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

**RISK ASSESSMENT OF A BIOCIDAL PRODUCT FOR NATIONAL AUTHORISATION APPLICATIONS**

(submitted by the eCA)



[Biopren 5 EC Larvicide concentrate]

Product type(s) [18]

[S-methoprene as included in the Union list of approved active substances]

Case Number in R4BP: [BC-QB019622-53]

Evaluating Competent Authority: Ctgb, Netherlands

Date: 31/08/2020

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# CONCLUSION

The physical and chemical properties of Biopren 5 EC have been addressed. Shelf life is 4 years in a plastic container (HDPE and HDPE/PA). Since emulsion stability was not addressed for the accelerated storage stability studies and low temperature stability was not performed, Biopren 5 EC should be stored at a temperature not higher than 30 °C and protected from direct sunlight and frost.

Based on its physical hazards and respective characteristics the product is classified as a category 3 flammable liquid.

The HPLC-UV analytical method used to determine the active substance in the product is sufficiently validated.

The authorised use of Biopren 5 EC will be as an insecticide against flea larvae (*Ctenocephalides*) as a spray treatment for (trained) professional use, indoor. 5 mL of Biopren 5 EC concentrate in 5 L of water is sufficient to spray 100 m2 surface, with a residual efficacy of 12 weeks.

The risk assessment suggests that no adverse systemic or local effects are expected for the professional users when gloves, coverall and eye protections are used during mixing and loading operations, when the product is used as insecticide against flea larvae (*Ctenocephalides*) according to the SPC. No PPE are prescribed during application by spraying.

The risk to the professional users, general public and animals posed by secondary exposure of BIOPREN 5 EC LARVICIDE CONCENTRATE is acceptable, when the product is used as insecticide against flea larvae (*Ctenocephalides*) according to the SPC.

Based on the available data, it can be concluded that BIOPREN 5 EC LARVICIDE CONCENTRATE, when used in accordance with the proposed label (SPC), complies with the environmental standards and will not cause unacceptable effects on the environment.

# ASSESSMENT REPORT

## Summary of the product assessment

### Administrative information

#### Identifier of the product

| **Identifier[[1]](#footnote-2)** | **Country (if relevant)** |
| --- | --- |
| Biopren 5 EC larvicide concentrate | NL |

#### Authorisation holder

|  |  |  |
| --- | --- | --- |
| **Name and address of the authorisation holder** | **Name** | Babolna Bioenvironmental Centre Ltd. |
| **Address** | H-1107 Budapest Szállás utca 6. |
| **Authorisation number** |  | |
| **Date of the authorisation** |  | |
| **Expiry date of the authorisation** |  | |

#### Manufacturer(s) of the products

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

#### Manufacturer(s) of the active substance(s)

|  |  |
| --- | --- |
| **Active substance** | S-methoprene |
| **Name of manufacturer** | Babolna Bioenvironmental Centre Ltd. |
| **Address of manufacturer** | Szállás utca 6, Budapest, 1107, Hungary |
| **Location of manufacturing sites** | Szállás utca 6, Budapest, 1107, Hungary |

### 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

#### Identity of the active substance

|  |  |
| --- | --- |
| **Main constituent(s)** | |
| **ISO name** | S-methoprene |
| **IUPAC or EC name** | Isopropyl-(2E,4E, 7S)-11-methoxy-3,7,11-trimethyl-2,4- dodecadienoate |
| **EC number** | not allocated |
| **CAS number** | 65733-16-6 |
| **Index number in Annex VI of CLP** | Not available |
| **Minimum purity / content** | 95 % |
| **Structural formula** |  |

#### Candidate(s) for substitution

S-methoprene is not a candidate for substitution.

#### Qualitative and quantitative information on the composition of the biocidal product

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Common name** | **IUPAC name** | **Function** | **CAS number** | **EC number** | **Content (%)** |
| S-methoprene  (min. 95%) | Isopropyl-(2E,4E, 7S)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate | Active substance | 65733-16-6 | Not allocated | 6.42  (pure 6.10) |
| Hydrocarbons, C10-C13, n-alkanes, isoalkanes, cyclics, < 2% | Hydrocarbons, C10-C13, n-alkanes, isoalkanes, cyclics, < 2% aromatics | Non-Active substance | - | EC no: N/A  List no.  918-481-9 | ≤ 83.67 |
| Benzenesulfonic acid, 4-C10-14-alkyl derivs., calcium salts | Benzenesulfonic acid, 4-C10-14-alkyl derivs., calcium salts | Non-active substance | 90194-26-6 | 290-635-1 | ≤4.32 |
| 2-methylpropan-1-ol | 2-methylpropan-1-ol | Non-active substance | 78-83-1 | 201-148-0 | ≤2.02 |

The composition details of the full formulation are contained within the confidential annex 3.6

#### Qualitative and quantitative information on the composition of the biocidal product family

Not applicable.

#### Information on technical equivalence

The notified source of S-methoprene is the same as that considered for Annex I inclusion under Council Directive 98/8/EC. Babolna Bio Ltd. is the Annex I notified source of S-methoprene.

#### Information on the substance(s) of concern

Identified substances of concern: Hydrocarbons, C10-C13, n-alkanes, isoalkanes, cyclics, < 2% aromatics, Benzenesulfonic acid, 4-C10-14-alkyl derivs., calcium salts (CAS 90194-26-6), and 2-methylpropan-1-ol (CAS 78-83-1). Please see section 2.1.2.3 and the confidential annex for further details.

No alert for endocrine disruption property was found. For more information please see “Others” in section 2.2.6.1 “Assessment of effects” for human health aspect, and “Further Ecotoxicological studies” in section 2.2.8.1 “Effects assessment on the environment” for environment aspect.

#### Type of formulation

|  |
| --- |
| EC - emulsifiable concentrate |

### Hazard and precautionary statements

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

| **Classification** | |
| --- | --- |
| Hazard category | Flammable Liquid Cat 3  Asp Tox. 1  Eye Dam. 1  Aquatic Chronic 2 |
| Hazard statement | H226 Flammable liquid and vapour  H304 May be fatal if swallowed and enters airways.  H318 Causes serious eye damage  H411 Toxic to aquatic life with long lasting effects  EUH066 Repeated exposure may cause skin dryness or cracking. |
| **Labelling** | |
| Signal words | Danger |
| Hazard statements | as above |
| Precautionary statements | P210 Keep away from heat/sparks/open flames/hot surfaces. — No smoking.  P280 Wear protective gloves/eye protection  P273 Avoid release to the environment  P301+P310 IF SWALLOWED: Immediately call a POISON CENTER/doctor.  P305+P351+P338+P310 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/doctor  P331 Do NOT induce vomiting.  P391 Collect spillage.  P403 + P235 Store in a well-ventilated place. Keep cool.  P405 Store locked up.  P501 Dispose of contents/container to: Residues and packaging of the product must be disposed of as hazardous waste. |
| Note | Hydrocarbons, C10-C13, n-alkanes, isoalkanes, cyclics, < 2% contribute to the classification for H304.  Benzenesulfonic acid, 4-C10-14-alkyl derivs., calcium salts (CAS 90194-26-6), and 2-methylpropan-1-ol (CAS 78-83-1)contribute to the classification for H318 |

### Authorised use(s)

#### Use description

Table 1. Use # 1 – Fleas – professional - indoor

|  |  |
| --- | --- |
| **Product Type** | PT18 - Insecticides, acaricides and products to control other arthropods (Pest control) |
| **Where relevant, an exact description of the authorised use** | Insecticide |
| **Target organism (including development stage)** | *Ctenocephalides­ -* Fleas - Larvae |
| **Field of use** | Indoor  For the treatment of areas where flea larvae might develop and where imagoes are seen, in resting places of pets, on carpets and upholstered furniture. |
| **Application method(s)** | Spraying (a hand-held spraying applicator) |
| Application rate(s) and frequency | Apply the spray to the places where flea larvae develop and where imagoes are seen (as the location of the imagoes is an indication of the location of the flea larvae).  Mix 5 ml of Biopren 5 EC concentrate with water up to a total of 5 L (dilution = 0.1% (1:1000)). 5 litres of working solution is enough to treat 100 m2 surface.  Residual efficacy: Observing the above directions for use and applied at the recommended dose, a 12-week residual effect may be achieved.  Maximum 4 applications of the product per year. |
| **Category(ies) of users** | Professional, trained professional |
| **Pack sizes and packaging material** | HDPE or COEX HDPE/PA opaque bottle:  100, 200, 250, 300, 500, 750, 1000 mL  HDPE or COEX HDPE/PA opaque can:  1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 L |

#### Use-specific instructions for use

|  |
| --- |
| See general directions for use. |

#### Use-specific risk mitigation measures

|  |
| --- |
| See general directions for use. |

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

|  |
| --- |
| See general directions for use. |

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

|  |
| --- |
| See general directions for use. |

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

|  |
| --- |
| See general directions for use. |

### General directions for use

#### Instructions for use

|  |
| --- |
| - Products should always be used in accordance with label instructions.  -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.  -Complementary treatment using adulticide products with prompt effect may be necessary to achieve immediate control of already emerged adult fleas.  Prior to preparing the working solution, shake the concentrate well and reclose the  bottle once the required quantity is measured.  Fill the sprayer (a hand-held spraying applicator of 1-3 bar pressure) with water to half of its volume, measure the quantity of Biopren 5 EC concentrate given below and pour it into the sprayer. After that, fill the sprayer to the desired volume, then mix the working solution thoroughly. Keep the prepared working solution closed and use it up within 48 hours. Shake the working solution from time to time during treatment or every time following longer standing.  It is unlikely that Biopren 5 EC concentrate will damage the treated surfaces, however - in order to prevent it - it is recommended to make a trial application on an inconspicuous area. This is particularly important when treating carpets and upholstery. When used on highly porous surfaces (such as brick, plaster, cement, etc.), efficacy may be reduced.  Mix 5 ml of Biopren® 5 EC concentrate with water up to a total of 5L.  5 litres of working solution is enough to treat 100 m2 surface.  For the treatment of areas where flea larvae might develop and where imagoes are seen, in resting places of pets, on carpets and upholstered furniture. Apply thorough ventilation after treatment.  Do not use the product at outdoor places for domestic animal keeping.  Animals should be kept away during spraying. Do not spray the animals directly. Make sure that pets can re-enter the treated area or lairs only when the spray is fully dried.  Residual efficacy: Observing the above directions for use and applied at the recommended dose, a 12-week residual effect may be achieved. Cleaning and walking on the treated surfaces can lower the residual efficacy.  -Maximum 4 applications of the product per year.  - It is advised to use insecticides with different mode of action (rotation) in the pest control program.  - Where possible, chemical treatments should be recommended to be combined with application of non-chemical measures.  - Complete elimination of pest insects should be attempted in infested areas  - Where an extended period of control is required, treatments should be alternated with products with different modes of action.  - Levels of effectiveness should be monitored, and instances of reduced effectiveness should be investigated for possible evidence of resistance.  -Inform the registration holder if the treatment is ineffective.  -Avoid continuous use of the product. |

#### Risk mitigation measures

|  |
| --- |
| Do not use in animal housing where livestock is kept.  To be used only for insect control and according to the directions for use.  Keep out of reach of children  Do not apply directly on or near food, feed or drinks, or on surfaces or utensils likely to be in direct contact with food, feed, drinks and animals  Do not apply the product directly to humans, domestic animals, plants and bed-clothes.  During application, observe the relevant regulations.  Thoroughly wash hands in hot water and soap after work.  Ensure adequate ventilation during the application.  Wear protective chemical resistant gloves and a protective coverall during product handling phase (glove and coverall material to be specified by the authorisation holder within the product information).  The use of eye/face protection during handling of the product is mandatory.Unprotected persons and animals should be kept away from treated areas until surfaces are dry. After treatment, the treated premises may be re-entered following full drying of the spray and thorough ventilation. |

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

|  |
| --- |
| Inhalation*:* Remove the wounded to fresh air, loosen the tight clothes, rest and keep warm. Get medical attention if feeling unwell.  Skin:Remove the contaminated clothes; wash thoroughly with plenty of water then rinse with soap and water.  Eye*:* Wash out with plenty of water for a few minutes; remove the contact lenses if it’s possible. Rest for 30 minutes and seek an optometrist in case of bulging, redness, and bleary eyes.  Ingestion*:* Do not induce vomiting! Wash the conscious person’s mouth with plenty of water.  Get medical attention if feeling unwell. If swallowed: Immediately call a poison center or doctor. |

#### Instructions for safe disposal of the product and its packaging

|  |
| --- |
| Dispose of the material and the packaging as a hazardous waste.  Recommended disposal: burning. |

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

|  |
| --- |
| Store in original opaque, closed packaging in a dry, cool and well-ventilated place. Protect from radiant heat, direct sunlight and frost. Do not store at temperature higher than 30 °C.  Shelf life is 4 years. |

### Other information

|  |
| --- |
| - |

### 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)** |
| Opaque bottle | 100, 200, 250, 300, 500, 750, 1000 mL | in case of all pack sizes:HDPE or COEX PE/PA (HDPE/PA) | tamper evident plastic cap, the material of the closure is identical to the packaging material | professional | yes |
| Opaque can | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25 L | in case of all pack sizes:HDPE or COEX PE/PA , (HDPE/PA) | tamper evident plastic cap, the material of the closure is identical to the packaging material | professional | yes |

### Documentation

#### Data submitted in relation to product application

Please find the list of studies under 3.3 New information on the active substance point.

#### Access to documentation

Babolna Bio Ltd is the owner of the S-methoprene active substance dossier and also the sponsor of the studies prepared for the BIOPREN 5 EC authorisaton process.

## Assessment of the biocidal product

### Intended use(s) as applied for by the applicant

The uses below are the ones applied for by the applicant, without any changes by the eCA. These uses are assessed in the following chapters.

See 2.1.4 for the authorised uses, after assessment of the dossier.

Table. Intended use # 1 – spraying[[2]](#footnote-3)

|  |  |
| --- | --- |
| Product Type(s) | PT18 - Insecticides, acaricides and products to control other arthropods (Pest control) |
| Where relevant, an exact description of the authorised use | For bed bug control: mix 60 ml of Biopren® 5 EC concentrate with 5 l of water.  As far as possible, apply the spray directly to the insects’ harbourages activity areas.  For flea control: mix 5 ml of Biopren 5 EC concentrate with 5 l of water.  Apply the spray to the places where flea larvae develop and where imagoes are seen.  For moth control: mix 5 ml of Biopren 5 EC concentrate with 5 l of water.  Use a low-pressure sprayer typically used for indoor applications.  On the average, 5 litres of working solution is enough to treat 100 m2 surface. |
| Target organism (including development stage) | Larvae of bed bug, larvae of cat flea, egg and larvae of Indian mealmoth |
| Field of use | indoor |
| Application method(s) | spraying |
| Application rate(s) and frequency | against cat flea and meal moth 5 mL product in 5L water, against bed bug 60 mL product in 5 L water  Frequency depends on the rate of infestation |
| Category(ies) of user(s) | PCO |
| Pack sizes and packaging material | Please see the relevant section. |

Table 2. Intended use # 2 – fogging

|  |  |
| --- | --- |
| Product Type(s) | PT18 - Insecticides, acaricides and products to control other arthropods (Pest control) |
| Where relevant, an exact description of the authorised use |  |
| Target organism (including development stage) | Larvae of Indian mealmoth |
| Field of use | indoor |
| Application method(s) | fogging |
| Application rate(s) and frequency | 20 ml/100 air m3. , frequency depends on the rate of infestation |
| Category(ies) of user(s) | PCO |
| Pack sizes and packaging material | Please see the relevant section. |

