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**



BIOPREN 4 GR FLY LARVICIDE GRANULE

Product type 18

Insecticides, acaricides and products to control other arthropods

S-methoprene

Case Number in R4BP: BC-LS019395-17

Evaluating Competent Authority: Ctgb

Date:29/10/2019

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# CONCLUSION

The Dutch CA considers the information provided for the intended uses sufficient for the authorisation of the product. Therefore the authorised uses of Biopren 4 GR Fly Larvicide granule will be as a insecticide against the larvae of houseflies (*Musca domestica*), larvae of stable flies (*Stomoxys calcitrans*) and larvae of drone flies (*Eristalis tenax*) for professional and non-professional use. Indoor use is authorised in dung in closed piggeries, cow and poultry houses, as well as in stables and other livestock breeding buildings. Outdoor use is authorised in dung-pits which are leak-proof and insulated.

The product consists of >95% carrier to which S-methoprene is added in encapsulated and free form in a ratio of 3:1. The physical, chemical and technical characteristics of the product have been tested and are considered acceptable. The shelf life is 3 years in PP and extrapolation of these data to all other commercial packages is acceptable. No classification is required with regard to physical and chemical hazards. The analytical method for S-methoprene determination in Biopren 4GR larvicide granule is validated. Analytical methods for monitoring are addressed sufficiently.

Regarding the environment the product is classified as H412. The precautionary statements P273 and P501 are therefore added. Emission of residues of the product to the sewer results in unacceptable risks for the aquatic environment, but emission to the manure is acceptable. Therefore a risk mitigation measure stating that residues of the product must be disposed to the manure storage and not to the sewer is added.

**Issues to be addressed at product renewal**

Although the risk assessment shows a safe use, the following issues were not fully addressed by the applicant and should be further clarified upon product renewal:

1. The use of less destructive extraction techniques should be further investigated to see whether it is possible to distinguish between encapsulated and free S-methoprene. If possible, the shelf-life study would need to be redone to be able to judge if S-methoprene capsules remain stable during storage.
2. Considering the product is based on encapsulated substance, it is possible the environment is exposed to S-methoprene, even though the substance has a DT90 of < 3 days. Therefore, the need for an analytical method for residues in soil should be reconsidered.

# ASSESSMENT REPORT

## Summary of the product assessment

### Administrative information

#### Identifier of the product

| **Identifier** | **Country (if relevant)** |
| --- | --- |
| BIOPREN 4 GR FLY LARVICIDE GRANULE | NL |

#### Authorisation holder

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

#### Manufacturer(s) of the product

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

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

|  |  |
| --- | --- |
| **Active substance** | S-methoprene |
| **Name of manufacturer** | Babolna Bio Ltd |
| **Address of manufacturer** | Szállás utca 6, Budapest, H-1107 |
| **Location of manufacturing sites** | Szállás utca 6, Budapest, H-1107 |

### 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

**X 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** | - |
| **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 | Isopropyl-(2E,4E, 7S)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate | Active substance | 65733-16-6 | - | 0.4% (pure, 0.1 % free and 0.3 % microencapsulated\*)  (0.421 % technical) |

\* The ratio in which encapsulated and free S-methoprene are mixed is 3:1. This ratio is not experimentally confirmed, but it is the ratio used for manufacture of the product.

The composition details of the full formulation are contained within the confidential annex 3.6.1.

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

Not relevant

#### 

#### 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. The applicant Babolna Bio Ltd. is the Annex I notified source of S-methoprene active substance.

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

No substances of concern are identified as none of the co-formulants fulfilled the requirements as set in the quidance part B and C. Please see the confidential annex for further details.

As a result of screening no need for ED assessment was identified for any of the co-formulants. See chapter 2.2.6.1 for human health aspect and 2.2.8.1 for environment aspect for further details.

