation is necessary.

Measures to protect the environment

When used in accordance with the label instructions for Use, BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE complies with the environmental standards and will not cause unacceptable effects to the environment. It is recommended to not apply before 10 days from the first treatment.

2.2.10 Assessment of a combination of biocidal products

BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is not intended to be used with other products, therefore no combined assessment is necessary.

2.2.11 Comparative assessment

Not relevant. S-methoprene is not a candidate for comparative assessment.

2.2.11.1 Screening phase

Not relevant.

2.2.11.2 Tier IA

Not relevant.

2.2.11.3 Tier IB

Not relevant.

2.2.11.4 Tier II

Not relevant.

2.2.11.5 Overall conclusion

Not relevant. S-methoprene is not a candidate for comparative assessment.

3 ANNEXES

3.1 List of studies for the biocidal product XXXXXXXXXXXXXXX

3.2 Output tables from exposure assessment tools

Primary professional exposure scenarios:

Exposure during loading of the product:

Exposure to professional users, Scenario 1 – Mixing: PHED *scenario 3*, All liquids, open mixing and loading

Exposure to professional users, Scenario 2 – Applying: PHED *scenario 13* – Groundboom / Open Cab

Exposure to professional users, Scenario 3 – Mixing & loading PHED *scenario 29* – Groundboom / Open Cab

XXXXXXX

Exposure to professional users, Scenario 4 – Applying: US EPA Occupational Pesticide Handler Unit Exposure Surrogate Reference Table (June 2018)

XXXXXXXXXXX

Exposure to professional users, Scenario 5 – Applying: US EPA Occupational Pesticide Handler Unit Exposure Surrogate Reference Table (June 2018)

XXXXXXXXXX

3.3 New information on the active substance

XXXXXXXXXXX

3.4 Residue behaviour

Not applicable.

3.5 Summaries of the efficacy studies (B.5.10.1-xx)

See IUCLID section 6.7

3.6 Confidential annex

See separate confidential document.

3.7 Other

None.