### Physical, chemical and technical properties

| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **Reference** |
| --- | --- | --- | --- | --- |
| Physical state at 20 °C and 101.3 kPa | OPPTS 830.6303/  physical state | Biopren 5 EC larvicide concentrate  batch: FN-338  6.3% w/w | Liquid | xxxx. Study 484-630-0680 |
| Colour at 20 °C and 101.3 kPa | OPPTS 830.6302/  colour | Biopren 5 EC larvicide concentrate  batch: FN-338  6.3% w/w | Light yellow | xxxx. Study 484-630-0680 |
| Odour at 20 °C and 101.3 kPa | OPPTS 830.6304/  odour | Biopren 5 EC larvicide concentrate  batch: FN-338  6.3% w/w | Slightly organic solvent like, reminiscent of petroleum | xxxx. Study 484-630-0680 |
| Acidity / alkalinity | CIPAC MT 75.3 | Biopren 5 EC larvicide concentrate  batch: FN-338  6.3% w/w | pH (1% solution): 5.4 at 20±1 °C.  after 4 years of storage:  pH (1% solution): 6.2 at 20±1 °C.  Since 4<pH<10, the acidity or alkalinity are not required. | xxxx. Study 484-122-0701  xxxx. Study 484-122-4095 |
| eCA remark: The pH of the undiluted product is not required as the product is not aqueous. | | | | |
| Relative density / bulk density | OECD 109 | Biopren 5 EC larvicide concentrate  batch: FN-338  6.3% w/w | D204 = 0.811 | xxxx. Study 484-109-0703 |
| Storage stability test – **accelerated storage** | CIPAC MT 46, Validated HPLC-UV method | Biopren 5 EC larvicide concentrate  batch: FN-338  6.3% w/w | The product was stored for 14 days at 54 +/- 2 °C  Active substance content:  Initial: 6.23 %w/w  After: 6.28 %w/w  Appearance: Initial: light yellow liquid, Slightly organic solvent like, reminiscent of petroleum  After: just odour changed a little-Organic solvent like, reminiscent of petroleum  packaging type: HDPE bottle  Appearance of the package did not change.\nce 4<pH<10, the acidity or alkalinity are not required. the authorisation. . kabel, door te kijken of kabels binnen twee ma | xxxx. Study 484-160-0681 |
| eCA remark: The accelerated storage stability study does not comply with the data requirements for an EC formulation. The acidity, alkalinity and/or pH were not determined. In addition, the emulsion stability and re-emulsification were not addressed for the stability at elevated temperature. The label should therefore indicate a temperature restriction: do not store at temperature higher than 30 °C.  The packaging material is specified as “plastic bottle” in the study report. The applicant confirmed the plastic bottle corresponds to a HDPE bottle. | | | | |
| Storage stability test – **long term storage at ambient temperature** | GIFAP Technical Monograph N°17, OPPTS 830.6303 OPPTS 830.6302 OPPTS 830.6304  Active substance content was determined using HPLC (see section 2.2.4) | Biopren 5 EC larvicide concentrate  batch: FN-338  6.3% w/w | The product was stored for 48 months at 20 ± 2 °C. This report contains the results of the real-time stability test after 6, 12, 18, 24, 36, and 48 months. At the beginning and at each analytical occasion the following parameters were assessed:  - active substance content (with validated method)  -appearance of the samples  -appearance of the packaging.  packaging type: HDPE bottle  The parameters remained within acceptable limits.  Active substance content:  initial: 6.13%w/w  6 months: 6.30%w/w  12 months: 6.08%w/w  18 months:  6.11%w/w  24 months: 6.12%w/w  36 months: 6.28%w/w  48 months  5.75%w/w  Decrease: 6.2% w/w  A shelf-life of 4 years is supported. | xxxx. 484-170-0682 |
| eCA remark: The packaging material is specified as “plastic bottle” in the study report. The applicant confirmed the plastic bottle corresponds to an HDPE bottle.  The physical properties required for an Emulsifiable concentrate (EC), i.e. pH and emulsion stability and re-emulsification, were not determined in the long term storage stability study but in a separate study. The pH and emulsion stability, before and after storage, can be found in the corresponding section in this table. | | | | |
| Storage stability test – **low temperature stability test for liquids** | - | - | Waiver:  The melting point of active substance, S-methoprene is  -22 °C so crystallization at 0 °C is improbable. In addition, the mixture is solvent based, more than 80% is hydrocarbons, C10-C13, n-alkanes, isoalkanes, cyclics. Low temperature has no effect on the stability. | - |
| eCA remark: The BPR guidance states that this data requirement applies to all liquids and not just water-based products. Therefore, this waiver is not acceptable. The temperature restriction “protect from frost” will be included on the label. | | | | |
| Effects on content of the active substance and technical characteristics of the biocidal product - **light** | - | - | Waiver:  The opapaque pakaging of the product ensures protection from direct sunlight | - |
| Effects on content of the active substance and technical characteristics of the biocidal product – **temperature and humidity** | - | - | Waiver:  The packaging of the product is waterproof, it ensures protection from the effect of humidity. | - |
| eCA remark: The effect of humidity was sufficiently addressed. The effect of temperature is covered given the long-term stability tests and label requirements stating that the product should be protected from frost and stored at room temperature. | | | | |
| Effects on content of the active substance and technical characteristics of the biocidal product - **reactivity towards container material** | - | - | The accelerated and long-term stability study demonstrated that the plastic (HDPE) packaging material has not reacted with the product. No visible changes were observed in the appearance of the product and packing of the test item during the study. The results can be extrapolated to HDPE PE/PA packaging material according to the relevant guidance. | - |
| eCA remark: Acceptable The relevant guidance is the guidance to the BPR, in which it is stated that data from HDPE can be extrapolated to HDPE/PA. Hence, both packaging materials applied for are supported. | | | | |
| Wettability | - | - | Not required for emulsifiable concentrates. | - |
| Suspensibility, spontaneity and dispersion stability | - | - | Not required for emulsifiable concentrates. | - |
| Wet sieve analysis and dry sieve test | - | - | Not required for emulsifiable concentrates. | - |
| Emulsifiability, re-emulsifiability and emulsion stability | CIPAC MT 36.3 | Biopren 5 EC larvicide concentrate  batch: FN-338  6.3% w/w | Dilutions:  1.2% v/v and 0.1% v/v product in CIPAC Water D.  Complete emulsion was observed for all tests for the 1.2% v/v dilution, except after 24h standing (ca. 1 mL white separate layer at the top of the sample). Re-emulsification resulted in a complete emulsion again and finaly remained complete.  The 0.1% v/v dilution showed complete emulsion or a white precipitation at the top layer. Re-emulsification resulted in a complete emulsion again but a white separate phase formed a ring at the wall of the cylinder.  After storage (4 years):  Dilutions:  1.2% v/v and 0.1% v/v product in CIPAC Water A.  1.2% v/v:  Complete emulsion and 2mL foam was observed at the start, after 30 min and after 2 hours. After 24 hours, ca 1 mL white, ring forming separate phase was observed at the top of the sample. Re-emulsification results in a complete emulsion again and finaly remained complete.  0.1% v/v:  Complete emulsion and 2mL foam was observed at the start, after 30 min and after 2 hours. After 24 hours, ca 1 mL white, ring forming separate phase was observed at the top of the sample. Re-emulsification results in a complete emulsion again and finaly remained complete.  Dilutions:  1.2% v/v and 0.1% v/v product in CIPAC Water D.  1.2% v/v:  Complete emulsion was observed at the start, after 30 min and after 2 hours. After 24 hours, ca 1 mL white, ring forming separate phase was observed at the top of the sample. Re-emulsification results in a complete emulsion again and finaly remained complete.  0.1% v/v:  Complete emulsion was observed at the start, after 30 min and after 2 hours. After 24 hours, ca 1 mL white, ring forming separate phase was observed at the top of the sample. Re-emulsification results in a complete emulsion again and finaly remained complete. | xxxx. Study 484-167-0805  xxxx. Study 484-167-4797 |
| eCA remark: Acceptable. The in-use concentration (0.1% v/v) was used. No emulsion stability and re-emulsification was tested in CIPAC water A prior to storage. Since all tested samples showed <2mL cream after 30 minutes and re-emulsification was complete after 24 h, there is no indication that the emulsion stability and re-emulsification would be different in CIPAC water A prior to storage.  Futhermore, this sentence is included in the use instruction: ‘Shake the working solution from time to time during treatment or every time following longer standing.’ | | | | |
| Disintegration time | - | - | Not required for emulsifiable concentrates. | - |
| Particle size distribution, content of dust/fines, attrition, friability | - | - | Not required for emulsifiable concentrates. MMAD is not required as input parameter for human health as human exposure is based on an indicative value from a spraying model which comprises also inhalative exposure. MMAD is not relevant for efficacy assessment. | - |
| Persistent foaming | CIPAC MT 47.2 | Biopren 5 EC larvicide concentrate  batch:  134168  5.84%w/w  After storage:  Biopren 5 EC larvicide concentrate  batch: FN-338  6.3% w/w | Three replicate measurements were performed  at the in-use concentration (0.1% v/v).  Before storage:  foam after 1 min: 7 mL  foam after 12 min: 0 mL  After 4 years storage:  After 10 sec all foam has disappeared.  Conclusion: after 1 and 12 min: 0 mL foam. | xxxx. Study 484-158-4069  xxxx. Study 484-158-4070 |
| Flowability/Pourability/Dustability | - | - | Not required for emulsifiable concentrates. | - |
| Burning rate — smoke generators | - | - | Not required for emulsifiable concentrates. | - |
| Burning completeness — smoke generators | - | - | Not required for emulsifiable concentrates. | - |
| Composition of smoke — smoke generators | - | - | Not required for emulsifiable concentrates. | - |
| Spraying pattern — aerosols | - | - | Not required for emulsifiable concentrates. The products are not sold in a spraying device of any sort nor in a sparying can and the spraying can is not part of the authorization. | - |
| Physical compatibility | - | - | Not relevant. The product not suggested to use in tank-mix with other products. | - |
| Chemical compatibility | - | - | Not relevant. The product not suggested to use in tank-mix with other products. | - |
| Degree of dissolution and dilution stability | - | - | Not required for emulsifiable concentrate. | - |
| Surface tension | OECD 115  (ring method) | Biopren 5 EC larvicide concentrate  batch: FN-338  6.3% w/w | Aqueous solution (0.1 g / 100 mL) 32.2 mN/m at 20 °C , aqueous solution (1.2 mL / 100 mL) 30.3 mN/m at 20 °C. | xxxx. Study 484-115-0804 |
| eCA remark: Acceptable, given the hydrocarbon content and the kinematic viscosity of the product, the surface tension should have been measured at 25 °C, but given that H304 is assigned regardless of the result of the test at 25 °C, no new study is required. | | | | |
| Viscosity | OECD 114  Viscosity of Liquids;  DIN 53015 Viscometry (falling ball viscometer) | Biopren 5 EC larvicide concentrate  batch: FN-338  6.3% w/w | 20 °C (dynamic): 2.1 mPa\*s,  40 °C (dynamic): 1.5 mPa\*s | xxxx. Study 484-114-0704 |
| eCA remark: An approximation of the kinematic viscosity is 1.85 mm2/s. This was calculated from the density and the dynamic viscosity at 40 °C. Due to the kinematic viscosity and >10% H304 labelled components, H304 is assigned. | | | | |

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| **Conclusion on the physical, chemical and technical properties of the product** |
| Biopren 5 EC larvicide concentrate is a light yellow liquid with slightly organic solvent odour, which is reminiscent of petroleum. The pH of 1% (w/v) aqueous mixture of test item: 5.4 at 20 °C. The relative density of Biopren 5 EC larvicide concentrate is 0.811 at 20 °C. The surface tension of the product (in concentration 0.1 g / 100 mL) was found to be 32.2 mN/m at 20 °C and its dynamic viscosity is 2.1 mPa\*s at 20 °C. The emulsion stability studies of Biopren 5 EC larvicide concentrate show complete emulsion in the initial state and after re-emulsification 24 h later. The results after 48 months storage are acceptable so it supports the 4 years shelf life in the plastic container (HDPE and HDPE/PA). Since emulsion stability was not addressed for the accelerated storage stability studies and low temperature stability was not tested, the product should be stored at a temperature not higher than 30 °C and protected from frost.  H304 is assigned because the product contains a >10% H304 classified component and has a kinematic viscosity of < 20.5 mm2/s. |

### Physical hazards and respective characteristics

| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **Reference** |
| --- | --- | --- | --- | --- |
| Explosives | - | - | Test not relevant to be conducted since none of the components present in the formulated biocide contain groups which may indicate explosive properties as listed in section 2.1.4.2 of the Guidance on the Application of the CLP Criteria. | - |
| Flammable gases | - | - | Test not relevant to be conducted as the biocidal product is not a gas. | - |
| Flammable aerosols | - | - | Not relevant: the product is not sold as an aerosol. | - |
| Oxidising gases | - | - | The product does not need to be considered for this hazard class as it is not a gas. The product is a liquid. | - |
| Gases under pressure | - | - | Not relevant: because the product is not a gas under pressure. The product is a liquid. | - |
| Flash point  Flammable liquids | 440/2008, A.9.  ASTM D93 - 13e1  ASTM D 6450 – 05  ASTM D 7094 - 04  UN Transport subsection 32.5.2 | Biopren 5 EC larvicide concentrate  batch: FN-338  6.3% w/w | The flash point is: 48 °C.  Sustained combustion at 60 °C after 60s heating: the sample ignites and continues to burn for more than 15s.  Conclusion: the product is a category 3 flammable liquid. | xxxx, 484-150-0700  2015  EHT 15145b/RWL, 2015 |
| Flammable solids | - | - | Not relevant, the product is a liquid. | - |
| Self-reactive substances and mixtures | - | - | Based on the composition, there are no chemical groups associated with explosive or self-reactive properties present in any of the constituents’ molecules. | - |
| Pyrophoric liquids | - | - | None of the constituents have pyrophoric properties and according to experience of other studies, the product has no ability to spontaneously ignite in contact with air. | - |
| Pyrophoric solids | - | - | Not relevant the product is a liquid. | - |
| Self-heating substances and mixtures | - | - | Test not considered to be conducted, therefore based on the accelerated- and long-term storage stability studies the product has no self-heating property. | - |
| eCA remark: The product is not a solid nor a liquid adsorbed on large surfaces. Therefore testing is not required. The product is not self-heating. | | | | |
| Substances and mixtures which in contact with water emit flammable gases | - | - | This product is an emusifiable concentrate, it is used after dilution in water. Based on the experience of the other studies conducted on it, the product is not considered to be able to emit any kind of gases when it comes in contact with water. | - |
| Oxidising liquids | - | - | Test not considered to be conducted, ingredients of the product have no oxidizing property. | - |
| Oxidising solids | - | - | Not relevant the product is a liquid. | - |
| Organic peroxides | - | - | None of the constituents of the product contain the bivalent -O-O- moiety, therefore it is not considered to be organic peroxide. | - |
| Corrosive to metals | - | - | Not relevant because the product, Biopren 5 EC larvicide concentrate, is halogen-free, contains no base, no complexing agents and is pH neutral. The low concentration of free sulphonic acids is expected to create a very low ablation rate. | - |
| Auto-ignition temperatures of products (liquids and gases) | DIN 51794 | Biopren 5 EC larvicide concentrate  batch: FN-338  5.86 % w/w | Three replicate main tests were performed under atmospheric pressure.  The lowest ignition temperature was 235 °C in the course of the three main A2 test series. | Determination of the Auto-Ignition Temperature of BIOPREN 5 EC larvicide concentrate, xxxx, Study No.: 484-153-5119 |
| Relative self-ignition temperature for solids | - | - | Not relevant, the product is a liquid. | - |
| Dust explosion hazard | - | - | Not relevant, the product is a liquid. It has no ability to form dust. | - |

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| **Conclusion on the** **physical hazards and respective characteristics of the product** |
| The flash point of the product was determined to be 48 °C, the product sustained combustion, meaning it is classified as a category 3 flammable liquid. Therefore, H226 is assigned. |

### Methods for detection and identification

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Analytical methods for the analysis of the product as such including the active substance, impurities and residues** | | | | | | | | | |
| **Analyte (type of analyte e.g. active substance)** | **Analytical method** | **Fortification range / Number of measurements** | **Linearity** | **Specificity** | **Recovery rate (%)** | | | **Limit of quantification (LOQ) or other limits** | **Reference** |
| Range | Mean | RSD |
| S-methoprene | 0.1g samples are dissolved in 25mL ethanol and diluted 20x with acetonitrile prior to analysis  reverse phase HPLC method with UV detection on a Luna 3μ C18 (2) 100A column | 5.6 and 6.6 %,  5 measurements per concentration | Range:  10 - 14 μg/mL (82-115% of nominal content)  n = 5 (duplicate injection)  y= 102895x + 2729,  r2 = 0.9998 | No significant interference. Representative chromatograms were included in the report (blank formulation, standard, spiked blank formulation). | 98 – 102  100-104 | 100  102 | 1.5  1.5  System precision:  RSD: 0.5%  (n = 7)  Complies with Horwitz criterion (10%): 1.90 | Not required for active substance content determination in a product. | xxxx. Study 484-100-0679 |

eCA remark: The range that is checked for linearity, is 82-115% of the nominal content instead of 80-120% which is required. The active substance content as measured in the storage stability reports stays well within the 82-115% boundaries, therefore these limits are acceptable.

No validated analytical methods for the identified SoCs have been included as for all SoCs it is known that their content is not affected by storage and no new SoCs are formed during storage.

**Analytical methods for water**

This study was evaluated and accepted at active substance level. It is a GC-MS method with an LOQ of 0.1 µg/L.

**Analytical methods for soil**

No analytical methods for soil are necessary for the product based on the following considerations.

According to the ECHA guidance Volume I, Part A, 2.8.2.1 Point 5.2.1 Soil:

“If the active substance degrades very quickly, i.e. DegT50 and DegT90 values of the active substance and the relevant metabolites are lower than two and three days; respectively, analytical methods for residues in soil are not required except in the case of continuous exposure.”

For S-methoprene and its metabolites, none of the criteria above are met. Therefore, no validated analytical method is needed for S-methoprene monitoring.

According to the guidance, in general an environmental risk assessment for the relevant compartments needs to be performed for major metabolites. If there is any reason for concern, a risk assessment also needs to be performed for minor metabolites which are ecotoxicologically relevant. For S-methoprene, no major metabolites have been identified in the soil degradation study.

Minor metabolites lack any environmental relevance as S-methoprene’s mode of action is an insect growth hormone regulator. After degradation, the degradation product will lose that mode of action. According to the degradation pathway described in the soil biodegradation study report, the identified degradation products are intermediates and they are further degrading to “several minor and transient fractions” and as a terminal degradation, significant CO2 production was measured. Therefore, the degradation products are not relevant for environmental risk assessment. Monitoring is not relevant in soil, consequently an analytical method in soil is not necessary.

**Analytical methods for air**

Because the active is non volatile and based on the use pattern, a method of analysis in air is not required.

Biopren 50 LML mosquito larvicide concentrate (case number in R4BP: BC-SN019523-27) is product from the same applicant based on the same active substance and is also used in spray applications. The waiver below is taken from the authorization of Biopren 50 LML mosquito larvicide concentrate:

*No analytical method for S-methoprene residues in air is available in the CAR of the a.s. (PT 18). No analytical method for S-methoprene residues was submitted by the applicant for the authorization of BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE, either.*

*However, BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE is not used as a ‘space spray’; the only application method is ‘surface spraying’ performed in a downwards direction, by backpack or hand-held sprayers, which produce coarse droplets. The VMD of a coarse spray is ca. 400 μm, therefore the droplets settle down quickly.*

*For the application of BIOPREN® 50 LML MOSQUITO LARVICIDE CONCENTRATE, only coarse sprays with big droplets (MMAD >50 μm) are recommended (see ‘Instructions for use’), so the inhalable amount of product is expected to be negligible.*

*The exposure of the atmospheric compartment to S-methoprene is not expected, either. Further, S-methoprene is non-volatile (VP = 1.08 mPa at 25°C) and is sensitive to light; thus, an accumulation of S-methoprene in air and long-range transport of the product is unlikely. The need for monitoring is, therefore, not envisaged.*

Downward spraying is not mentioned as a possible waiver in the guidance and does not actually prevent exposure to air (see section 2.8.2.2: ‘If the substance is volatile (i.e. if the vapour pressure >0.01 Pa) or sprayed, or occurrence in air is otherwise probable, the respective analytical methods need to be submitted’). Considering the waiver was accepted for Biopren 50 LML mosquito larvicide concentrate, the eCA considers that the waiver should be accepted for Biopren 5 EC larvicide concentrate as well and that accepting the waiver should be reconsidered upon renewal of the substance approval.

**Analytical methods for animal and human body fluids and tissues**

S-methoprene is not classified as being toxic or highly toxic. It is therefore proposed in the Assessment Report of the active substance that analytical methods in animal and human body fluids and tissues are not required.

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| **Conclusion on the methods for detection and identification of the product** |
| Validation of the analytical method using a reverse phase HPLC method with UV detection on a Luna 3μ C18 (2) 100A column for the determination of S-Methoprene in BIOPREN 5 EC larvicide concentrate was performed. The procedure was found to be suitable for the analysis. |

### Efficacy against target organisms

#### Function and field of use

Biopren 5 EC is an insecticidal (PT18) concentrate based on S-methoprene as the active substance. The product is intended for the indoor control of flea larvae in domestic, industrial and public areas. The product is to be used by professional and trained professional users.

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

The organisms to be controlled by the product are larvae of fleas (*Ctenocephalides*).

The intended target species bed bug (*Cimex lectularius)* andIndian meal moth (*Plodia interpunctella)* will not be authorised*.* The originally submitted efficacy data with these target species were not sufficient to validate these target species. Therefore, these target species were withdrawn at the request of the applicant. Bed bugs and Indian meal moth are not further discussed in the PAR and no efficacy tests for these species are provided and evaluated.

#### Effects on target organisms, including unacceptable suffering

Juvenile hormone analogues (JHAs) – like the active substance, S-methoprene – act by disrupting developmental processes of holometabolous insects at certain phases of metamorphosis. JHAs have no effect on adult insects exposed at fully developed stage. JHAs’ population control effect is caused by increased mortality in the intermediate developmental stages (during larval-pupal and pupal-adult transformation). In conclusion, S-methoprene prevents new adults from emergence, helping to reduce flea population in infested homes.

The product was tested in the laboratory on *Ctenocephalides felis* resulting in a significant effect (100% reduction) on adult emergence. The product does not cause unacceptable suffering and is highly selective and specific for insect larvae. It is non-toxic to humans and other vertebrates (mammals, birds, etc.).

#### Mode of action, including time delay

Juvenile hormone analogue (JHA) insecticides impair the endocrine system of insects by blocking larval–pupal transformation and pupal-adult metamorphosis. S-methoprene acts as a JH agonist, it mimics the action of JH III. Juvenile hormone is normally produced by larvae and modulates the action of ecdysone burst which occurs at larval molts leading to maintaining larval development. During the early phases of metamorphosis, JH level decreases and thus, the effect of ecdysone can be expressed leading to metamorphic changes. If external JHA is applied during early metamorphosis, it binds to JH-interacting proteins forming a complex which alters the expression of early ecdysone-regulated metamorphic genes required for normal developmental changes. This results in developmental disruption: failure in egg hatching (probably due to the impairment of early embryonic development), increased mortality during pupal development, and - in some species - sterility in the emerged adults. The presence of external JHAs during the last instar phase can also result in the formation of non-viable larval–pupal or pupal–adult intermediates.

Since JHA-type insecticides affect insect development only at specific, susceptible developmental stages, it takes some time before their effects are clearly visible at the level of the entire insect population. Depending on severity of the infestation and life cycle of the target insect, it takes 2-4 weeks to achieve full effect. Based on the results of efficacy tests, the product provides 100% reduction in the emergence of adult fleas within 4 weeks following application, and 12-week-long residuality was achieved on porous and non-porous surfaces. Therefore the product is suitable for reducing flea population indoors applied by spraying on the surfaces as a residual spray treatment.