#### Type of formulation

|  |
| --- |
| GR - granule |

### Hazard and precautionary statements

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

| **Classification** | |
| --- | --- |
| Hazard category | -- |
| Hazard statement | H412 Harmful to aquatic life with long lasting effects  EUH208 Contains Polyethyleneglycol-15-hydroxystearat. May produce an allergic reaction. |
|  | |
| **Labelling** | |
| Signal words | -- |
| Hazard statements | H412 Harmful to aquatic life with long lasting effects  EUH208 Contains Polyethyleneglycol-15-hydroxystearat. May produce an allergic reaction. |
| Precautionary statements | P101 If medical advice is needed, have product container or label at hand.  P102 Keep out of reach of children.  P273 Avoid release to the environment  P501 Dispose of contents/ container in accordance with national regulations. |
|  | |
| Note | **-** |

### Authorised use(s)

#### Use description

Table 1. Fly larvae- general public and professional

|  |  |
| --- | --- |
| **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)** | *Musca domestica* - House fly - larvae  *Stomoxys calcitrans* - Stable fly - larvae  *Eristalis tenax* - Drone fly - larvae |
| **Field of use** | Indoor:  dung in closed piggeries, cow and poultry houses, as well as in stables and other livestock breeding buildings.  Outdoor:  dung-pit which is leak-proof, insulated. |
| **Application method(s)** | Spreading |
| **Application rate(s) and frequency** | Dosage: 30 g/ m2  The product has to be spread onto the manure’s surface either by hand, with a measuring cup or with an appropriate device, eg. hand held granule applicator according to the following dosing:  Piggeries, Cattle Stables:  -Slatted floor: Apply on the 3rd day after the introduction of new livestock. Treat the whole floor of manure-pit. It is necessary to repeat treatment after each removal of dung.  -Deep litter: Apply on every new layer of litter and repeat the treatment after every 8 - 10 cm increase of the layer.  Poultry Farms:  -Cage: Treat the accumulated manure (every 10 cm thick layer) under the cages.  -Deep litter: Apply on every new layer of litter and repeat the treatment after every 10 cm increase of the layer.  In the case of very dry substrates (e.g. chicken litter), effect of the product may develop slower. Adding 100-200 mL water/m2 to the substrate may facilitate development of larvicide effect in the case of very dry environmental conditions.  Dung stored outdoors:  it should only be treated if it is placed in a dung-pit which is leak-proof, insulated and corresponds to other requirements of safe dung storage. When treating dung stored outdoors, apply the product at the dosage of 30 g/m2.  Stop treating the dung with the larvicide at least two months before spreading/ processing the dung in the fields  The product can control the number of newly hatched adult flies for a period up to 12 weeks after treatment if above instructions for application are respected. The maximum number of annual applications is six. |
| **Category(ies) of users** | Trained professional, Professional, General public (non-professional) |
| **Pack sizes and packaging material** | Professional:  paper bag with LDPE inner layer 10, 15, 20, 25kg  PP or HDPE Bag/sack 10, 15, 20, 25kg  carton box with LDPE inner layer 100, 200, 250, 500, 750, 1000, 1500, 2000g  PP or HDPE bucket 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, 10, 12.5, 15, 20, 25kg  PP or HDPE box or bottle 100, 200, 250, 500, 1000g  general public:  carton box with LDPE inner layer 100, 200, 250, 500, 750, 1000, 1500, 2000g  PP or HDPE bucket 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5  PP or HDPE box or bottle 100, 200, 250, 500, 1000g |

#### Use-specific instructions for use

|  |
| --- |
| See general instructions for use |

#### Use-specific risk mitigation measures

|  |
| --- |
| See general instructions 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 instructions for use |