#### Efficacy data

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Experimental data on the efficacy of the biocidal product against target organism(s)** | | | | | | | |
| **Function** | **Field of use envisaged** | **Test substance** | **Test organism(s)** | **Test method** | **Test system / concentrations applied / exposure time** | **Test results: effects** | **Reference** |
| Insecticide | Indoor | Biopren 5 EC larvicide concentrate  –S-methoprene (6.1 w/w%) | *Ctenocephalides felis*(cat flea) | Laboratory test (screening test, no choice),  supportive data  Spray application  This study used a protocol adapted from the C.E.B. method No. 135 (1st edition: April 1987 Revised:  March 2007) and CEB 159 | Dose calculation: 0.04% is equivalent to 2.00 ml of product in 5 L of water applied on 100 m²,  50 ml/m² of the diluted product. Dose range varied between 1 ml product in 5 L of water (0.02% dilution) and 10 mL product in 5 L of water (0.2% dilution) applied on 100 m2 surface.  Medium: real house dust  5 different treatment doses (0.02%, 0.05%, 0.075%, 0.1% & 0.2% dilution) + untreated control (medium treated by water). 2 replicate per treatment. 25 last instar larvae per replicate.  Treatment: after 30 min incubation on the treated medium , larvae are placed on control medium and maintained for 4 weeks at 24+/-1 °C, 65 +/-5 % RH, light 1200 lux 8 hours + 16 hours darkness, without ventilation.  After 4 weeks, emerged adults are counted. | Inhibition of emergence (%IE) results at the end of the 4 weeks long observation period for cat flea:   |  |  | | --- | --- | | Dilution | Inhibition of emergence | | 0.02 % | 93 % | | 0.05 % | 100% | | 0.075 % | 100% | | 0.1 % | 100% | | 0.2 % | 100% |   Control emergence rate of untreated series was high enough to validate the trial. (88%). | LABORATORY MEASUREMENT OF THE EFFECTIVENESS OF AN  IGR-INSECTICIDE SPECIALITY INTENDED FOR THE CONTROL OF  INSECTS, xxxx, Study number 1873a/1214R |
| Insecticide | Indoor | BIOPREN 5 EC larvicide concentrate –S-methoprene (6.1 w/w%) | *Ctenocephalides felis* (cat flea) | Laboratory test,no choice  Spray application  Combined study: direct spray treatment + residual efficacy study  C.E.B. method No. 135 / 159 (1st edition: April 1987 Revised: March 2007) | Dilution rate: 5 ml product in 5 L water for 100 m2 surface(0.1% dilution).  Tested on carpet (porous surface; 1420 g/m², 4.5 mm hairs) and ceramic tiles (non-porous surface). (The materials were checked as having no effect on the target species before the trial.)  Untreated control treatment: using water without biocide in the same volume.  Storage dimensions: T=22°C+/- 2°C; RH=70+/- 5%;  photoperiod: 16h/8h (light/darkness).  Lighting: typical for agri-food premises, covered with UV protective plastic film. Smooth ventilation: 1 m3/h.  Treatment: in a closed room (60 m3, ca. 22 m2), sheltered from draughts; 15x15 cm pieces of typical surfaces were placed flat on the floor, distributed  randomly within the area treated excluding the edges. Complete drying was achieved 2 hrs after treatment, before the introduction of flea larvae. Conditions: T=21.5-23.1 °C; RH=69-73%, light 700 lux: smooth ventilation 1 m3/h.  50 pcs of 2nd instar larvae were used per replicates.  -4 treated replicates  -4 untreated replicates  Larvae were exposed for 1 hour to the product. Then the insects were removed by  gentle suction and transferred to untreated, inert surfaces  with a nutritious substratum and water available and were kept under control conditions until the emergence of adults.  monitoring period: 4 weeks  Complementary trial was conducted by directly spraying the product onto the target  Organisms (2 ml).    Residual efficacy was tested on aged surfaces: 4, 8, 12 & 16 weeks of aging under the same conditions. | The product applied by spraying on the surfaces as a residual spray treatment, showed:  Inhibition of emergence (%IE) for both surface types:   |  |  | | --- | --- | | Spray trail | Inhibition of emergence | | Direct spray trial | 100 % | | 4 weeks aging | 100% | | 8 weeks aging | 100% | | 12 weeks aging | 100% | | 16 weeks aging | 46% |   data are % of reduction of emergence    Control emergence rates:   |  |  | | --- | --- | | Spray trail | Emergence | | Direct spray trial | 97% | | 4 weeks aging | 96% | | 8 weeks aging | 91% | | 12 weeks aging | 89% | | 16 weeks aging | 95% |   Caution: here the data are  the % of emergence    Control emergence rate of untreated series was high enough to validate the trial. (> 88%). | LABORATORY ASSESSMENT OF AN INSECTICIDE SPECIALITY  INTENDED TO CONTROL FLEAS AS A RESIDUAL SPRAY  TREATMENT, xxxx, 1931-B5EC-F/0515R  This study is mentioned twice in the table to make it clear that two different types of tests are performed. |

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| **Conclusion on the efficacy of the product** |
| Efficacy against fleas was demonstrated in two laboratory tests of which one test was considered as supportive data only.. Both tests were performed with the product to be authorised.  For an evaluation of the label claims, see section 2.2.5.8.  Based on the provided efficacy studies, sufficient efficacy against flea larvae was shown for spray application of 5 ml product diluted with water up to a total of 5 L. 5L is sufficient to treat 100m2 surface. The efficacy tests show 12 weeks long residual efficacy. |

#### Occurrence of resistance and resistance management

The product is intended to be used only indoors, at more or less enclosed, limited locations. Area of use specified in the label claims prevents spreading of affected insects and breeding with wild, naive insect populations which also helps to avoid the development of insecticide resistance.

However, observing the following rules while applying the product is recommended to prevent the development of insecticide resistance:

- It is advised to use insecticides with different mode of action (rotation) in the pest control program.

- Where possible, chemical treatments should be recommended to be combined with application of non-chemical measures.

- Products should always be used in accordance with label instructions.

- Complete elimination of pest insects should be attempted in infested areas

- Where an extended period of control is required, treatments should be alternated with products with different modes of action.

- Levels of effectiveness should be monitored, and instances of reduced effectiveness should be investigated for possible evidence of resistance.

#### Known limitations

Since JHA-type insecticides affect insect development only at specific, susceptible developmental stages, it takes some time before their effects are clearly visible at the level of the entire insect population. Depending on severity of the infestation and life cycle of the target insect, it takes 2-4 weeks to achieve full effect. Complementary treatment using adulticide products with prompt effect may be necessary to achieve immediate control of already emerged adult fleas.

The product is toxic to aquatic life with long lasting effects, therefore it is not recommended to use the product outdoors (in the garden or near water pools and natural water bodies). The product is not suitable for treating clothes and bed linen. Treating of animals (pets) with the product is not allowed, proper veterinary products should be used for this purpose.

When used on highly porous surfaces (such as brick, plaster, cement, etc.), efficacy may be reduced.

#### Evaluation of the label claims

To show efficacy against fleas with a residual efficay of 12 weeks two laboratory tests were provided, both with model species *Ctenocephalides felis*. The first test was considered as supportive data only.

In the first laboratory test,which is considered as supportive data, 5 different treatment doses (0.02%, 0.05%, 0.075%, 0.1% & 0.2% dilution) were tested on a medium of real house dust. After 30 minutes incubation of larvae on the treated medium, larvae were placed on control medium. After 4 weeks emerged adults were counted and sufficient (>80%) inhibition of emergence of adult cat fleas was found for all treatment doses. The claimed treatment dose of 0.1% dilution (5 mL product diluted with water up to 5 litres for treatment of 100 m2 surface) caused a 100% emergence inhibition. Control emergence rate of untreated series (88%) was high enough to validate the trial.

In the second laboratory test both porous/absorbent (carpet, 1420g/m2, 4.5 mm hairs) and non-porous (ceramic tiles) surfaces were tested with a treatment dose of 0.1% dilution. For the direct spray trial 2 ml of product was sprayed directly on the target organisms. For the residual efficacy claim larvae were exposed to the product for 1 hour on aged surfaces (after 4, 8, 12 and 16 weeks). After exposure the flea larvae were placed on a control medium and emergence was observed for 4 weeks. For the direct spray test and for the larvae exposed to aged surfaces up to 12 weeks a 100% inhibition of emergence was observed after 4 weeks, justifying a residual efficacy claim of 12 weeks. Control emergence rate of untreated series (>88%) was high enough to validate the trial.

No simulated use test or field test were provided with flea larvae. However, the eCA considers efficacy of the product to be sufficiently shown with the laboratory test due to the behaviour and biology of the larvae of flea (see justification below).

Flea larvae have limited crawling capacity and usually remain near the spot where they have hatched from the eggs since females lay eggs typically at the same sites where food sources of larvae (skin scales and adult flea fecal material) are available in higher amount (at the nests and resting sites of host animals) (*Dryden and Rust, 1994)[[3]](#footnote-4).*

Flea egg development is highly sensitive to changes in temperature and relative humidity, they require a warm, moist environment to hatch and will desiccate rapidly in dry conditions (*Marchiondo et al., 1999*)[[4]](#footnote-5). Thus, eggs laid close to the host are more likely to hatch. In addition, the negatively phototactic, vermiform larvae are susceptible to heat and desiccation, lack ocelli and legs and move by means of wriggling motions aided by a pair of anal struts in their microhabitats. This process does not allow the larvae to cover long distances (*Rust and Dryden, 1997*)[[5]](#footnote-6), which is also not necessary due to the fact that the right habitat and food are usually already provided. Moreover, prior to spinning of the cocoon, the larvae become even less active.

To sum up, flea larvae can only survive in small, protected microhabitats, and they do not perform significant migration. Due to this fact and because of the microscopic size of the larvae, smaller-scale laboratory trials using the same materials (e.g. carpets) which serve as hiding places for flea larvae can model their living environment in human homes successfully. The addition of free choice in which both treated and non-treated areas are provided in equal reach to the flea larvae (as is one of the main requirements for usual simulated use tests) is practically impossible to produce inside those microhabitats.

Larvae will behave and react the same way on small or large treated pieces of fabrics because they do not move too far from the site where they were placed. As such, in the case of flea larvae it is not expected that larger-scale simulated or field studies would show different results than smaller-scale studies.

Therefore, the eCA considers the results of the laboratory test provided sufficient to show efficacy of the product against flea larvae.

This conclusion is the result of expert’s judgement and is applicable to this particular authorisation only. At product renewal, a field study (or new simulated use study) should be submitted to confirm the efficacy of the product against flea larvae.

Larval stages tested:

Although the tests were conducted with L2-L3 larvae, read across is considered possible to authorise this product as efficacious against all larval stages. Later (L2-3) larval stages represent the worst case scenario in efficacy studies against flea larvae as they are bigger in size and have a thicker and harder cuticle than early larval stages. Therefore, if the product is effective against later larval stages, it can be reasonably assumed, that it is also effective against early larval stages, so read-across can be used.

Using L2-3 flea larval stages in efficacy studies provides more reliable results due to the fact that natural mortality of early larval stages are higher than later stages, moreover, early larval stages are smaller, less visible and it is more difficult to collect and handle them without causing any harm which may have significant impact on the outcome of the study (may cause false positive results) as the number of living larvae after treatment is a critical endpoint in these tests.

Also, since different larval stages do not occur alone under real-life situation, but always in a mixed population, it does not make sense to specify them in the label as the operator can not treat them separately."

Therefore a claim against all larval stages is considered possible.

The intended target species bed bug (*Cimex lectularius)* andIndian meal moth (*Plodia interpunctella)* were withdrawn at the request of the applicant. Therefore, no efficacy tests for these species were provided.

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

Not intended to be used as tank mix. Complementary treatment using proper adulticide products with prompt effect may be allowed to achieve immediate control of already emerged adult fleas since active ingredient of BIOPREN 5 EC has only larvicide effect as an IGR-type substance. If pets are also involved in the insect infestation (e.g. by fleas), using proper veterinary products is recommended to cure them parallel with biocide treatment of the living habitat (using the product directly on vertebrates or other non-target organisms is not recommended).

### Risk assessment for human health

#### Assessment of effects on Human Health

***Skin corrosion and irritation***

No tests with the product are available. 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. See IUCLID section 8.1.1. Based on the calculation method described in Annex I of Regulation 1272/2008/EC, BIOPREN 5 EC LARVICIDE CONCENTRATE is considered not irritating to the skin.

|  |  |
| --- | --- |
| **Conclusion used in Risk Assessment – Skin corrosion and irritation** | |
| Value/conclusion | BIOPREN 5 EC LARVICIDE CONCENTRATE is not a skin irritant |
| Justification for the value/conclusion | On the basis of reactions observed in the S-methoprene skin irritation study S-methoprene is not a skin irritant The co-formulants are present in the biocidal product at concentrations insufficient to trigger the classification of the product. Consequently, based on the criteria defined in CLP Regulation (EC) No. 1272/2008, the product is not a skin irritant or corrosive. |
| Classification of the product according to CLP and DSD | No classification required according to CLP. |

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | Skin corrosion and irritation test on the product |
| Justification | 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. |

***Eye irritation***

No tests with the product are available. 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. See IUCLID section 8.1.2 Based on the calculation method described in Annex I of Regulation 1272/2008/EC, BIOPREN 5 EC LARVICIDE CONCENTRATE is considered to cause damage to eye, and therefore is classified with H318.

|  |  |
| --- | --- |
| **Conclusion used in Risk Assessment – Eye irritation** | |
| Value/conclusion | BIOPREN 5 EC LARVICIDE CONCENTRATE is considered to cause damage to eye, and therefore is classified with H318. |
| Justification for the value/conclusion | The active ingredient S-methoprene is not an eye irritant. The co-formulants (Benzenesulfonic acid, 4-C10-14-alkyl derivs., calcium salts (CAS 90194-26-6), and 2-methylpropan-1-ol (CAS 78-83-1)) however are present in the biocidal product at concentrations sufficient to trigger the classification of the product with H318. |
| Classification of the product according to CLP and DSD | H318 is required according to CLP |

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | Eye irritation test on the product |
| Justification | 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. |

***Respiratory tract irritation***

No tests with the product are available. 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. Based on the calculation method described in Annex I of Regulation 1272/2008/EC, BIOPREN 5 EC LARVICIDE CONCENTRATE is considered not irritating to the respiratory tract.

|  |  |
| --- | --- |
| **Conclusion used in the Risk Assessment – Respiratory tract irritation** | |
| Justification for the conclusion | BIOPREN 5 EC LARVICIDE CONCENTRATE is considered not an irritant to the respiratory tract. |
| Justification for the  conclusion | The active ingredient S-methoprene is not an irritant for the respiratory tract. The co-formulants that are present in the biocidal product do not trigger classification of the product. |
| Classification of the product according to CLP and DSD | No classification required according to CLP |

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | Respiratory tract irritation test on the product |
| Justification | 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. The active ingredient S-methoprene is not an irritant for the respiratory tract. The co-formulants that are present in the biocidal product do not trigger classification of the product. |

***Skin sensitization***

No tests with the product are available. 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. See IUCLID section 8.3.1. Based on the calculation method described in Annex I of Regulation 1272/2008/EC, BIOPREN 5 EC LARVICIDE CONCENTRATE is considered not sensitizing to the skin.

|  |  |
| --- | --- |
| **Conclusion used in Risk Assessment – Skin sensitisation** | |
| Value/conclusion | BIOPREN 5 EC LARVICIDE CONCENTRATE does not need to be classified for skin sensitizing properties. |
| Justification for the value/conclusion | The active ingredient S-methoprene and the co-formulants do not have sensitizing properties. |
| Classification of the product according to CLP and DSD | No classification required according to CLP |

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | Skin sensitisation test on the product |
| Justification | 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. |

***Respiratory sensitization (ADS)***

The active ingredient S-methoprene and the co-formulants do not have sensitizing properties for the respiratory system. Therefore, BIOPREN 5 EC LARVICIDE CONCENTRATE does not need to be classified for respiratory sensitizing properties.

***Acute toxicity***

*Acute toxicity by oral route*

No tests with the product are available. 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. See IUCLID section 8.5.1. Based on the calculation method described in Annex I of Regulation 1272/2008/EC, BIOPREN 5 EC LARVICIDE CONCENTRATE is considered not acute oral toxic.

|  |  |
| --- | --- |
| **Value used in the Risk Assessment – Acute oral toxicity** | |
| Value | BIOPREN 5 EC LARVICIDE CONCENTRATE does not need to be classified for acute oral toxicity. |
| Justification for the selected value | The active ingredient S-methoprene and the co-formulants do not have acute oral toxic properties. |
| Classification of the product according to CLP and DSD | No classification required according to CLP |

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | Acute oral toxicity test on the product |
| Justification | 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. |

*Acute toxicity by inhalation*

No tests with the product are available. 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. See IUCLID section 8.5.2. Based on the calculation method described in Annex I of Regulation 1272/2008/EC, BIOPREN 5 EC LARVICIDE CONCENTRATE is considered not acute inhalation toxic.

|  |  |
| --- | --- |
| **Value used in the Risk Assessment – Acute inhalation toxicity** | |
| Value | BIOPREN 5 EC LARVICIDE CONCENTRATE does not need to be classified for acute inhalation toxicity. |
| Justification for the selected value | The active ingredient S-methoprene and the co-formulants do not have acute inhalation toxic properties. |
| Classification of the product according to CLP and DSD | No classification required according to CLP |

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | Acute inhalation toxicity test on the product |
| Justification | 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. |

*Acute toxicity by dermal route*

No tests with the product are available. 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. See IUCLID section 8.5.3. Based on the calculation method described in Annex I of Regulation 1272/2008/EC, BIOPREN 5 EC LARVICIDE CONCENTRATE is considered not acute dermal toxic.

|  |  |
| --- | --- |
| **Value used in the Risk Assessment – Acute dermal toxicity** | |
| Value | BIOPREN 5 EC LARVICIDE CONCENTRATE does not need to be classified for acute dermal toxicity. |
| Justification for the selected value | The active ingredient S-methoprene and the co-formulants do not have acute dermal toxic properties. |
| Classification of the product according to CLP and DSD | No classification required according to CLP |

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | Acute dermal toxicity test on the product |
| Justification | 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. |

***Information on dermal absorption***

|  |  |
| --- | --- |
| **Value(s) used in the Risk Assessment – Dermal absorption** | |
| Substance | S-methoprene |
| Value(s)\* | 25 % for the concentrate and 35% for the in-use dilutions |
| Justification for the selected value(s) | No data is available for Biopren 5 EC larvicide concentrate. For the concentrate the default values described in Guidance on dermal absorption (EFSA, 2017) 25% for organic solvent formulated formulation is applied. Regarding the dilution 35%, the value determined for oral absorption is applied according to the Guidance on dermal absorption (EFSA, 2017, p20), because in the CAR oral absorption was determined to be 35% for S-methoprene, which is lower than 70% as indicated for organic solvent-based formulations. The actual dermal absorption of S-methoprene from the dilution is not expected to be greater than this value. |

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | Dermal absorption test on the product |
| Justification | The default values described in Guidance on dermal absorption (EFSA, 2017) are applied. |

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

No relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg) was identified in the S-methoprene Assessment Report.

Furthermore, in accordance to the guidance on Substances of Concern (CA-Nov14-Doc.5.11) Benzenesulfonic acid, 4-C10-14-alkyl derivs., calcium salts (CAS 90194-26-6), and 2-methylpropan-1-ol (CAS 78-83-1) are identified as substances of concern, as they contribute to the eye damaging effect of the product, being H318 classified. H318 falls into band B, according to the guidance.

Also, Hydrocarbons, C10-C13, n-alkanes, isoalkanes, cyclics, < 2% aromatics (EC-No 918-481-9) is identified as a SoC, because this substance leads to the assignment of Asp Tox 1 (H304 May be fatal if swallowed and enters airways). H304 falls into band A, according to the guidance.

For this band the application of P-statements normally associated with concerned H statement is considered sufficient. P-statements that are highly recommended for mixutre with H318 for professional use, include

- P280 “Wear protective gloves/eye protection.”,

- P305+P351+P338 “IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.” and

- P310 “Immediately call a POISON CENTER/doctor/…”

are included in the classification and labelling of BIOPREN 5 EC LARVICIDE CONCENTRATE.

Also for H304, highly recommended P-statements

- P301+P310 “IF SWALLOWED: Immediately call a POISON CENTER/doctor.”,

- P331 “Do NOT induce vomiting” and

- P405 “Store locked up”

are included in the classification and labelling of BIOPREN 5 EC LARVICIDE CONCENTRATE.

More details of the SoCs are included in the confidential annex.

***Available toxicological data relating to a mixture***

No tests with the product are available. 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.

***Others***

***Endocrine disruption activity of the biocidal product***

Regarding the active substance, it was concluded in the CAR that, whilst S-methoprene is a juvenile (insect) hormone analogue, there is no evidence of any endocrine disruption potential in the human health or ecotoxicological studies presented in the dossier.

To examine if any of the co-formulants contained in the product may possess ED properties, a screening was performed by examining the co-formulants are

* Classified as CMR or PBT;
  + Identified as ED in the DG Santé’s Impact Assessment study on Screening of available evidence on chemical substances for the identification of endocrine disruptors;
  + Identified as ED in the EU list of potential endocrine disruptors; or
  + Listed in CoRAP linked to ED concerns.

For one co-formulant X (see confidential Annex), an ED concern has been raised and the inclusion of this substance on the CoRAP list has been proposed by one of the EU Member States. Regarding the current application for Biopren 5 EC larvicide concentrate CA NL considers that the ED assessment for this co-formulant X does not need to be included and should await the outcome of the discussions at EU level. If this co-formulant X is concluded to possess ED potency the authorisation granted for Biopren 5 EC larvicide concentrate needs to be re-evaluated. Except for this co-formulant X none of the co-formulants triggered an alert for ED property from this screening. Therefore ED potency of co-formulants was not examined further.

#### Exposure assessment

The active substance, S-methoprene and the product BIOPREN 5 EC LARVICIDE CONCENTRATE is manufactured and formulated in Hungary. Production and formulation of the biocidal product is covered by other legislation.

Potential exposure to S-methoprene from BIOPREN 5 EC LARVICIDE CONCENTRATE will occur through use of the product.

The preparation has to be sprayed onto the floor as a general surface treatment or the hiding places of the pests with an appropriate device, e.g. backpack sprayer, according to the following dosing: 5 ml/100 m2 against fleas.

For exposure assessment, the pure cocnentration instead of the technical concentration S-methoprene was used. However, this does not affect the conclusion.

**Inhalation exposure**

The vapour pressure of the active substance is very low. However, as the product is sprayed, inhalation exposure to spray cannot be excluded.

**Dermal exposure**

The main route of exposure is dermal exposure of users during loading, application and post-application cleaning. After application, non-users might come into contact with BIOPREN 5 EC LARVICIDE CONCENTRATE: infants crawling on the floor in treated areas.

**Oral exposure**

BIOPREN 5 EC LARVICIDE CONCENTRATE is not likely to directly reach the mouth of 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. It is possible however that dermal contamination may lead to oral exposure, if the hands are not washed properly after handling, or by infant due to hand-to-mouth exposure.

**Primary exposure (Professional user):**

The professional user is expected to use gloves and protective clothes. However dermal and inhalation exposure is expected during application or post-application. PPE (gloves and protective clothes) are not considered in Tier 1 exposure calculations.

**Secondary exposure:**

Infants might be exposed dermally and orally while crawling on the floor.

**Local effects:**

BIOPREN 5 EC LARVICIDE CONCENTRATE is classified with H318.

| **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 | no | n.a. |
| Dermal | n.a. | yes | n.a. | n.a. | no | yes | n.a |
| Oral | n.a. | n.a. | n.a. | n.a. | n.a | yes | n.a |

***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. | Open mixing and loading | Primary exposure  Loading of concentrate into spraying device for flea treatment  RISKOFDERM dermal model | Professional |
| 2. | Application | Primary exposure  Spray – surface treatment, against Flea  RISKOFDERM and ART models | Professional |
| 3. | Post-application | Primary exposure  Cleaning spraying equipment  HEAdhoc Recommendation no. 4 | Professional |
| 4. | Indirect | Secondary exposure - Via crawling, General surface treatment  ConsExpo | Infant crawling |

***Industrial exposure***

The active substance, S-methoprene and the product BIOPREN 5 EC LARVICIDE CONCENTRATE manufactured and formulated in Hungary. Production and formulation of the biocidal product is covered by other legislation. Industrial use of BIOPREN 5 EC LARVICIDE CONCENTRATE is not foreseen.

***Professional exposure***

Professional exposure refers to professional users such as a Pest Control Operator (PCO) and / or farmers but they are considered as professionals. In general the 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 biocidal product BIOPREN 5 EC LARVICIDE CONCENTRATE is an emulsifiable concentrate formulation insecticide containing 6.1 % w/w S-methoprene. The product is applied as a diluted surface spray by professional users only. The density of the concentrate product is 0.811 g/ml.

Primary exposure to biocidal products occurs to the individual who directly uses /applies the product. Exposure may occur during the task of mixing&loading, application and cleaning of equipment. During the mixing&loading phase, only dermal exposure is relevant, as the active substance is not volatile and the formation of inhalable droplets is not expected.

Application of the product BIOPREN 5 EC LARVICIDE CONCENTRATE may result in primary exposure via skin contact or via inhalation. Professional pest control operators are trained in the application of biocidal products and as such contamination by ingestion is not expected to occur. The oral route is not considered further.

A separate scenario is included for the **post-application** phase (cleaning of the equipment). For this step, only dermal exposure is considered relevant. Exposure may occur only to the diluted solution during this step.

The product BIOPREN 5 EC LARVICIDE CONCENTRATE is applied diluted as a surface spray to indoor areas at an application rate of 2.5 mg S-methoprene / m2 against fleas.

Professional users are assumed to wear protective gloves when handling the product. However, PPE was not included for Tier 1 exposure calculation assessments.

It is assumed that 100% of inhalation exposure is absorbed. For dermal absorption of the concentrate, the default value according to the EFSA dermal absorption guidance (2017) was used in the calculations (25%). For the dermal absorption of the dilution, the default valueof 50%, based on the EFSA Guidance on dermal absorption as the formulation of 5 mL is diluted in 5 L water, so the default value for water-based solution can be applied according to the EFSA guidance (2017). Moreover, considering the relatively low oral absorption (35%) and based on the available studies performed with comparable formulations demonstarting a relatively low dermal absorption value of up to 5%. Thus based on a weight of evidence approach, the actual dermal absorption of S-methoprene from the dilution is not expected to be greater than this default value of 50%.

*Scenario 1:* Professional use, Open mixing and loading

For the treatment of fleas, **5 ml** concentrate has to be diluted into **5 L** working solution. This amount of working solution is sufficient for the treatment of **100 m2** surface (i.e. 5 ml product/100 m2). Based on the intended use and the ECHA recommended treatment areas (draft ENV WG document 7.3), the maximum application area in one location is 93 m2 for professional flea treatment (general surface, carpet, furniture treatment). The content of an applicator device (**5 L**) is therefore sufficient for the treatment of one location.

During a working day, the pest control operator can usually visit maximum 8-10 locations. This means that as a worst case, **10** mixing&loading events may occur during a day.

For repeated loading of liquids, HEEG Opinion 1 recommends the use of the RISKOFDERM Dermal model or BEAT. As exposure estimations for the application scenario are modelled using RISKOFDERM (Liquid manual loading/pouring), this model has been selected for the mixing&loading scenario as well.

| **Description of Scenario 1:** Flea treatment professional user, mixing and loading | | |
| --- | --- | --- |
| **Professional user** loading the product. Only dermal exposure is included as inhalation exposure during mixing and loading is considered negligible (active substance is considered non-volatile and no aerosols are formed during mixing and loading). | | |
|  | Parameters | Value |
| Tier 1 (no PPE) | Dermal exposure (Hands)1 | 9.2 mg/min |
| Dermal exposure (body) 1 | 28.3 mg/min |
| Task duration | 1 min |
| Number of mixing&loading events/day (worst case) | 10 |
| dermal absorption | 25 % |
| User body weight2 | 60 kg |
| Tier 2 (gloves, coverall) | Protection factor (gloves, coverall)3 | 90% (hands)  80% (body) |

1: RISKOFDERM Toolkit Loading liquid, HEEG opinion 1

2:HEAdhoc Recommendation 14 replacing HEEG Opinion No 17, Default human factor values

3: HEEG opinon 9

Tier 1:Dermal exposure

(9.2 + 28.3) mg/min x 1 min x 10 times/day x 6.1% a.s. x 25% absorption / 60 kgbw

=0.095 mg/kgbw

Tier 2: Dermal exposure

(9.2 mg/min x 10% + (28.3 mg/min x 20%) x 1 min x 10 times/day x 6.1% a.s. x 25% absorption / 60 kgbw

=0.0167 mg/kgbw/day

*Scenario 2:* Professional use, Application – Spray, general surface treatment (flea treatment)

| **Description of Scenario 2:** Spray, general surface treatment against fleas – Estimated with **RISKOFDERM and ART** | | |
| --- | --- | --- |
| **Professional user** applying the diluted product onto surfaces against fleas with the use of a hand-held spraying applicator (1-3 bar pressure)  5 ml product is diluted to 5 L working solution, sufficient for the treatment of 100 m2  Active substance content in the working solution: 0.00495%; density: 1  The settings used for the simulations are the followings:  **Dermal exposure (RISKOFDERM):**   * indoor application * spraying downward * direction of airflow not clearly away from worker * no segregation of the worker from the source * source less than 1 meter from the worker * liquid not highly volatile * application rate 1 L/min * percentile 75th * exposure duration: 480 min (full shift)   **inhalation exposure (ART):**   * indoor application * spraying downward * no segregation of the worker from the source * source less than 1 meter from the worker (near field) * liquid non-volatile * application rate 0.3-3 L/min * natural good ventilation\*1 * vapour pressure 0.000623 Pa * exposure duration: 480 min (full shift)   Furthermore the following parameters were used for the calculation. | | |
|  | Parameters | Value |
| Tier 1 (no PPE) | dermal absorption | 50 % |
| Inhalation absorption | 100 % |
| User body weight | 60 kg |

\*1 natural good ventilation is assured by a RMM “Ensure adequate ventilation during the application”

According to the ECHA Biocides Human Health Exposure Methodology (2015) and HEAdhoc Recommendation No. 6, no specific model is mentioned for general surface spraying against fleas. However, for the professional control of fly larvae by spraying, the HEAdhoc Recommendation no.3 is indicated to be followed.

In HEAdhoc Recommendation 3, it was proposed to use a combination of the exposure assessment models ART and RISKOFDERM for the estimation of inhalation and dermal exposure, respectively. Consequently, an assessment is presented below based on this approach.

For both above-mentioned models, an important parameter to be specified is the application rate. As the product is a concentrate to be diluted and used with spraying applicators (1-3 bar pressure), the application rate will depend on the type of device and nozzle being used for the application. For flea control purposes, this application rate is usually around 0.3-0.5 L/min. As a worst-case approach, the calculations in RISKOFDERM were performed with the rate of 1 L/min and in ART with the application rate range of 0.3-3 L/min.

The model of ART is optimised for the exposure duration of 480 min and this is the default value also appearing in RISKOFDERM, therefore as a wors-case first approach this value was implemented. It is clear however that it is unreasonable that the professional user will be spraying continuously during his whole work shift (the task of loading also needs to be performed and also moving to the locations to be treated).

For further details, output tables and calculations see Annex 3.2.

As a comparison, exposure estimates based on the classical **Spraying model 1** are also included below. This model does not rely on the application rate as the models presented above.

| **Description of Scenario 2:** Spray, general surface treatment – Estimated with **Spraying Model 1** | | |
| --- | --- | --- |
| **Professional user: Exposure values:** Hands (without gloves) = 181 mg/minute, Body = 92 mg/minute, Inhalation =104 mg/m3. Exposure duration 480 min (for better comparability with the models presented above). **Clothes scenario:** Tier 1 – no PPE | | |
|  | Parameters | Value |
| Tier 1 (no PPE) | Indicative value without protective gloves [mg of in-use dilution/minute], dermal exposure | 181 |
| Indicative value [mg in-use dilution/minute], dermal exposure | 92 |
| Indicative value [mg of in-use dilution/m3], inhalation exposure | 104 |
| Active substance content in the working solution | 0.00495% |
| Task duration | 480 min |
| dermal absorption | 50 % |
| Inhalation absorption | 100 % |
| Inhalation rate | 1.25 m3/hour |
| User body weight1 | 60 kg |

1: HEAdhoc Recommendation 14 replacing HEEG Opinion No. 17, Default human factor values

Calculations are included in Annex 3.2.

For dermal exposure, Spraying Model 1 gives higher exposure than RISKOFDERM (0.029 mg/kg bw/day from RISKOFDERM and 0.0757 mg/kg bw/day from Spraying Model 1).

Regarding inhalation exposure, it is evident that Spraying Model 1 estimates higher exposure (0.00008 mg/kg bw/day from ART, 0.0009 mg/kg bw/day from Spraying Model 1), this is due to the fact that Spraying Model 1 is also based on overhead use data, which is not relevant for the current product. This is also indicated in HEAdhoc Recommendation no. 3 - if the application is only downward, Spraying Model 1 will overestimate the exposure.

As in the HEAdhoc Recommendation the RISKOFDERM and ART models are recommended, and based on the intended use pattern these models seem more relevant, the values calculated with these models are taken forward to risk assessment calculations.

*Scenario 3:* Professional use, Post-application – Cleaning after treatment

| **Description of Scenario 3:** Post application step, cleaning of spray equipment – Estimated on the basis of 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.  5 ml product was diluted to 5 L working solution. Active substance content in concentrate: 6,1%, density: 0.811 g/mL. Dilution density may be considered as 1 g/ml. | | |
|  | Parameters | Value |
| Tier 1 (no PPE) | body exposure (HEAdhoc 4) | 19.28 μl/min |
| hand exposure (HEAdhoc 4) | 35.87 μl/min |
| duration of cleaning (HEAdhoc 4) | 20 min |
| dermal absorption | 50 % |
| user body weight1 | 60 kg |

1: HEAdhoc Recommendation 14 replacing HEEG Opinion No 17, Default human factor values

Calculations are included in Annex 3.2.

A separate scenario is included for the cleaning of the spray equipment. Calculations are based on Recommendation no. 4 of the BPC Ad hoc Working Group on Human Exposure (HEAdhoc) (2014).

This recommendation may be considered as an absolute worse case for the current scenario as HEAdhoc recommendation 4 concerns the cleaning of spray equipment in antifouling use (paint spray equipment). The working solution of Biopren 5EC 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. The default value suggested in the Recommendation was 20 minutes, this value was used in the calculations as an absolute worst case, which may be considered as an overestimation of actual expected exposure.

Based on the HEAdhoc Recommendation 4 and realistic post-application conditions, only dermal exposure was considered relevant for this scenario.**Calculations for Scenario 1-3**

| **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 Professional user, mixing & loading | Tier1/no PPE | negligible | 0.095 mg/kg bw/day | n.a. | 0.095 mg/kg bw/day |
| Tier 2/gloves and coverall | negligible | 0.0167 mg/kg bw/day | n.a. | 0.0167 mg/kg bw/day |
| Scenario 2 Professional user, application | Tier1/no PPE | 0.0008 6mg/kg bw/day | 0.054 mg/kg bw/day | n.a. | 0.055 mg /kg bw/day |
| Scenario 3 Professional user, post-application, cleaning of equipment | Tier1/no PPE | negligible | 4.55 x 10-4 mg/kg bw/day | n.a. | 4.55 x 10-4 mg/kg bw/day |

**Further information and considerations on scenario 1-3**

**Relevant information for risk characterisation for local effects:** a risk characterisation for local effects is relevant for the product concentrate, as it is classified as H318, Causes serious eye damage. The professional user only encounters the concentrate when filling the spraying device. In order to prepare the in-use dilution, 5 ml concentrate is diluted to 5 L working solution. In the in-use dilutions, the irritative propreties of the concentrate are no longer relevant and no other local effects are to be expected based on the composition and the concentration of the co-formulants that are classified to be eye damaging/irritating. Consequently, local risk characterisation is only relevant for Scenario 1, mixing&loading. A qualitative assessment is presented for the local effects in risk characterisation section.

*Combined scenarios*

A professional user may be exposed by various scenarios in the same day. It is considered realistic that a professional user is exposed the same day by mixing and loading, application and post application.

| **Summary table: combined systemic exposure from professional uses** | | | | |
| --- | --- | --- | --- | --- |
| **Scenarios combined** | **Estimated inhalation uptake** | **Estimated dermal uptake** | **Estimated oral uptake** | **Estimated total uptake** |
| Scenarios [1+2+3]  Tier 1, no PPE | 0.00008 mg/kg bw/day | 0.15 mg/kg bw/day | n.a. | 0.15 mg/kg bw/day |
| Scenarios [1+2+3]  Tier 2 (gloves and coverall) for scenario 1,  Tier 1, no PPE for scenario 2 and 3 | 0.00008 mg/kg bw/day | 0.072 mg/kg bw/day | n.a. | 0.072 mg/kg bw/day |

***Non-professional exposure***

Not applicable. BIOPREN 5 EC LARVICIDE CONCENTRATE is not intended for non-professional use.

***Exposure of the general public***

Indirect exposure

A secondary exposure scenario describes the exposure of people to a substance through being present during an application task, or being present in places where a substance had been used. Secondary exposure to S-methoprene may occur where an individual is present in a room either during or following the application of the product BIOPREN 5 EC LARVICIDE CONCENTRATE. Possible situations where contact may occur are:

* direct contact with the treated surface. The worst-case scenario for this situation is an infant crawling across the treated surface, with possible dermal and subsequent oral exposure from hand-to-mouth contact.
* residues dislodged from the treated surface (e.g. carpet) during or after vacuuming.
* laundering of contaminated work clothing

The scenario of a infant touching a treated surface represents the worst-case scenario for secondary exposure from these situations. Please see below for detailed calculations for this scenario (scenario 4). The other two scenarios are assessed qualitatively: based on the vapour pressure of the active substance, volatilisation is negligible. Inhalation exposure is not expected to be a relevant route, and it was confirmed to be negligible by screening performed in accordance with HEEG opinion 13 as presented below. Oral exposure, due to hand-to-mouth contact may be considered negligible for adults. Dermal exposure may occur to some extent. Secondary exposure situations represent much lower contact. Additionally, the person applying the product will most likely be different from the person exposed secondarily, thus a combined scenario is not relevant (and if the pest control operator would wash his clothes for himself, this exposure may be considered covered by the 8-hour full shift application scenario). The calculations presented for the quantitatively assessed scenarios represent worst-case exposure, which cover any other possible exposure situations as a risk envelope.

Screening to determine whether inhalation exposure can be considered negligible:

The Human Exposure Expert Group (HEEG) opinion 13 on the assessment of inhalation exposure to volatilised biocides[[6]](#footnote-7) provides the following screening tool to determine whether inhalation exposure can be considered negligible:

Where mw and vp denote the molecular weight (in g/mol) and the vapour pressure (in Pa), for a toddler (based on an inhalation rate of 8 m3/24 hr and bw of 10 kg) and using an AEL expressed in mg a.s./kg bw/d, if



then the risk from inhalation exposure is considered negligible. The assessment assumes that the individual is exposed to the saturated vapour concentration of the active substance for 24 hours a day and therefore reflects a ‘worst-case’ scenario. The calculation of toddler inhalation exposure represents a ‘worst case’ scenario and as such forms the risk envelope for the assessment of an infant, child and/or adult.

The active substance S-methoprene has a molecular weight of 311 g/mol and a vapour pressure of 6.23 x 10-4 Pa at 20°C. The AEL (long term) is 0.076 mg/kg bw/d.

Therefore applying the above equation:



= 0.84

The value of 0.84 is <1 therefore the risk from inhalation exposure to S-methoprene is considered negligible.

In light of the HEEG screening assessment detailed above, secondary inhalation exposure to volatilised S-methoprene has not been considered further.

*Scenario 4:* Secondary exposure - Via crawling, infant, after general surface treatment

| **Description of Scenario 4:** Secondary exposure - Via crawling, infant, general surface treatment. Following flea treatment on relevant surfaces, a (<1 year old) may crawl over the treated area and dermal contact may occur. Hand-to-mouth behaviour can also result in oral exposure. Inhalation exposure is not relevant for this scenario.  “Rubbing off” model from ConsExpo for dermal exposure.  “Constant rate” model from ConsExpo for oral exposure. | | |
| --- | --- | --- |
| **Infant crawling on the treated surface** | | |
|  | Parameters | Value |
| Tier 1 | Dermal absorption | 50% |
| Oral absorption  (from active substance Assessment Report) | 35% |
| Exposed area1 | 2122 cm2 |
| Transfer coefficient  (based on HEAdhoc recommendation 12) | 2000 cm2/h = 0.2 m2/h |
|  |  |
| Dislodgeable amount2 | 0.0122 g product/m2 |
| Ingestion rate3 | 0.004055 mg product/min |
| Exposure frequency4 | once a day |
| Exposure time  (based on RIVM Pest Control Products Fact Sheet) | 1 h |
| Body weight infant  (based on HEAdhoc Recommendation 14) | 8 kg |

1 According to the Pest Control Products Fact Sheet for ConsExpo, dermal exposure of children can take place on any uncovered skin, i.ewhole body excluding the trunk. Based on the HEAdhoc Recommendation no. 14 revising HEEG opinion 17, default body surface areas of infants are 4100 cm2 for the whole body and 1977.6 cm2 for the trunk. Total uncovered area is thus 2122 m2.

2 5 ml product concentrate is applied/100 m2. Product density is 0.811 g/ml. Consequently, 0.04055 g product is applied /m2. According to the Pest Control Products Fact Sheet for ConsExpo, 30% of this amount is dislodgeable, which is 0.0122 g/m2.