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

|  |
| --- |
| See general instructions for use |

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

|  |
| --- |
| See general instructions for use |

### General directions for use

#### Instructions for use

|  |
| --- |
| Always read the label or leaflet before use and follow all the instructions provided.  Avoid continuous use of the product.  Take into account the life cycle and characteristics of target insects to adapt treatments. In particular, target the most susceptible stage of the pest, timing of applications and areas to be treated.  Adopt integrated pest management methods such as the combination of chemical, physical control methods and other public health measures, taking into account local specificities (climatic conditions, target species, conditions of use, etc).  Alternate use of this product with products containing active substances with a different mode of action, (to remove resistant individuals from the population).  It is important to disperse the granules over the surface of the dung within 3 days after introduction of livestock and then treat every new 10 cm thick dung layer. Disperse the granules evenly over the surface of the remaining dung after each removal of the dung.  The product has to be spread onto the manure’s surface either with a measuring cup, or with an appropriate device, e.g. hand held granule applicator according to the following dosing:  **Piggeries, Cattle Stables:**  Slatted floor: Apply on the 3rd day after the introduction of new livestock. Treat the whole floor of manure-pit. It is necessary to repeat treatment after each removal of dung.  Deep litter: Apply on every new layer of litter and repeat the treatment after every 8 - 10 cm increase of the layer.  **Poultry Farms**:  Cage: Treat the accumulated manure (every 10 cm thick layer) under the cages.  Deep litter: apply this dosage on 10 cm thick manure.  **Dung stored outdoors:**  it should only be treated if it is placed in a dung-pit which is leak-proof, insulated and corresponds to other requirements of safe dung storage. When treating dung stored outdoors, apply the product at the dosage of 30 g/m2.  Stop treating the dung with the larvicide at least two months before spreading/ processing the dung in the fields. |

#### Risk mitigation measures

|  |
| --- |
| During application, observe the relevant regulations in order to avoid risk the environment or human health.  Prevent livestock from getting in contact with the product. Should this not be feasible, remove livestock for the duration of the treatment. Treat the dung accumulated under the slatted floor, metal grid, deep litter system or the cages. Do not disperse the granules in the immediate surroundings of feeding and watering places or where the animals may consume the product.  Keep out of reach of children and domestic animals.  Keep away from food, drink and animal feedingstuffs.  DO NOT store with food, feedstuffs, seed and fertilisers.  Do not use in animal housings where exposure to a STP or direct emission to surface water cannot be prevented.  Resistance management  To prevent the development of resistance it is advised to use insecticides with a different mode of action as well in the pest control program. In the case of Biopren 4 GR fly larvicide granule it is advised to use an adulticidal product, sticky traps and UV lamps after a few applications of the larvicidal product. Sticky traps can also be used for monitoring purposes. |

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

|  |
| --- |
| Likely direct or indirect adverse effects:  • Repeated exposure may cause allergic disorders.  First aid measures:  • IF IN EYES: Rinse cautiously with water for 15 minutes. Remove contact lenses, if present and easy to do.  • IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water/shower.  • IF exposed or concerned: Get medical advice/attention. |

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

|  |
| --- |
| The empty containers and the remains of product should be disposed as hazardous waste. |

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

|  |
| --- |
| Store in original closed packaging in a dry and cool place protected from radiant heat and at max. 35 ºC.  Store unused product in a well ventilated area and out of direct sunlight.  Shelf life: 3 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)** |
| Bag/sack | 10, 15, 20, 25 kg | Paper bag with inner LDPE layer | Sewn | professional | yes |
| Bag/sack | 10, 15, 20, 25 kg | PP or HDPE | Sewn | professional | yes |
| Box | 100, 200, 250, 500, 750, 1000, 1500, 2000 g | carton with LDPE inner layer | sticking / seal | professional | yes |
| Bucket | 0.5, 0.75, 1,1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, 10, 12.5, 15, 20, 25 kg | PP or HDPE | PP or HDPE lid closure | Professional | yes |
| Container (box or bottle) | 100, 200, 250, 500, 1000 g | PP or HDPE | PP or HDPE closure (lid or cap) | Professional | yes |
| Box | 100, 200, 250, 500, 750, 1000, 1500, 2000 g | carton with LDPE inner layer | sticking / seal | non-professional | yes |
| Bucket | 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 5kg | PP or HDPE | PP or HDPE lid closure | non-professional | yes |
| Container (box or bottle) | 100, 200, 250, 500, 1000 g | PP or HDPE | PP or HDPE closure (lid or cap) | non-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 S-methoprene active substance dossier and also the sponsor of the studies prepared for the BIOPREN 4 GR FLY LARVICIDE GRANULE 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 e-CA. These uses are assessed in the following chapters.