3 According to the Pest Control Products Fact Sheet for ConsExpo (chap 2.2.7), the ingestion rate can be calculated based on the assumption that from the total dermal exposure 10% is taken in orally due to hand-mouth contact. The dislodgeable amount was 0.0122 g/m2 (rounded value, the accurate number of dislodgeable product is 0.012165 g/m2) and according to the transfer coefficient, 0.2 m2 is wiped per hour due to skin contact. The resulting dislodgeable amount and potential dermal exposure is thus 0.002433 g product/h = 0.04055 mg product/min. From this amount, 10% may be taken in orally, which is 0.004055 mg product/min.

4 for the assessment using ConsExpo only the acute values were used to assess the exposure per day and not the chronic values, as these values are averaged taken into account the exposure frequency.

Calculations - ConsExpo output table is included in Annex 3.2.

**Calculations for Scenario 4**

| **Summary table: systemic exposure to the general public** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake** | **Estimated dermal uptake** | **Estimated oral uptake** | **Estimated total uptake** |
| Scenario 4  Via crawling, infant, Surface treatment | no PPE | n.a | 9.3x10-3 mg/kg bw/day | 6.5x10-4 mg/kg bw/day | 10x10-3 mg/kg bw/day |

**Further information and considerations on scenario 4**

Secondary Non-Professional Exposure: infant crawling across the floor after general surface spray application:

A risk characterisation for local effects is not relevant for the secondary exposure scenarios. The general public only are exposed the applied dilution, which is a 1000-fold dilution of the concentrate and does not have any properties that are expected to cause adverse local effects.

The product Biopren 5 EC larvicide concentrate may be applied to carpets and/or floor areas for the treatment of fleas. An infant may then crawl across the treated floor area. In addition to the dermal exposure from crawling across the floor, it is further assumed that the infant could be exposed orally due to hand to mouth contact. This scenario has been modelled in ConsExpo Web (version 1.0.3.) in accordance with the RIVM pest control products fact sheet and general fact sheet.

The RIVM pest control products fact sheet states that the “rubbing off” model is used to calculate the dermal exposure to children crawling over a floor surface after any type of spray application. It is assumed that a child crawls over the floor of the treated room for 1 hour a day (RIVM pest control products fact sheet p43).

The transfer coefficient (TC) provides a measure of surface-to-skin residue transfer and is derived from concurrent measurements of exposure and surface residue. The TC value of 0.2 m2/hr has been used based on HEAdhoc Recommendation 12.

Secondary exposure to the product has been calculated using the ‘general’ room dimensions (RIVM general fact sheet p14). The dermal absorption value of 50 % for S-methoprene and an infant bodyweight of 8 kg have been considered for the assessment.

The RIVM pest control products fact sheet (p43) states that the constant rate model should be used to assess oral exposure. The ingestion rate is calculated on the basis that 10% of the dermal exposure is ingested as hand to mouth contact (RIVM pest control products fact sheet p28).

ConsExpo output table is included in Annex 3.2.

*Combined scenarios*

Combined scenarios are not relevant for secondary exposure of BIOPREN 5 EC LARVICIDE CONCENTRATE. Only one scenario was identified.

***Monitoring data***

No monitoring data is available.

***Dietary exposure***

BIOPREN 5 EC LARVICIDE CONCENTRATE is for professional use only. It is expected that the professional user will follow label instructions and will keep general safety rules, therefore oral exposure due to contamination of the product on food can be excluded. Treatment of livestock housings is not intended therefore exposure via this source can be excluded.

The following relevant RMMs are assigned:

*Do not use in animal housing where livestock is kept.*

*Keep out of reach of children*

*Do not apply directly on or near food, feed or drinks, or on surfaces or utensils likely to be in direct contact with food, feed, drinks and animals*

*Unprotected persons and animals should be kept away from treated areas until surfaces are dry’ is included.*

*Thoroughly wash hands in hot water and soap after work.*

*Information of non-biocidal use of the active substance*

In Europe S-methoprene is authorized for biocide and veterinary use. In Australia it is also used for grain treatment.

Residue definitions

| *[***Summary table of other (non-biocidal) uses** | | | |
| --- | --- | --- | --- |
|  | **Sector of use1** | **Intended use** | **Reference value(s) 2** |
| 1. | Biocide, EU |  | Not establised |
| 2. | Veterinary, EU | Spot-on products | Not establised |
| 3. | Agriculture, Australia | Grain treatment |  |
| 4. | No approved for Plant Protection Products |  | As the Maximum Residue Levels in animal products are 0.05\* mg/kg based on the lower limit of analytical determination (in some of the products 0.1 mg/kg as edible offal of swine, bovine, sheep or 0.2 mg/kg as fat free of lean meat of swine, bovine, sheep (see Regulation 899/2012/EC for PPP) |

1 e.g. plant protection products, veterinary use, food or feed additives

2 e.g. MRLs. Use footnotes for references.

*Estimating Livestock Exposure to Active Substances used in Biocidal Products*

The product is applied where flea larvae develop including cracks and crevices. Livestock housings are not intended to be treated thus exposure of livestock can be excluded. To ensure that the product is not used for livestock the following RMM is included:

*Do not use in animal housing where livestock is kept.*

*Do not use on surfaces which may come in direct contact with food feeding stuff and livestock animals*.

**Conclusion**

BIOPREN 5 EC LARVICIDE CONCENTRATE does not pose a concern for consumers. Livestock will be not exposed to BIOPREN 5 EC LARVICIDE CONCENTRATE.

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

The BIOPREN 5 EC LARVICIDE CONCENTRATE is for professional use only.

**Conclusion**

No exposure assessment is needed. No food contamination would occur during the use of BIOPREN 5 EC LARVICIDE CONCENTRATE.

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

Production and formulation is addressed under other EU legislation (e.g. Directive 98/24/EC) and not repeated under Regulation 528/2012 (this principle was agreed at Biocides Technical Meeting TMI06).

***Aggregated exposure***

No metholodology has been developed yet.

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

***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. mixing & Loading, surface treatment | Professional | Tier 1, no PPE | 0.095 mg/kg bw/day |
| Professional | Tier 2/gloves and coverall | 0.0167 mg/kg bw/day |
| 2. Appl., surface treatment | Professional | Tier 1, no PPE | 0.055 mg/kg bw/day |
| 3. Post-applciation, surface treatment | Professional | Tier 1, no PPE | 4.55 x 10-4 mg/kg bw/day |
| 4. Indirect, surface treatment | infant crawling | Tier 1, no PPE | 10 x 10-3 mg/kg bw/day |

| **Summary table: combined systemic exposure from professional uses** | | | | |
| --- | --- | --- | --- | --- |
| **Scenarios combined** | **Estimated inhalation uptake** | **Estimated dermal uptake** | **Estimated oral uptake** | **Estimated total uptake** |
| Scenarios [1+2+3]  Tier 1, no PPE | 0.00008 mg/kg bw/day | 0.124 mg/kg bw/day | n.a. | 0.15 mg/kg bw/day |
| Scenarios [1+2+3]  Tier 2 (gloves and coverall) for scenario 1,  Tier 1, no PPE for scenario 2 and 3 | 0.00008 mg/kg bw/day | 0.072 mg/kg bw/day | n.a. | 0.072 mg/kg bw/day |

#### Risk characterisation for human health

**Reference values to be used in Risk Characterisation**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Reference** | **Study** | **NOAEL (LOAEL)**  **(mg/kg bw/day)** | **AF1** | **Correction for oral absorption** | **Value**  **(mg/kg bw/day)** |
| AELshort-term | developmental rabbit study | 100 | 100 | 0.35 | 0.35 |
| AELmedium-term | dog 90-day repeat oral | 100 | 100 | 0.35 | 0.35 |
| AELlong-term | combined chronic toxicity and carcinogenicity | 21.7 | 100 | 0.35 | 0.076 |
| ARfD | Not established |  |  |  | -- |
| ADI | Not established |  |  |  | -- |

1 10 for interspecies, 10 for intraspecies variability

The ARfD of a chemical can be defined as "an estimate of a substance in food and/or drinking water, normally expressed on a body weight basis, that can be ingested in a period of 24 hours or less, without appreciable health risk to the consumer on the basis of all the known facts at the time of evaluation” (EU guidance, 7199/VI/99/rev 6). Hovewer the setting of ARfD for S-methoprene for which the representative product applied in closed bait boxes indoor was not established.

AELmedium-term:

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

AELlong-term

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

AELshort-term:

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

**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.

***Risk for industrial users***

Not applicable. The product is not intended for use by industrial users.

***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)** |
| Scenario 1 mixing and loading, Surface treatment | Tier 1 | 21.7 | 0.076 | 0.095 | 125 | no |
| Tier 2 (gloves and coverall) | 21.7 | 0.076 | 0.0167 | 22 | yes |
| Scenario 2, Application, Surface treatment | Tier 1 | 21.7 | 0.076 | 0.055 | 72 | yes |
| Scenario 3: Professional use, Post-application | Tier 1 | 21.7 | 0.076 | 4.55 x 10-4 | 0.60 | yes |

**Combined scenarios**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **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)** |
| Scenario 1+2+3  Loading + application + post-application | Tier 1 | 21.7 | 0.076 | 0.15 | 197 | No |
| Scenarios [1+2+3] | Tier 2 (gloves and coverall) for scenario 1,  Tier 1, no PPE for scenario 2 and 3 | 21.7 | 0.076 | 0.072 | 95 | yes |

**Local effects**

S-methoprene does not produce local effects, neither after a single nor repeated exposure.

However, as Biopren 5 EC larvicide concentrate is classified as H318, Causes serious eye damage, a risk characterisation for local effects is relevant. The professional user only encounters the concentrate when filling the spraying device. In order to prepare the in-use dilution, 5 ml concentrate is diluted to 5 L working solution. At this concentration, the irritative propreties of the concentrate are no longer relevant and no other local effects are to be expected based on the composition and concentration of the dilution.

Consequently local risk characterisation is only relevant for Scenario 1, mixing&loading.

A qualitative assessment is presented for the local effects: during the loading step, the user pours 5 ml concentrate into the applicator. For scenario 2 and 3, local risks are not relevant. During spraying the users will only exposed to a working solution, which is a 1000-fold dilution of the concentrate and does not have any properties that are expected to cause adverse local effects.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Hazard** | | | **Exposure** | | | | | | | **Risk** |
| Hazard Cate-  gory | effects in terms of C&L | additional relevant hazard information | PT | Who is exposed? | Tasks, uses, processes | Potential exposure route | Frequency and duration of potential exposure | Potential degree of exposure | Relevant RMM & PPE | Conclusion on risk |
| High | Eye dam. Cat 1, H318 | - | 18 | Professional users | Mixing & loading step – filling the spraying device | splashes to skin and eye | max. 10 mixing & loading events per day.  Less than 1 minute per loading event. | n.r. | labelling for eye damage  instructions for use    use of appropriate PPE (gloves and eye protection) is required for loading,  washing of hands after use (P280 Wear protective gloves/ eye protection) | Acceptable  +appropriate RMM, PPE required  + low chance for eye exposure  +professionals following instructions for use |

**Conclusion**

The risk assessment suggests that no adverse systemic or local effects are expected for the professional users when gloves, coverall and eye protections are used during mixing and loading operations, when the product is used according to the SPC. Further no PPE are prescribed during application by spraying.

Furthremore, no adverse systemic or local effects are expected from the secondary exposure when the product is used according to the SPC.

***Risk for non-professional users***

Not applicable. BIOPREN 5 EC LARVICIDE CONCENTRATE is not intended for non-professional use. The product will not be authorized for non-professional use.

***Risk for the general public***

**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)** |
| Scenario 4 Indirect exp.,  Via crawling, Surface treatment | Tier 1 | 21.7\* | 0.076\* | 10 x 10-3 | 13 | yes |

\*: As exposure of 1/day is assumed for this scenario the use of the long-term AEL is relevant.

The general public only are exposed to the applied dilution, which is a 1000-fold dilution of the concentrate and does not have any properties that are expected to cause adverse local effects. Local effects will not be relevant for this scenario.

From the above risk characterization it can be concluded that the BIOPREN 5 EC LARVICIDE CONCENTRATE has an acceptable human risk based on the evaluated scenario:

* toddler crawling on treated surfaces

**Conclusion**

The risk to the general public posed by secondary exposure of BIOPREN 5 EC LARVICIDE CONCENTRATE is acceptable in the calculated scenario, when the product is used in accordance with the SPC.

***Risk for consumers via residues in food***

BIOPREN 5 EC LARVICIDE CONCENTRATE does not pose a concern for consumers. It is expected that the professional user will follow label instructions and will keep general safety rules. Therefore no exposure on food expected. Treatment of livestock housings is not intended, therefore exposure via this source is not relevant. The following relevant RMMs are prescribed:

*Do not use in animal housing where livestock is kept.*

*Keep out of reach of children*

*Do not apply directly on or near food, feed or drinks, or on surfaces or utensils likely to be in direct contact with food, feed, drinks and animals*

*Unprotected persons and animals should be kept away from treated areas until surfaces are dry’ is included.*

*Thoroughly wash hands in hot water and soap after work.*

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

No relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg) was identified in the S-methoprene Assessment Report.

Based on the Substances of Concern guidance (CA-Nov14-Doc.5.11) Benzenesulfonic acid, 4-C10-14-alkyl derivs., calcium salts and 2-methylpropan-1-ol are identified as substances of concern, as they contribute to the eye damaging effect of the product, being H318 classified. Hydrocarbons, C-10-C13 is also a Substance of concern as it is responsible for the classification for aspiration toxicity, H304. The combined effect of the eye damaging/irritating components has been assessed (see local risk assessment considerations) and the product is classified accordingly. Other combined effects between the active ingredient and the substances of concern are not expected, therefore a combined risk assessment of these components is not relevant.

### Risk assessment for animal health

Treatment of livestock buildings is not intended, and the exposure of livestock is not expected. Domestic animals such as dogs may however come into contact with the product. To minimize the contact the instructions for use include the following measures:

*In case of places used for domestic animal keeping, e.g. dog kennels,**treat the floor and side walls up to a height of about 1 m. Pay special attention to cracks and crevices.* Animals should be kept away during spraying. *Do not spray the animals directly. Make sure that pets can re-enter the treated area or lairs only when the spray is fully dried.*

In addition a RMM “*Unprotected persons and animals should be kept away from treated areas until surfaces are dry*” is included.

. The risk assessment for the general public including an infant did not result in unacceptable risk. Furthermore, as the calucalations for the infant resulted in 8.5% of the long-term AEL, it is not expected that the exposure of smaller domestic animals result in exceedance of the AEL. Therefore all in all no unacceptable risk for animal health was identified.

### Risk assessment for the environment

#### 2.2.8.1 Effects assessment on the environment

PNEC determination on active ingredient S-methoprene:

Details of PNEC determinations are provided in the S-methoprene Assessment Report (2013). PNECs relevant to risk characterisation in the affected compartments are as follows:

PNECs relevant to risk characterisation in the aquatic compartment (hydrosphere) are as follows:

PNECSTP micro-organisms = 6.85 mg/L

PNECaquatic (SW) = 0.00019 mg/L

PNECsediment = 0.00038\* mg/kg wwt

\*At risk assessment stage, according to the guidance, the PNECsed is lowered by a factor of 10 due to the log Kow >5.

***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 *Daphnia magna* with an EC50 of 0.22 mg/L.

A summary of the aquatic ecotoxicological data presented for acute exposure indicates the following key endpoints:

|  |  |
| --- | --- |
| Fish toxicity: | 96 h LC50 in Zebrafish (*Brachydanio rerio*) = 4.26 mg/L |
| Invertebrate toxicity: | 48 h EC50 in Cladoceran (*Daphnia magna*) = 0.22 mg/L |
| Algal toxicity: | 72 h ErC50 in *Selenastrum capricornutum* = 2.264 mg/L |

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

|  |  |
| --- | --- |
| Invertebrate 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 and the product.

***Further Ecotoxicological studies***

Further ecotoxicological studies on terrestrial organisms other than included in the current list of endpoints are submitted by the applicant for risk assessment puposes. The studies have been evaluated by the Dutch eCa. The evaluations are added to the IUCLID dossier. A new PNEC has been derived for soils. The PNECs for STP, surface water and sediment were taken from the current assessment report.

**Summary table - Further ecotoxicological studies**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Summary table of further ecotoxicological studies** | | | | | | | | |
| **Method, Guideline, GLP status, Reliability** | **Species** | **End point** | **Exposure** | | **Results (mg/kg dwt)** | | **Remarks** | **Refe-rence** |
| **Design** | **Dura-tion** | **NOEC** | **EC50 / LC50** |
| OECD 222,  ISO No.: 11268-2GLP, Reliability: 1 | Earthworm (*Eisenia fetida*) | reproduction (56 d)  mortality (28 d) | Reproduction test | 56 d  28 d | 106  213 | 241  (EC50)  404  (LC50) | Nominal 5% OM | IUCLID section 9.2.2.2 |
| OECD 232,  ISO No.: 11267-2GLP, Reliability: 1 | Collembola (*Folsomia candida*) | reproduction (56 d) | Reproduction test | 28 d | 47 | 79.85  (EC50)  24.75 (EC10) | Nominal 5% OM | IUCLID section 9.2.5 |

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| **Conclusion used in Risk Assessment – Further ecotoxicological studies** | |
| Value/conclusion | From the terrestrial study results the *Folsomia candida* (Collembola) EC10 of 24.75 mg/kg dry soil was used for PNECsoil calculation.  The study has been conducted with a high content of organic material in the artificial soil (i.e. 5% peat), the resulting endpoints have 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% is used to convert the endpoint to a standard soil for biocides resulting in a EC10 of 16.83 mg/kg soil dwt.  PNECsoil = 0.168 mg/kg dwt (= 0.148 mg/kg wwt) |
| Justification for the value/conclusion | The most sensitive organism among the species tested is the Collembolan. As two chronic studies were submitted, an assessment factor of 100 is applied because the available terrestrial ecotox data are derived for species belonging to a single trophic level. |

The value of PNECsoil in the Assessment Report of S-methoprene was estimated using the equilibrium partitioning method. (PNECsoil = 0.0003 mg/kg wwt). However new terrestrial studies with S-methoprene have been submitted at time of the BIOPREN 5 EC LARVICIDE CONCENTRATE product dossier submission. The 28 days study result on *Folsomia candida* (Collembola) was a NOECreproduction of 47 mg/kg soil dry weight and for Earthworm the NOECreproduction was 106 mg/kg soil dry weight (56 day) and the NOECmortality was 213 mg/kg soil dry weight (28 day).

Since in the study with *Folsomia candida* already 20% inhibition of reproduction was observed at the level of the NOEC, the 28-d EC10 of 24.75 mg/kg dw is preferred over the NOEC of 47 mg/kg dw. The derivation of the EC10 is described in the study report and the dose-response curve seems to fit very wel to the observed effect percentages.

The study has been conducted with a high content of organic material in the artificial soil (i.e. 5% peat). This means that the resulting endpoints have 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% is used to convert the endpoint to a standard soil for biocides resulting in a EC10 of 16.83 mg/kg soil dwt. As two chronic studies were submitted, an assessment factor of 100 is applied because the available terrestrial ecotox data are derived for species belonging to a single trophic level.

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

Note from the CA evaluator: The derived PNEC is fully in line with guidance in Vol IV Part B+C (2017) and agreed at the 28th BPC meeting, but should be considered with care. From the PPP area it is well known that especially larvicides have very specific modes of action. Therefore possibly sensitive species have not been tested. At present, however, there are no tools on how to address this further.

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

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| --- | --- |
| **Data waiving** | |
| Information requirement | Not relevant |
| Justification | No additional test on other target organisms is needed on the basis of intended uses, data available on the active substance or risk assessment. |

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

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | Not relevant |
| Justification | Not applicable. The product is not applied directly on non-target organisms 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 | Not submitted |
| Justification | No study on acceptance by ingestion of the biocidal product by any non-target organisms thought to be at risk is needed on the basis of intended uses, data available on the active substance or risk assessment. |

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

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | Not relevant |
| Justification | No additional test on secondary ecological effect is needed on the basis of intended uses, data available on the active substance or risk assessment. |

***Endocrine disruption activity of non-active substances***

The Commission Delegated Regulation (EU) 2017/2100 specifying the scientific criteria for the determination of endocrine-disrupting properties (ED criteria) under Regulation (EU) No 528/2012 (BPR) establishes that the ED criteria become applicable by 7 June 2018 for biocides (<https://www.ctgb.nl/onderwerpen/hormoon-verstoorders>).

No further ecotoxicological studies are available for BIOPREN 5 EC LARVICIDE CONCENTRATE. The product was not tested for potential endocrine disruption properties. BIOPREN 5 EC LARVICIDE CONCENTRATE contains the active substance s-methoprene and various co-formulants (see confidential annex).

For s-methoprene no ED assessment is required because for active substances which have been approved, the EU assessment should be followed. The Assessment Report (September 2016) states that s-methoprene is not included in the Commission staff working document on implementation of the EU Strategy for Endocrine Disrupters. Whilst s-methoprene is a juvenile (insect) hormone analogue, there is no evidence of any endocrine disruption potential in the human health or ecotoxicological studies presented in the dossier. As such it has been agreed that S-methoprene should be further assessed with regards to its potential endocrine disruptor properties once further guidance is available and preferably before the product authorisation stage. The conclusion of that assessment might lead to review of the active substance approval.

For the co-formulants a screening was performed by consulting:

* ECHA data for identification of ED and PBT, under REACH or BPR or CLP
* Identified as ED by United States EPA (https://comptox.epa.gov/dashboard/)
* Identified as ED by the United Nations Environment (July 2017) Programme(<http://wedocs.unep.org/bitstream/handle/20.500.11822/25634/edc_report2.pdf?sequence=1&isAllowed=y> and https://wedocs.unep.org/bitstream/handle/20.500.11822/25635/edc\_report2\_factsheet.pdf?sequence=1&isAllowed=y)

Only the co-formulant X triggered an alert for ED property. This co-formulant is included in the United Nations Environment Programme. And this is the same co-formulant that raised a concern based on the available toxicological information (see Section 2.2.6.1). As discussed in Section 2.2.6.1, CA NL considers that the ED assessment should await the outcome of the discussions at EU level. If this co-formulant X is concluded to possess ED potency the authorisation granted for Biopren 5 EC larvicide concentrate needs to be re-evaluated.

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

The product comes in the form of an emulsifiable concentrate. The product is intended for use against against fleas and is applied by professionals indoors by spraying. When treated surfaces are cleaned, the active substance will enter the STP and subsequently the aquatic environment. The active substance in the STP is distributed to the activated sewage sludge which is spread on agricultural land.

The environmental exposure of S-methoprene was assessed in accordance with the OECD Emission Scenario Document No 18., “Emission scenario document for insecticides, acaricides and products to control other arthropods for household and professional uses”.

The preparation has to be sprayed onto the floor as a general surface treatment or the hiding places of the pests. On the average, 5 litres of working solution is enough to treat 100 m2 surface. As product residuality is 12 weeks, frequency of use will be between 3-11 times per year (if re-treatment is considered every 12 weeks, the result is 4 treatments per year). The product needs to be applied with an appropriate device, e.g. backpack sprayers according to the following dosing: 5 ml/100 m2 against fleas.

For the exposure and risk assessment of BIOPREN 5 EC LARVICIDE CONCENTRATE on the environment the representative use scenario was evaluated.

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

Further studies on fate and behaviour have been submitted by the applicant for risk assessment puposes. It concerns a study on biodegradability in sewage sludge to determine if the active substance may be inherently biodegradable, one study on biodegradation in soils, and one study on degradation in water-sediment systems.

These studies were already included as the post-approval studies in the CAR for S-methoprene (and discussed by member states during BPC-15 and BPC-16). The additional studies were submitted for commenting at BPC-15 (2016). eCA IE received comments from both DE and DK. After a three-week commenting period, it was addressed at BPC-16 that there were no further comments and IE updated the CAR addendum and LoEP based on the comments received.

The evaluation of the study on biodegradation of S-methoprene in sewage sludge by the eCA IE is included below for completeness.

##### **Biodegradability (ready/inherent)**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Summary table - biodegradation studies (ready/inherent)** | | | | | | | | | | | |
| Method, Guideline, GLP status, Realibility | **Test type1** | **Test parameter** | **Inoculum** | | | **Additional substrate** | **Test sub-stance concentr.** | **Degradation** | | **Remarks** | **Reference** |
| Type | Concen­tration | Adap­tation | Incuba-tion period | Degree [%] |
| Modified MITI Test (II), OECD guideline 302C, GLP,  The study was considered acceptable with a Reliability score of 1. | Inherent Biodegradability | See below | Activated sludge | 100 ppm | None | n/a | 30 ppm | 28 days | > 70% | See below | xxxx; Inherent Biodegradability of S-Methoprene In Modified MITI Test (II). xxxx, unpublished report No.: 484.462.3617  IUCLID section 10.2 |
| 1 Test on inherent or ready biodegradability according to OECD criteria | | | | | | | | | | | |

|  |  |
| --- | --- |
| **Conclusion used in Risk Assessment – Further studies on fate and behaviour in the environment** | |
| Value/conclusion | kdeg for the STP = 0/d |
| Justification for the value/conclusion | The biochemical oxygen demand (BOD) values were measured continuously during the experiment.   * Under the test conditions the percentage biodegradation of S-Methoprene reached a mean of 4.2 % after 7 days, 24.5 % after 14 days, 77.5 % after 21 days and 85.8 % after 28 days based on its ThOD. * The Inherent biodegradability of S-Methoprene Technical was determined from the BOD measurement over 28 days according to OECD guideline 302C. The percentage of degradation of S-Methoprene Technical was calculated using the BOD method, and supplemental chemical analysis was also carried out using HPLC method with UV detection on a Phenomenex, Luna 3µ C18 column.   From the BOD method the biodegradability was calculated to be 85.8% and by chemical analysis the degradation was found to be 74.2%.  This 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. |

***Leaching behaviour (ADS)***

For product type 18 Insecticides a leaching study is not relevant.

***Testing for distribution and dissipation in soil (ADS)***

A study considering aerobic degradation of S-methoprene in soil was submitted by the applicant for risk assessment puposes. This study is already included as post-approval study in the CAR for S-methoprene (and discussed by member states during BPC-15 and BPC-16). The additional studies were submitted for commenting at BPC-15 (2016). eCA IE received comments from both DE and DK. After a three-week commenting period, it was addressed at BPC-16 that there were no further comments and IE updated the CAR addendum and LoEP based on the comments received. The evaluation of the study on aerobic degradation of S-methoprene in soil by the eCA IE is included below for completeness.

**Aerobic biodegradation**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Summary table – aerobic biodegradation in soil- laboratory study** | | | | | | | | | | |
| **Method, Guideline, GLP status, Reliability** | **Test type1** | **Test system** | | | | **Test sub-stance concentra-tion** | **Incu-bation period** | **Degra-dation**  **DT50\*** | **Remarks** | **Reference** |
| Soil origin | Soil type | pH | OC % |
| Aerobic transformation in soil, OECD 307, GLP, The study was considered acceptable with a Reliability score of 1. | Soil degradation study | Germany | Loamy sand | 5.5 | 1.61 | 0.52 mg/kg | 120 days | 1.76 days | See below | xxxx, Degradation and Metabolism in Four Soils of [14C] S-methoprene Incubated under Aerobic Conditions. xxxx  IUCLID section 10.2 |
| Germany | Sandy Loam | 6.0 | 0.67 | 1.38 days |
| Germany | Clay | 7.1 | 1.73 | 1.50 days |
| Germany | Silt Loam | 6.29 | 1.13 | 1.57 days |

\* Geomean DT50 for the four soils = 1.55 days

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| --- | --- |
| **Conclusion used in Risk Assessment –Distribution and dissipation in soil** | |
| Value/conclusion | DT50 is 1.55 d at 12°C (geometric mean, n=4) |
| Justification for the value/conclusion | The route and rate of degradation of [14C]S-methoprene in four soils incubated under aerobic conditions at 20  2 °C in the dark were investigated.   * [14C]S-methoprene degraded rapidly in all four soils with DT50 values of 0.93, 0.78, 0.79 and 0.83 days in soils I, II, III and IV, respectively. When coverted to 12 °C, this gives DT50 values of 1.76, 1.38, 1.50 and 1.57 days in soils I, II, III and IV, respectively. * Besides the parent compound one metabolite was identified by co-chromatography as Isopropyl (2E,4E)-11-hydroxy-3,7,11-trimethyldodeca-2,4-dienoate (R4) reaching maximum mean amounts of 2.3%, 2.5%, 2.5% and 3.5% of applied on day 1 in soils I to IV, respectively. * All other radioactive fractions were minor and transient, not exceeding 5.9% of the applied radioactivity at any sampling interval. * High mineralisation of the radioactive residues to radiolabeled carbon dioxide was observed in all soils reaching maximum levels of 51.1%, 61.5%, 52.4% and 52.4% of the applied radioactivity for soils I to IV, respectively, on day 118. * The amount of non-extractable radioactivity was also significant, amounting to maximum mean values of 48.6% to 54.1% of the applied radioactivity during the 118-day incubation period. By the end of the study (day 118), the level of bound residues had declined. Organic matter fractionation on day 28 indicated that the majority of the non-extractable radioactivity was bound to the immobile humic acids and humins (26.7 – 41.4% of the applied radioactivity). Lower amounts of radioactivity (6.7 – 12.1% of applied) were detected in the more mobile fulvic acid fraction. * The main degradation pathway of S-methoprene in soil proceeds via biodegradation beyond Isopropyl (2E,4E)-11-hydroxy-3,7,11-trimethyldodeca-2,4-dienoate (R4) as degradation inter-mediate and several minor and transient fractions. In addition, a significant 14CO2 production and formation of bound residues was observed. |

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

A water/sediment dissipation study was submitted by the applicant for risk assessment puposes. This study is already included as post-approval study in the CAR for S-methoprene (and discussed by member states during BPC-15 and BPC-16). The additional studies were submitted for commenting at BPC-15 (2016). eCA IE received comments from both DE and DK. After a three-week commenting period, it was addressed at BPC-16 that there were no further comments and IE updated the CAR addendum and LoEP based on the comments received. The evaluation of the water/sediment dissipation study by the eCA IE is included below for completeness.

**Water/sediment degradation test**

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Summary table – fresh water/sediment degradation** | | | | | | | | |
| **Method, Guideline, GLP status, Reliability** | **Test type1** | **Test system** | | **Test substance concentra-tion** | **Incubation period** | **Degradation**  **(DT50 /days)** | **Remarks** | **Reference** |
| Water | Sediment |
| Aerobic transformation in aquatic sediment systems, OECD 308, GLP, The study was considered acceptable with a Reliability score of 1. | Biodegradation in freshwater | River Rhine, Mumpf, AG, Switzerland | | 0.059 mg/kg total system | 100 days | |  |  | | --- | --- | | Parent |  | | total system | 2.50 | | Metabolite M2 |  | | total system | 5.40 | | Metabolite M3 |  | | total system | 2.29 | | See below | xxxx, Route and Rate of Degradation of [14C]S-Methoprene in Aerobic Aquatic Sediment Systems. xxxx, unpublished report no.: D93728  IUCLID section 10.2 |
| Fröschweiher pond, Möhlin, AG/Switzerland | | 0.061mg/kg total system | |  |  | | --- | --- | | Parent |  | | total system | 1.65\* | | Metabolite M2 |  | | total system | 9.88 | | Metabolite M3 |  | | total system | 3.64 | |

\* parameter was derived using DFOP kinetics. Comparison of biphasic kinetic parameters with trigger cutoffs is not ideal. Therefore calculation of the DT50 from the slow phase of the degradation yields a more conservative estimate of degradation:

DT50 = ln2/k1 = 0.6931/0.1089 = 6.4 days @ T = 20 °C or 12.1 days @ T = 12 °C.

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| **Conclusion used in Risk Assessment –distribution and dissipation in water and sediment** | |
| Value/conclusion | DT50 at 20°C are 0.65 d in water, 5.01 d in sediment, and 1.07 d for the whole system (geometric mean, n=2), corresponding to respectively 1.23, 9.50, and 2.03 d at 12°C. |
| Justification for the value/conclusion | Data indicated that [14C] *S*-Methoprene and metabolites degraded at a very rapid rate and showed rapid dissipation from the total system.   * Total recoveries of the applied radioactivity (material balances) averaged 92.7 ± 7.2% and 96.1 ± 10.7% of the applied radioactivity for the river and pond systems, respectively. * After treatment, the majority of the radioactivity applied was detected in the water phase, representing 100.5% and 104.5% of the applied radioactivity for river and pond, respectively. In both systems the level of radioactivity in the water phase rapidly decreased over time, mainly by degradation and adsorption to the sediment. Within two days, the amount in the water phase had decreased to 38.2% and 28.5% of applied radioactivity for river and pond systems respectively. On Day 100, corresponding values were 1.2% and 0.6% of the applied radioactivity for river and pond, respectively. * The total extractable radioactivity from sediments initially increased reaching maximum mean amounts of 21.2% (river) and 25.5% (pond) of applied after two days. Thereafter, levels decreased and on Day 100, 3.4% and 2.0% of the applied radioactivity was still extractable from the river and pond sediments, respectively. Soxhlet extractions were performed from Day 2 onwards, recovered up to 3.4% (river system, Day 2) and 4.7% (pond system, Day 14) of the applied radioactivity. * The formation of radioactive carbon dioxide was significant, and constantly increased throughout incubation in both systems, reaching maximum mean amounts of 54.9% (river) and 67.5% (pond) of the applied radioactivity after 100 days of incubation. Organic volatile compounds never exceeded 0.6% of the applied radioactivity in either system. * The relative amounts of [14C]*S*-Methoprene and degradation products present in water and the sediment extracts were determined by chromatographic profiling by normal phase TLC. * Significant metabolites in the water phase were M2 (R4 = NL 3.1.1.1) and M3 (R1 = FN 263). M2 reached up to 7.8% in the river and 6.2% in the pond waters by Day 2, and was detected until Day 21 in some samples. Maximum mean levels of M3 were 10.2% (river) and 5.8% pond, observed on Day 2. On all other sampling days, the concentrations of Metabolite M3 remained below 1%. * The amounts of the test item reached maximum values after two days of incubation. At this interval the mean concentrations of [14C]*S*-Methoprene in the river sediment were 16.6% and 20.8% in the pond sediment. These amounts decreased to 3.3% of applied in the river sediment and to 1.7% in the pond sediment by Day 49. In both sediments M2 (R4 = NL 3.1.1.1) and M3 (R1 = FN 263) were the predominant metabolites, but the levels did not exceed 1.9% of applied in either sediment, and had decreased to levels below 1% by Day 49. One additional metabolite M1 was detected which appeared to be less polar that the parent [14C]*S-*Methoprene. M1 reached maximum mean levels 1.9% (river, Day 21) and 2.5% (pond, Day 14).   S-Methoprene degrades at a very rapid rate when applied to an aerobic aquatic environment. 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.   |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | **S-Methoprene** | **Test System @ T = 20°C** | | | | | | | | **Converted to T = 12°C** | | | **Best fit** | **M(0) %** | **K1(d-1)** | **K2(d-1)** | **g** | **DT50 (d)\*** | **DT90 (d)\*** | **x2 error** | **DT 50 (d)\*** | **DT 90 (d)\*** | | River (water) | SFO | 95.9 | 0.8862 | - | - | 0.78 | 2.60 | 0.554 | 1.48 | 4.93 | | Pond (water) | SFO | 99.1 | 1.2950 | - | - | 0.54 | 1.78 | 0.982 | 1.02 | 3.38 | | River (sediment) | SFO | 16.1 | 0.1855 | - | - | 3.74 | 12.4 | 34.2 | 7.09 | 23.5 | | Pond (sediment) | SFO | 20.9 | 0.1032 | - | - | 6.72 | 22.3 | 7.23 | 12.8 | 42.3 | | River (total system) | SFO | 95.7 | 0.5235 | - | - | 1.32 | 4.40 | 9.98 | 2.50 | 8.34 | | Pond (total system) | DFOP | 99.1 | 0.109 | 1.223 | 0.2756 | 0.87 | 9.31 | 3.12 | 1.65 | 17.7 | | **M2 (NL 3.1.1.1)** |  |  |  |  |  |  |  |  |  |  | | River (total system) | SFO | 0 | 0.2429 | - | - | 2.85 | 9.48 | 18.5 | 5.40 | 18.0 | | Pond (total system | SFO | 0 | 0.1329 | - | - | 5.21 | 17.32 | 28.2 | 9.88 | 32.9 | | **M3 (FN 263)** |  |  |  |  |  |  |  |  |  |  | | River (total system) | SFO | 0 | 0.5745 | - | - | 1.21 | 4.01 | 21.0 | 2.29 | 7.60 | | Pond (total system | SFO | 0 | 0.3613 | - | - | 1.92 | 6.37 | 28.6 | 3.64 | 12.1 |   \* The values quoted for water and sediiment phases refer to dissipation. The total system values refer to degradation |

***Testing for distribution and dissipation in air (ADS)***

|  |  |
| --- | --- |
| **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 possibility of long-range environmental transport (LRT) has been evaluated in the AR of S-methoprene and it was concluded that it was not expected that the substance will fulfil  the screening criteria for the potential for LRT. S-methoprene is also not a persistent organic pollutant (POP).  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 therefopre 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. BIOPREN 5 EC LARVICIDE CONCENTRATE is applied indoors and therefore an overspray study is not required.

***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)***

Not applicable. BIOPREN 5 EC LARVICIDE CONCENTRATE is applied indoors and therefore an overspray study is not required.

#### 2.2.8.2 Exposure assessment

**General information**

|  |  |
| --- | --- |
| Assessed PT | PT 18 |
| Assessed scenarios | Scenario 1: Flea treatment |
| ESD(s) used | OECD Emission Scenario Document No 18: “Emission scenario document for insecticides, acaricides and products to control other arthropods for household and professional uses, July 2008  Technical Agreements for Biocides. European Chemicals Agency, Report no. ECHA-17-R-19-EN, Helsinki, Finland, August 2017. |
| Approach | Average consumption  Scenario 1: spray application against fleas – carpets, furniture, surfaces |
| Distribution in the environment | Calculated based on Guidance on BPR Vol IV Part B+C (2017) and SimpleTreat version 3 |
| Groundwater simulation | No |
| Confidential Annexes | No |
| Life cycle steps assessed | Scenario 1:  Production: No  Formulation No  Use: Yes  Service life: Yes |
| Remarks | None |

**Release pathways:**

Insecticides applied indoors will generally reach the treated surfaces (furniture, equipment, clothes, walls, floor…), the walls and the floor (even if not directly targeted), the applicator and the indoor air in the building. As a result, insecticides will generally not reach directly the environmental compartments usually considered in emission scenario documents: surface water (including sediments), soil (including groundwater) and air. Therefore, indoor receiving materials will be considered as “intermediate compartments”. As a matter of fact most surfaces (either target or not) will be cleaned. The cleaning step will therefore lead to releases either to wastes (e.g. through dry cleaning methods like vacuuming) or to waste water (e.g. through wet cleaning methods). Therefore the sewage treatment plants (STP) is considered as one of the main “receiving compartments” where insecticides will be released through wet cleaning events. As a worst case, it is considered that emissions to indoor air are completely released to the outdoor air compartment during e.g. venting of the room.

**Scenarios:**

For the use of BIOPREN 5 EC LARVICIDE CONCENTRATE the following scenario can be identified for the risk assessment:

Scenario 1 Flea treatment:

The environmental exposure of S-methoprene was assessed in accordance with the OECD Emission Scenario Document No 18., “Emission scenario document for insecticides, acaricides and products to control other arthropods for household and professional uses” and default values agreed at TMI and II 2010.

The preparation has to be sprayed against fleas onto infested surfaces, carpets or furniture. On the average, 5 litres of working solution is enough to treat 100 m2 surface. As product residuality is 12 weeks, frequency of use will be between 3-11 times per year (if re-treatment is considered every 12 weeks, the result is 4 treatments per year). The product needs to be applied with an appropriate device, e.g. backpack sprayers according to the following dosing: 5 ml/100 m2 against fleas.

***Emission estimation***

Scenario 1 Flea treatment:

In this scenario the product is applied as spray application as general surface treatment (e.g. resting places of dogs and cats kept in the flat, carpets, upholstered furniture).

According to the ESD for PT 18 (2008), emissions to the STP from indoor surface treatment occur due to wet cleaning of the floor/treated area and due to wet cleaning of the clothes of the applicator.

Treated areas were selected as 22 m2 in standard houses and 93 m2 in larger buildings, based on ECHA recommendations on generic treatment areas (currently in draft version; ENV WG item 7.3e) and the Technical Agreements for Biocides (TAB, 2017). The corresponding wet cleaned areas are 5.9 m2 in standard houses and 27 m2 in larger buildings. Larger treated surfaces are not relevant for this scenario, as the fleas typically appear nearby their host organisms, e.g. the resting places of dogs or cats, carpets, furniture, etc. The majority of adult fleas can be found on the host animals, while eggs, larvae and pupae are mainly present around the hosts, e.g. between fibres of the carpet, and typically develop in these microhabitats, with limited access to escaping from the treated area. Whole houses and whole large buildings do not have to be treated in order to achieve appropriate control. The treatment pattern is closer to spot treatment, furthermore carpets or furniture are not relevant for wet cleaning. The above-mentioned treatment areas represent a realistic worst-case value for this use.

By default the e-CA performs the risk assessment with a pure concentration active substance instead of a technical concentration. The issue of using a pure versus a technical concentration in the risk assessment should be discussed elsewhere. For this specific PAR, the difference does not change the conclusions.

The frequency of treatment was set at maximum 3-11 times per year. Product residuality against fleas was proven to be 12 weeks, therefore more frequent treatments than this are not necessary (if re-treatment is considered every 12 weeks, the result is 4 treatments per year). Consequently, the simultaneity factor is 0.00815 (0.815%) based on the ESD.

Taking the default parameters for sprays onto surfaces described in the ESD into account, the use of the product results in the following emissions during the preparation and application step.

| **Emissions during preparation and application for surface treatment of fleas in houses and larger buildings** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Parameter** | **Symbol** | **Unit** | **Houses** | **Larger buildings** | **S/D/O\*** |
| Area treated | AREAtreated | m² | 22 | 93 | D |
| Area wet rooms | AREAwet rooms | m² | 5.9 | 27 | D |
| Fraction surfaces cleaned during the cleaning step with emission to waste water | F ww | - | 1 | 1 | O |
| Fraction of active substance in the commercial product | FAI | - | 0.061 | 0.061 | S |
| **Preparation** | | | | | |
| Container volume | - | L | 5 | 5 | S |
| Fraction emitted to applicator during preparation step | Fprep,applicator | - | 0.0012 | 0.0012 | D |
| Fraction emitted to floor during preparation step | Fprep,floor | - | 0.0004 | 0.0004 | D |
| Quantity of commercial product used per preparation\*\* | Qprod,prep | g | 4.055 | 4.055 | S |
| Number of preparations per day\*\*\* | Nprep,building | d-1 | 1 | 1 | S |
| Emission to the applicator during preparation step | Eprep,applicator | kg a.s./d | 2.97E-07 | 2.97E-07 | O |
| Emission to floor during preparation step | Eprep, floor | kg a.s./d | 9.89E-08 | 9.89E-08 | O |
| **Application** | | | | | |
| Fraction emitted to air during application | Fapplication,air | - | 0.02 | 0.02 | D |
| Fraction emitted to applicator during application | Fapplication,applicator | - | 0.02 | 0.02 | D |
| Fraction emitted to floor during application | Fapplication,floor | - | 0.11 | 0.11 | D |
| Fraction emitted to treated surfaces during application | Fapplication,treated | - | 0.85 | 0.85 | D |
| Number of applications per day per building | Napplication,building | d-1 | 1 | 1 | S |
| Quantity of commercial product applied | Qprod | kg/m² | 4.06-05 | 4.06E-05 | S |
| Emission to the air during application step | Eapplication, air | kg a.s./d | Negligible and not further assessed | | O |
| Emission to the applicator during application step | Eapplication, applicator | kg a.s./d | 1.09E-06 | 4.60E-06 | O |
| Emission to wet cleaned floor during application step | Eapplication, floor | kg a.s./d | 1.61E-06 | 7.35E-06 | O |
| Emission to wet cleaned treated surfaces during application | Eapplication, treated | kg a.s./d | 1.24E-05 | 5.68E-05 | O |
| **Preparation and application** | | | | | |
| Fraction emitted to waste water by the applicator during the cleaning step | Fapplicator,ww | - | 1 | 1 | D |
| Applicator | Eapplicator, ww | kg a.s./d | 1.39E-06 | 4.90E-06 | O |
| Emission to waste water preparation to floor step | Eprep,floor,ww | kg a.s./d | 9.89E-08 | 9.89E-08 | O |
| Cleaning efficiency for floor and treated surfaces | Fce | - | 0.5 | 0.5 | D |
| Floor/treated surface | Etreated, ww | kg a.s./d | 7.01E-06 | 3.22E-05 | O |
| Local emission to STP/building | Elocalww | kg a.s./d | 8.49E-06 | 3.72E-05 | O |
| Simultaneity factor | Fsimultaneity | - | 0.00815 | 0.00815 | D |
| Daily local emission to STP (total) | Elocal, ww, total | kg a.s./d | 3.68E-04 | | O |

\*S = set, D = default, O = output

\*\* Product density is 0.811 g/ml, thus 5 ml product = 4.055 g

\*\*\* 5L of working solution is sufficent for 100m2 therefore 22 m2 requires 1 preparation and 93 m2 treatment also requires 1 preparation

The emissions to STP are calculated applying a simultaneity factor of 0.815% and 4000 treated private houses and 300 larger buildings. This results in a total emission from both types of buildings of **3.68E-04 kg a.s./d**.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Overview emission to waste water (Elocal, wastewater) (kg a.s./d)** | | | | |
| **Emission to waste water after** | **Symbol** | **Houses** | **Larger buildings** | **Combined emission** |
| **Fleas - indoor treatment** | | | | |
| Emission to waste water from applicator | Eapplicator,ww | 1.39E-06 | 4.90E-06 | 5.71E-05 |
| Emission to waste water preparation to floor step | Eprep,floor,ww | 9.89E-08 | 9.89E-08 | 3.47E-06 |
| Emission to waste water from floor and treated surfaces | Etreated,ww | 7.01E-06 | 3.22E-05 | 3.07E-04 |

***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, Flea treatment | Yes | Yes | No | No | Yes | Not relevant | Yes | Yes | No |

\* Emission to the soil compartment concerns only the route after cleaning via sewer to an STP, adsorbed to sludge and brought on land.

The active substance’s properties applied for the exposure assessment are summarised below.

|  |  |  |  |
| --- | --- | --- | --- |
| **Input parameters for calculating the fate and distribution in the environment** | | | |
| **Input** | **Value** | **Unit** | **Remarks** |
| Concentration of active substance in the product | 61 | g/kg | - |
| Molecular weight of S-methoprene | 310.48 | g/mol | - |
| Melting point | 53.8 | °C | calculated with Epiweb 4.1 |
| Vapour pressure (20°C) | 6.23E-04 | Pa | - |
| Experimental solubility (20°C) | 6.85 | mg/L | - |
| Henry’s Law Constant (20 °C) | 0.0306 | Pa/m3/mol | calculated |
| Organic carbon-water partitioning coefficient (Koc) | 8.76E+02 | L/kg | - |
| Log Octanol/water partition coefficient | 6.34 | Log 10 | calculated |
| Biodegradability | Not Ready biodegradable |  | - |
| Half-life for biodegradation in soil (Geometric mean, 12 °C) | 1.55 | day | - |

Distribution in the sewage treatment plant was calculated according SimpleTreat. The

values applied in the risk assessment are summarised below.

|  |  |  |
| --- | --- | --- |
| **Calculated fate and distribution in the STP** | | |
| Compartment | Percentage [%] | Remarks |
| To air | n.r. | - |
| To water | 90.2 |
| Via sludge | 9.8 |
| - primary sludge | 7.0 |
| - surplus sludge | 2.7 |
| Degraded | 0 |

**Calculations**

***Calculated PEC values***

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Summary table on calculated PEC values** | | | | | |
| **Uses** | **PECSTP** | **PECwater** | **PECsed** | **PECsoil** | **PECGW** |
| [mg/L] | [mg/L] | [mg/kgwwt] | [mg/kg wwt] | [μg/L] |
| Fleas - indoor treatment | 1.66E-04 | 1.66E-05 | 3.27E-04 | 6.69E-05 | 3.21E-04 |

***Primary and secondary poisoning***

As the log Kow of the active substance is >3 (6.34 L/kg), the potential for bioaccumulation is considered high. As no experimental data is available, the expected bioconcentration factor (BCF) is calculated to be 516 L/kg. However, significant accumulation in terrestrial organisms (earthworms) is not expected as the active substance disappears quickly from soils (DT50 = 1.55 days at 12°C) and bioaccumulation of extreme hydrophobic compounds such as s-methoprene is slow (takes weeks to reach equilibrium), significant uptake is not expected.

The accompanied risks for birds and mammals is expected to be low regarding secondary poisoning as the active substance quickly disappears from soils as explained previously.

#### Risk characterisation

***Atmosphere***

Conclusion:

Criteria for the examination of environmental risks to air are not specified in the form of a numerical standard. The assessment of potential impacts on air quality is aimed to minimize the risk for stratospheric ozone depletion. There are no indications that S-methoprene contributes to depletion of the ozone layer as the compound is not listed as ‘controlled substance’ in Annex I of Regulation (EC) No 1005/2009 of the European Parliament. Moreover, AOPwin calculates for the active substance a half life of 4.6 hours in air (OH timeframe 24 hrs/day, 0.5×106 OH radicals/cm3). The calculated half life is below the trigger of 2 days, which is used as cut off value to identify chemicals that could be of potential concern for long range transport through the atmosphere. The environmental risk to air is therefore considered acceptable.

***Sewage treatment plant (STP)***

|  |  |
| --- | --- |
| **Summary table on calculated PEC/PNEC values** | |
| Uses | **PEC/PNECSTP** |
| Fleas - indoor treatment | < 0.001 |

Conclusion:

From the above results it can be concluded that the risk for micro-organisms in the STP is acceptable.

***Aquatic compartment***

|  |  |  |
| --- | --- | --- |
| **Summary table on calculated PEC/PNEC values for the aquatic compartment** | | |
|  | **PEC/PNECwater** | **PEC/PNECsediment** |
| Fleas - indoor treatment | 0.087 | 0.86 |

Conclusion:

From the above result it can be concluded that the risk to aquatic and sediment dwelling organisms is acceptable.

***Terrestrial compartment***

|  |  |
| --- | --- |
| **Summary table on calculated PEC/PNEC values for the receiving soil compartment** | |
|  | **PEC/PNECSoil** |
| Fleas - indoor treatment | < 0.001 |

Conclusion: From the above results it can be concluded that the risk for terrestrial organisms is acceptable.

The risk assessment to arthropods is considered to be similar to soil organisms due to their direct contact with soils. The standards for soil arthropods are therefore met. Because the active substance is expected to have a non-systemic mode of action, secondary exposure of bees through pollen is considered negligible. Hence, the risk for bees is considered acceptable for the active substance.

***Groundwater***

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).

|  |  |
| --- | --- |
| **Summary table on calculated PEC values for ground water** | |
|  | **PECporewater (µg/L)** |
| Fleas - indoor treatment | 3.21E-04 |

Conclusion: From the above results it can be concluded that the standards for groundwater are met.

***Primary and secondary poisoning***

Primary poisoning

As the log Kow of the active substance is >3 (6.34 L/kg), the potential for bioaccumulation is considered high. As no experimental data is available, the expected bioconcentration factor (BCF) is calculated to be 516 L/kg. However, significant accumulation in terrestrial organisms (earthworms) is not expected as the active substance disappears quickly from soils (DT50 = 1.55 days at 12°C) and bioaccumulation of extreme hydrophobic compounds such as S-methoprene is slow (takes weeks to reach equilibrium), significant uptake is not expected.

The accompanied risks for birds and mammals is expected to be low regarding secondary poisoning as the active substance quickly disappears from soils as explained previously. It is furthermore expected that birds and mammals are not directly exposed to contaminated larvae as the product is used indoor and the secondary exposure is only possible in case the STP sludge is spread on agricultural soil as a fertilizer. However the exposure is negligible as can be seen from the calculations.

***Mixture toxicity***

*Screening step*

Screening Step 1: Identification of the concerned environmental compartments

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

Screening Step 2: Identification of relevant substances

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

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

Conclusion: The only relevant component in the mixture is the active ingredient. No risk was identified for all relevant environmental compartments when applying the product against fleas.

***Aggregated exposure (combined for relevant emmission 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 is mainly used in biocide products in the EU. These products are used in different areas, therefore there is no overlapping use of the underlying products.

Decision steps:

Other regulatory areas?: Yes

Biocide use of a.s. < 10 %? No

Different user categories?: Yes

Overlap in time and sapace?: 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** |
| Based on the available data, it can be concluded that BIOPREN 5 EC LARVICIDE CONCENTRATE, when used in accordance with the proposed label (SPC), complies with the environmental standards and will not cause unacceptable effects on the environment. |

### Measures to protect man, animals and the environment

BIOPREN 5 EC LARVICIDE CONCENTRATE is used indoors against fleas.

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 5 EC LARVICIDE CONCENTRATE is recommended for use by professional pest control operators. Specific training is not required for the use of BIOPREN 5 EC LARVICIDE CONCENTRATE. |
| ***Methods and precautions concerning handling and use*** |
| Eye protection: Goggles  Respiratory protection: In the absence of suitable ventilation use face mask with  filter (A-type)!  Other protective equipment: Other protective equipment: gloves, normal protective clothes, take it off  after work  The usual precautionary measures for handling chemicals should be observed. |
| ***Methods and precautions concerning storage*** |
| Safe storage: Store in a cool, dry, well-ventilated room upright in original packaging. Keep away from heat, flames, other sources of ignition and strong oxidising agents (e.g. peroxides). If the quantity is higher, safe electrical equipment (against explosion) and lights are necessary. Keep away from food, feed! |
| ***Methods and precautions concerning transport*** |
| UN-number 1993  Proper shipping name according United Nations:  UN 1993 Flammable liquids, n.o.s (2-methylpropan-1-ol)  Danger class(es): 3  Packaging group: III |
| ***Methods and precautions concerning fire*** |
| Extinguishing media: carbon dioxide, alcohol resistant foam, water mist. Use water jet to cool containers.  Fire fighting procedures: wear self-contained breathing apparatus and usual protective clothes. |

**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 | Causes serious eye damage | Flush with water for a few minutes, seek an optometrist in case of bulging, redness, and bleary eyes. | | Skin | No known adverse effects | Wash affected area with soap and water. | | Inhalation |  | Inhalation exposure not likely. Get medical attention if feel unwell. | | Ingestion | No known adverse effects | Rinse mouth, drink some water | |
| ***Emergency measures to protect the environment*** |
| If spillageoccursadsorb with a suitable non-combustible material (sand, dry earth, etc.) and place into waste containers for disposal. Clean the spill area with detergent and hot water. Contain the spill. 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: Dispose off the material and the packaging as a hazardous waste. 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** |
| Not applicable as the product is applied indoors in controlled way. The active substance, S-methoprene is non-volatile (vapour pressure approximately 3.15 mPa) and therefore release to the air is not envisaged. |
| **Possibility of destruction or decontamination following release in water, including drinking water** |
| Release to water is not likely considering the use pattern of the product: indoor use 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 S-methoprene active ingredient which 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 fertilizing the soil with STP sludge. 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 S-methoprene active ingredient which is rapidly degrading in water. |

**Controlled incineration:**

Dispose of the material and the packaging as a hazardous waste. Recommended disposal: burning.

**Measures to protect animals:**

The product is used indoors therefore wild animals are not expected to get in contact with the product. Pets should not be present during application of the product. No risk mitigation is necessary.

**Measures to protect the environment**

When used in accordance with the label instructions for use, BIOPREN 5 EC LARVICIDE CONCENTRATE complies with the environmental standards and will not cause unacceptable effects to the environment. No risk mitigation measures are necessary.

### Assessment of a combination of biocidal products

BIOPREN 5 EC LARVICIDE CONCENTRATE is not intended to be used with other products, therefore no combined assessment is necessary.

### Comparative assessment

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

# Annexes[[7]](#footnote-8)

## List of studies for the biocidal product

| Section No / Reference No | Author(s) | Year | Title  Source (where different from company)  Company  Report No.  GLP (where relevant)  (Un)Published | Data Protection Claimed (Yes/No) | Owner |
| --- | --- | --- | --- | --- | --- |
| IUCLID  3.1. | xxxx | 2015 | Determination of the Appearance of BIOPREN 5 EC larvicide concentrate, xxxxx, Unpublished | Yes | Bábolna Bio Ltd. |
| IUCLID  3.2. | xxxx | 2015 | Determination of the pH Values of Biopren 5 EC larvicide concentrate, xxxx Unpublished | Yes | Bábolna Bio Ltd. |
| IUCLID  3.2. | xxxx | 2018 | Determination of the pH Values of Biopren 5 EC larvicide concentrate after storage | Yes | Bábolna Bio Ltd. |
| IUCLID  3.2. | xxxx | 2019 | Determination of the pH Values of Biopren 5 EC larvicide concentrate after storage | Yes | Bábolna Bio Ltd. |
| IUCLID  3.2. | xxxx | 2015 | Determination of the Acidity/Alkalinity of Biopren 5 EC larvicide concentrate ,xxxx, Unpublished | Yes | Bábolna Bio Ltd. |
| IUCLID  3.3. | xxxx | 2015 | Determination of the Relative Density of Biopren 5 EC larvicide concentrate, xxxx, Unpublished | Yes | Bábolna Bio Ltd. |
| IUCLID  3.4.1. | xxxx | 2015 | Determination of the Accelerated Storage Stability of BIOPREN 5 EC larvicide concentrate, xxxx, Unpublished | Yes | Bábolna Bio Ltd. |
| IUCLID  3.4.1. | xxxx | 2015-2019 | Determination of the Long-term Storage Stability of BIOPREN 5 EC larvicide concentrate, xxxx, Unpublished | Yes | Bábolna Bio Ltd. |
| IUCLID  3.5. | xxxx | 2015 | Determination of Flash Point of Biopren 5 EC larvicide concentrate, xxxx, Unpublished Y Bábolna Bio Ltd. | Yes | Bábolna Bio Ltd. |
| IUCLID  3.5. | xxxx | 2015 | Determination of the Emulsification Stability of Biopren 5 EC larvicide concentrate, xxxx, Unpublished | Yes | Bábolna Bio Ltd. |
| IUCLID  3.5. | xxxx | 2018 | Determination of the Emulsification Stability of Biopren 5 EC larvicide concentrate | Yes | Bábolna Bio Ltd. |
| IUCLID  3.5. | xxxx | 2019 | Determination of the Emulsification Stability of Biopren 5 EC larvicide concentrate | Yes | Bábolna Bio Ltd. |
| IUCLID  3.5. | xxxx | 2018 | Determination of the persistent foaming of Biopren 5 EC larvicide concentrate | Yes | Bábolna Bio Ltd. |
| IUCLID  3.5. | xxxx | 2018 | Determination of Persistent Foaming of BIOPREN 5 EC larvicide concentrate (after storage) | Yes | Bábolna Bio Ltd. |
| IUCLID  3.5. | xxxx | 2019 | Determination of Persistent Foaming of BIOPREN 5 EC larvicide concentrate  484-158-4796 | Yes | Bábolna Bio Ltd. |
| IUCLID  3.8. | xxxx | 2015 | Determination of the Surface Tension of Biopren 5 EC larvicide concentrate, xxxx, Unpublished | Yes | Bábolna Bio Ltd. |
| IUCLID  3.9. | xxxx | 2015 | Determination of the Viscosity of Biopren 5 EC larvicide concentrate, xxxx, Unpublished | Yes | Bábolna Bio Ltd. |
| IUCLID  4.2. | -- | 2015 | DETERMINATION OF THE SUSTAINED COMBUSTIBILITY TESTED TO UN TRANSPORT “MANUAL OF TESTS AND CRITERIA, PART III, SUBSECTION 32.5.2” OF A SAMPLE OF BIOPREN 5 EC LARVICIDE CONCENTRATE xxxx, xxxx, Study No: EHT15145b/RWL, Unpublished | Yes | Bábolna Bio Ltd. |
| IUCLID  4.17. | xxxx | 2019 | Study Report  Determination of the Auto-Ignition Temperature of  BIOPREN 5 EC larvicide concentrate | Yes | Bábolna Bio Ltd. |
| IUCLID  5. | xxxx | 2015 | Validation of the Analytical Method (HPLC) for the determination of S-Methoprene in BIOPREN 5 EC larvicide concentrate, xxxx, Unpublished | Yes | Bábolna Bio Ltd. |
| IUCLID  6.7. | xxxx | 2014 | Laboratory measurement of the effectiveness of an IGR-insecticide speciality intended for the control of insects, xxxx, Study No: 1873a/1214R, Unpublished | Yes | Bábolna Bio Ltd. |
| IUCLID  6.7. | xxxx | 2015 | Laboratory assessment of an insecticide speciality intended to control fleas as a residual spray treatment, xxxx, Study No: 1931-B5EC-F/0515R, Unpublished | Yes | Bábolna Bio Ltd. |
| IUCLID 9.2.2.2 | xxxx | 2015 | Effects of S-methoprene technical on earthworm (*Eisenia fetida*) reproduction in a chronic toxicity test, xxxx Study no. 484-222-0675, Unpublished | Y | Babolna Bio Ltd |
| IUCLID  9.2.5. | xxxx | 2015 | COLLEMBOLAN REPRODUCTION TEST IN SOIL WITH S-METHOPRENE TECHNICAL, xxxx, Study No: 484-232-0676, Unpublished | Yes | Bábolna Bio Ltd. |
| IUCLID  10.1. | xxxx | 2011 | Environmental distribution of S-Methoprene (Level 1 Fugacity Calculator ver1.2 by Karl Nieman), xxxx, Study No: RIV2011/03/08, Unpublished | Yes | Bábolna Bio Ltd. |
| IUCLID  10.2. | xxxx | 2015 | S-Methoprene: Route and Rate of Degradation of [14C]S-Methoprene in Aerobic Aquatic Sediment Systems, xxxx Study No: D93728, Unpublished | Yes | Bábolna Bio Ltd. |
| IUCLID  10.2. | xxxx | 2015 | S-methoprene: Degradation and Metabolism in Four Soils of [14C]S-methoprene Incubated under Aerobic Conditions, xxxx, Study No: D93717, Unpublished | Yes | Bábolna Bio Ltd. |
| IUCLID 10.2. | xxxx | 2014 | INHERENT BIODEGRADABILITY OF S-METHOPRENE  IN MODIFIED MITI TEST (II) | Y | Babolna Bio Ltd |

## Output tables from exposure assessment tools

**Human Health exposure**

***Scenario 2*** - **Professional use, Application – Spray, general surface treatment (flea treatment)**

**Dermal exposure (RISKOFDERM):**

The following model configurations were used in RISKOFDERM:

* indoor application
* spraying downward
* direction of airflow not clearly away from worker
* no segregation of the worker from the source
* source less than 1 meter from the worker
* liquid not highly volatile
* application rate 1 L/min
* percentile 75th
* exposure duration: 480 min (full shift)

Based on the model, the resulting exposure to the working solution is as follows:

|  |  |  |
| --- | --- | --- |
|  | **median** | **percentile distribution (75th)** |
| **Resulting exposure rate hands** | 11.2 µl/min | 37.6 µl/min |
| **Resulting exposure rate body** | 52.3 µl/min | 175 µl/min |
| **Exposure loading per shift hands** | 5390 µl | 18100 µl |
| **Exposure loading per shift body** | 25100 µl | 84100 µl |
| **Total dermal exposure per shift** | 30490 µl/day | **102200 µl/day** |

The concentrate product contains 6.1% S-metoprene. The dilution rate is 5 ml product to 5 L working solution, resulting in 0.00495% a.s. in the working solution. Consequently, the estimated daily dermal exposure of 102200 µl (102200 mg – as the dilution is mainly water, its density is considered 1) equals to an external dermal exposure of 5.056 mg active substance.

With the dermal absorption value of 50% and a user body weight of 60 kg, the resulting internal systemic exposure is **0.042 mg/kg bw/day**.

This value represents an absolute worst case as both the application rate and exposure duration values were worst case figures. For the above calculations the use of PPE was not considered (Tier 1).

**Inhalation exposure (ART):**

The following model configurations were used in ART:

* indoor application
* spraying downward
* no segregation of the worker from the source
* source less than 1 meter from the worker (near field)
* liquid non-volatile
* application rate 0.3-3 L/min
* natural good ventilation
* vapour pressure 0.000623 Pa
* exposure duration: 480 min (full shift)

As a result of ART inhalation modelling, it was concluded that the estimated inhalation exposure was **0.00048 mg/m³** active ingredient (75th percentile value).

Based on HEAdhoc Recommendation no. 14 revising HEEG Opinion 17 or ECHA’s Biocides Human Health Exposure Methodology, the default adult inhalation rate is **1.25 m3/h**. With an exposure duration of **480 min**, a total of **10 m3** air is inhaled. The resulting exposure is **0.0048 mg** active substance per day (worst case value, calculated with spraying during full shift, which is a clear overestimation). With a user body weight of **60 kg**, the resulting systemic exposure is **0.00008 mg/kg bw/d**.

**ART output tables:**

|  |  |  |
| --- | --- | --- |
| **ART REPORT – Biopren 5 EC larvicide concentrate – 11-Aug-18** | | |
|  |  |  |
| General surface treatment against fleas | | |
|  |  |  |
| **Chemical details** |  |  |
| Chemical | S-methoprene |  |
| CAS No. | 65733-16-6 |  |
|  |  |  |
| **Scenario details** |  |  |
| Number of activities | 1 |  |
| Total duration (mins) | 480 |  |
| Nonexposure period (mins) | 0 |  |
|  |  |  |
| **Metadata** |  |  |
| ART version | 1.5 |  |
| Creator | xxxx |  |
| Date created | 11-Aug-18 |  |
| Date last edited | 11-Aug-18 |  |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Details for Activity Application - general surface treatment against fleas** | | | | | | | | | | | |  | | |
|  |  |  |  |  |  |  |  |  | |  | |  | | |
| Emission sources: | Near field | 63d9ea7a-c694-4414-b65a-330b8adb001f   |  | | --- | |  | | |  |  | Duration (mins): | | | 480 | |  | |  | | |
|  |  |  |  |  |  | |  | |  | | |
|  | Far field |  |  |  |  |  |  |  | |  | |  | | |
|  |  |  |  |  |  |  |  |  | |  | |  | | |
| **Near-field exposure** | | | | | | | | | | | |  | | |
|  |  |  |  |  |  |  |  |  | |  | |  | | |
| ***Operational Conditions*** | | | | | |  |  |  | |  | |  | | |
|  |  |  |  |  |  |  |  |  | |  | |  | | |
| *Substance emission potential* | | | | | | |  | | | | | | |
| Substance product type | | | | | | | Liquids | | | | | | |
| Process temperature | | | | | | | Room temperature | | | | | | |
| Vapour pressure | | | | | | | 0.00108 Pa | | | | | | |
| Liquid weight fraction | | | | | | | 5E-05 | | | | | | |
| Viscosity | | | | | | | Low | | | | | | |
|  |  |  |  |  |  |  |  |  | | | | | | | |  |  |
| *Activity emission potential* | | | | | | |  | | | | | | |
| Activity class | | | | | | | Surface spraying of liquids | | | | | | |
| Situation | | | | | | | Moderate application rate (0.3 - 3 l/minute) | | | | | | |
| Spray direction | | | | | | | Only downward | | | | | | |
| Spray technique | | | | | | | Spraying with no or low compressed air use | | | | | | |
|  |  |  |  |  |  |  |  |  | | | | | | | |  |  |
| *Surface contamination* | | | | | | |  | | | | | | |
| Process fully enclosed? | | | | | | | No | | | | | | |
| Effective housekeeping practices in place? | | | | | | | No | | | | | | |
| General housekeeping practices in place? | | | | | | | No | | | | | | |
|  |  |  |  |  |  |  |  |  | | | | | | | |  |  |
| *Dispersion* | | | | | | |  | | | | | | |
| Work area | | | | | | | Indoors | | | | | | |
| Room size | | | | | | | Any size workroom | | | | | | |
|  |  |  |  |  |  |  |  |  |  | |  | |
| ***Risk Management Measures*** | | | |  |  |  |  |  |  | |  | |
|  |  |  |  |  |  |  |  |  |  | |  | |
| *Localised controls* | | | | | | |  | | | | | | |
| Primary | | | | | | | No localized controls (0.00 % reduction) | | | | | | |
| Secondary | | | | | | | No localized controls (0.00 % reduction) | | | | | | |
|  |  |  |  |  |  |  |  |  |  | |  | |
| *Dispersion* | | | | | | |  | | | | | | |
| Ventilation rate | | | | | | | Only good natural ventilation | | | | | | |

|  |  |  |
| --- | --- | --- |
| **Predicted exposure levels** | | |
|  |  |  |
| ART predicts air concentrations in a worker's personal breathing zone outside of any Respiratory Protection Equipment (RPE). The use of RPE must be considered separately. | | |
|  |  |  |
| **Mechanistic model results** |  |  |
|  |  |  |
| The predicted 75th percentile full-shift exposure is **0.0004 mg/m³**. | |  |
|  |  |  |
| The inter-quartile confidence interval is 0.00023 mg/m³ to 0.001 mg/m³. | |  |

*Scenario 2* - **Professional use, flea treatment, Spraying model 1 estimations**

|  |  |
| --- | --- |
| **Biopren 5 EC (Active substance S-methoprene)** | **Flea treatment** |
| **Exposure Descriptor** |  |
| **Hand Exposure** |  |
| Indicative value without gloves [mg of in-use dilution/minute] | 181 |
| Task duration [minutes] | 480 |
|  |  |
|  |  |
| Amount of in-use dilution on hands [mg] | 86880 |
| **Rest Of Body Exposure** |  |
| Indicative value [mg in-use dilution/minute] | 92 |
| Task duration [minutes] | 480 |
| Potential dermal deposit on body [mg in-use dilution] | 44160 |
| **Total amount of in-use dilution on feet, hands and rest of body [mg] Tier 1, no PPE** | **131040** |
| **Total amount of active substance on feet, hands and rest of body [mg a.s.] Tier 1, no PPE** | **6.486** |
| Skin penetration [%] | 50 |
| Body weight [kg] | 60 |
| **Total systemic dermal exposure [mg a.s./kg bw/day]** | **0.0541** |
| **Inhalation Exposure** |  |
| Indicative value [mg of in-use dilution/m3] | 104 |
| Task duration [minutes] | 480 |
| Inhalation rate of person [m3/h] | 1.25 |
| Volume of air inhaled over task duration [m3] | 10 |
| Potential inhalation exposure over task duration [mg in-use dilution] | 1040 |
| Potential inhalation exposure over task duration [mg a.s.] | 0.051 |
| Inhalation absorption [%] | 100 |
| Body weight [kg] | 60 |
| **Systemic inhalation exposure [mg a.s./kg bw/day]** | **0.00086** |
|  |  |
| **Total systemic dose (dermal+inhalation), Tier 1, no PPE [mg a.s./kg bw/day]** | **0.055** |

***Scenario 3*** - **Professional use, flea treatment, post-application (cleaning of spray equipment)**

The following default values and considerations were used based on HEAdhoc Recommendation no. 4:

* body exposure: **19.28 μl/min**
* hand exposure: **35.87 μl/min**
* exposure duration (cleaning): **20 min** in a working day
* only dermal exposure is relevant

On the basis of these data, the body exposure to the **working solution** (which is present in the spraying device and exposure may occur during cleaning), is **385.6 mg/day**. Hand exposure is **717.4 mg/day**. The density of the solution is 1 (it is mainly water). Thus, the total external dermal exposure is **1103 mg working solution**/day.

The active substance content of the concentrate is 6.1% and the dilution is prepared by diluting 5 ml product to 5 L working solution. Consequently, the total external dermal exposure is **0.0546 mg active substance**/day

Dermal absorption is **50%** so the absorbed dose is **0.027 mg/day**.

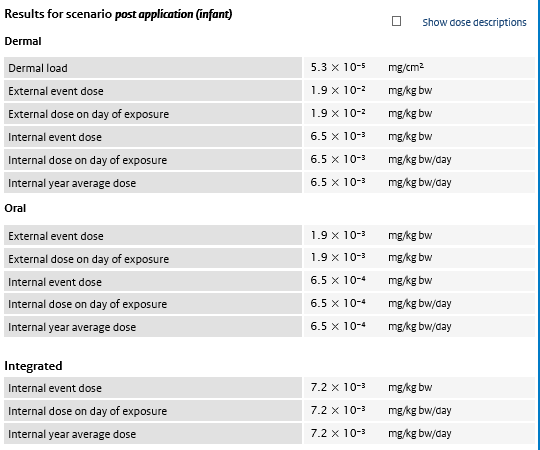
With a body weight of **60 kg**, the internal dose from this scenario is **4.55 x 10-4 mg active substance/kg bw/day.**

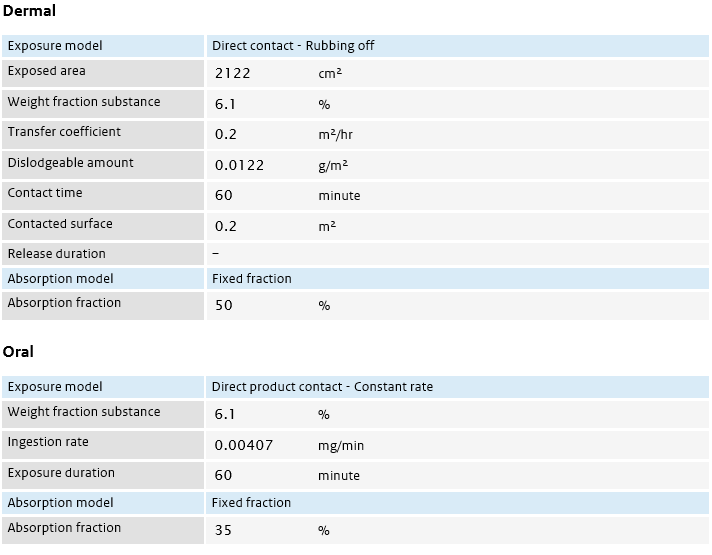
***Scenario 4*** - **toddler crawling across a floor after the general surface spray application of ‘Biopren 5 EC larvicide concentrate’ indoors.**

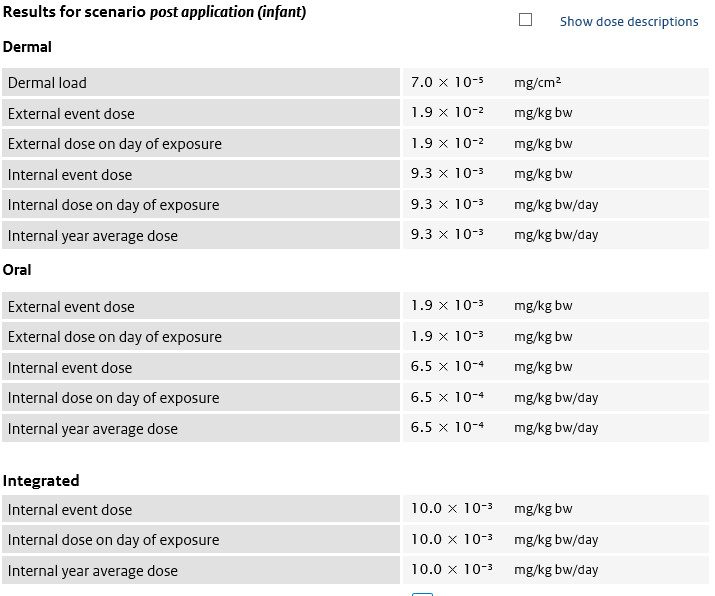
**ConsExpo Report**

**Report for assessment Biopren 5EC - General surface treatment**

ConsExpo Web – 20-12-2019







## New information on the active substance

New biodegradation studies:

1. S-methoprene: Degradation and Metabolism in Four Soils of [14C]S-methoprene Incubated under Aerobic Conditions,
2. S-Methoprene: Route and Rate of Degradation of [14C]S-Methoprene in Aerobic Aquatic Sediment Systems
3. Inherent Biodegradability Of S-Methoprene In Modified MITI Test (II)

See IUCLID section 10.2

New terrestrial non-target studies:

1. Collembolan reproduction test in soil with s-methoprene technical
2. Effects of S-methoprene technical on earthworm (*Eisenia fetida*) reproduction in a chronic toxicity test

See IUCLID section 9.2

## Residue behaviour

## Summaries of the efficacy studies (B.5.10.1-xx)[[8]](#footnote-9)

See IUCLID section 6.7

## Confidential annex

See separate document.

## Other

***Endocrine disruption activity of non- active substances***

The Commission Delegated Regulation (EU) 2017/2100 specifying the scientific criteria for the determination of endocrine-disrupting properties (ED criteria) under Regulation (EU) No 528/2012 (BPR) establishes that the ED criteria become applicable by 7 June 2018 for biocides  (<https://www.ctgb.nl/onderwerpen/hormoon-verstoorders>).

According to the Endocrine disruption criteria a substance shall be considered as having endocrine disrupting properties if it meets all of the following criteria:

a) it shows an adverse effect in [an intact organism or its progeny]/[non-target organisms], which is a change in the morphology, physiology, growth, development, reproduction or life span of an organism, system or (sub)population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress or an increase in susceptibility to other influences;

b) it has an endocrine mode of action, i.e. it alters the function(s) of the endocrine system;

c) the adverse effect is a consequence of the endocrine mode of action.

For one co-formulant, 2,6-di-tert-Butyl-p-cresol, ED concern has been raised by France:

<https://echa.europa.eu/documents/10162/7ddda8e5-d66c-4fad-b502-86cfdf2298bc> and they propose to include this substance on the CoRAP list. Regarding the current application CA NL considers that the ED assessment for this co-formulant does not need to be included in the PAR and can await the outcome of the discussions at EU level. If 2,6-di-tert-Butyl-p-cresol is concluded to possess ED potency the authorisation of the product needs to be re-evaluated.

No further ecotoxicological studies are available for BIOPREN 5 EC LARVICIDE CONCENTRATE. The product was not tested for potential endocrine disruption properties. BIOPREN 5 EC LARVICIDE CONCENTRATE contains the active substance S-methoprene and various co-formulants.

For S-methoprene no ED assessment is required because for active substances which have been approved, the EU assessment should be followed. The Assessment Report (September 2016) states that S-methoprene is not included in the Commission staff working document on implementation of the EU Strategy for Endocrine Disrupters. Whilst S-methoprene is a juvenile (insect) hormone analogue, there is no evidence of any endocrine disruption potential in the human health or ecotoxicological studies presented in the dossier. As such it has been agreed that S-methoprene should be further assessed with regards to its potential endocrine disruptor properties once further guidance is available and preferably before the product authorisation stage. The conclusion of that assessment might lead to review of the active substance approval.

For the co-formulants a screening was performed by consulting:

* ECHA data for identification of ED and PBT, under REACH or PPPR, BPR or CLP
* Identified as ED by United States EPA (https://comptox.epa.gov/dashboard/)
* Identified as ED by the United Nations Environment (July 2017) Programme(<http://wedocs.unep.org/bitstream/handle/20.500.11822/25634/edc_report2.pdf?sequence=1&isAllowed=y> and https://wedocs.unep.org/bitstream/handle/20.500.11822/25635/edc\_report2\_factsheet.pdf?sequence=1&isAllowed=y)

Only the co-formulant 2,6-di-tert-Butyl-p-cresol triggered an alert for ED property. This co-formulant is included in the United Nations Environment Programme. And this is the same co-formulant that raised a concern based on the available toxicological information, see above. CA NL considers that the ED assessment should await the outcome of the discussions at EU level. If this co-formulant is concluded to possess ED potency the authorisation granted for BIOPREN 5 EC LARVICIDE CONCENTRATE needs to be re-evaluated.

1. Please fill in here the identifying product name from R4BP. [↑](#footnote-ref-2)
2. [↑](#footnote-ref-3)
3. Dryden, M. W. & Rust, M. K. (1994) The cat flea: biology, ecology and control. Veterinary Parasitology 52, 1–19. [↑](#footnote-ref-4)
4. Marchiondo, A. A., Meola, S. M., Palma, K. G., Slusser, J. H. & Meolla, R. W. (1999) Chorion formation and ultrastructure of the egg of the cat flea (Siphonaptera: Pulicidae). Journal of Medical Entomology 36, 149-157. [↑](#footnote-ref-5)
5. Rust, M. K. & Dryden, M. W. (1997) The Biology, Ecology, and Management of the Cat Flea. *Annual Review of Entomology* 42, 451–473. [↑](#footnote-ref-6)
6. HEEG Opinion 13: Assessment of inhalation exposure of volatilised biocide active substance. [↑](#footnote-ref-7)
7. When an annex in not relevant, please do not delete the title, but indicate the reason why the annex should not be included. [↑](#footnote-ref-8)
8. If an IUCLID file is not available, please indicate here the summaries of the efficacy studies. [↑](#footnote-ref-9)