See 1.1.4 for the authorised uses, after assessment of the dossier.

Table 2. Intended use # 1 – PCO

|  |  |
| --- | --- |
| Product Type(s) | PT18 - Insecticides, acaricides and products to control other arthropods (Pest control) |
| Where relevant, an exact description of the authorised use | The product is an S-methoprene based insect growth regulator, a juvenile hormone analogue. The use of the product makes possible to eliminate the less visible part of fly population. This part consist the early developmental stages ( maggots and pupae) which represent more than 80 % of the full population.  The product will significantly reduce the number of newly hatched adult flies for a period of 12 weeks after the larvicide treatment. Treated larvae continue to develop to the pupal stage after which they fail to emerge |
| Target organism (including development stage) | Muscidae:House fly Larvae  Muscidae:Stable flies Larvae  Muscidae:Rat-tailed maggot Larvae, drone fly, Eristalis Tenax |
| Field of use | Indoor , Outdoor  Apply the product to inhibit the transformation of fly larvae breeding in the dung into imagoes in closed piggeries, cow and poultry houses, as well as stables, goat-folds, sheep-pens and other livestock breeding buildings. Outdoor: dung-pit which is leak-proof, insulated. |
| Application method(s) | Spreading |
| Application rate(s) and frequency | Dosage: 30 g/ m2  frequency depends on the rate of infestation. The product can control the number of newly hatched adult flies for a period of 12 weeks after treatment. |
| Category(ies) of user(s) | Professionals |
| Pack sizes and packaging material | - 10, 15, 20, 25 kg in foil layered paper bag  - 10,15.20,25 kg in plastic bag (PP or HDPE)  - 100, 200, 250, 500, 750, 1000, 1500, 2000 grams in foil layered carton box  - 0.5, 0.75, 1,1.5, 2,2.5, 3,4,5,6,7,8,9,10,12.5, 15, 20, 25 kg in plastic bucket (PP or HDPE)  - 100, 200, 250, 500, 1000 grams in plastic container (PP or HDPE) |

Table 3. Intended use # 2 – non-PCO

|  |  |
| --- | --- |
| Product Type(s) | PT18 - Insecticides, acaricides and products to control other arthropods (Pest control) |
| Where relevant, an exact description of the authorised use | The product is an S-methoprene based insect growth regulator, a juvenile hormone analogue. The use of the product makes possible to eliminate the less visible part of fly population. This part consist the early developmental stages (maggots and pupae) which represent more than 80 % of the full population.  The product will significantly reduce the number of newly hatched adult flies for a period of 12 weeks after the larvicide treatment. Treated larvae continue to develop to the pupal stage after which they fail to emerge |
| Target organism (including development stage) | Muscidae:House fly Larvae  Muscidae:Stable flies Larvae  Muscidae:Rat-tailed maggot Larvae, drone fly, Eristalis Tenax |
| Field of use | Indoor , Outdoor  Apply the product to inhibit the transformation of fly larvae breeding in the dung into imagoes in closed piggeries, cow and poultry houses, as well as stables, goat-folds, sheep-pens and other livestock breeding buildings. Outdoor: dung-pit which is leak-proof, insulated. |
| Application method(s) | Spreading |
| Application rate(s) and frequency | Dosage: 30 g/ m2  frequency depends on the rate of infestation. The product can control the number of newly hatched adult flies for a period of 12 weeks after treatment. |
| Category(ies) of user(s) | non-Professionals |
| Pack sizes and packaging material | - 100, 200, 250, 500, 750, 1000, 1500, 2000 grams in foil layered carton box  - 0.5, 0.75, 1,1.5, 2, 2.5, 3,4,5 kg in plastic bucket (PP or HDPE)  - 100, 250, 200, 500, 1000 grams in plastic container (PP or HDPE) |

### Physical, chemical and technical properties

eCA remark: the product consists of a carrier mixed with active substance (both free and encapsulated).

| **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, US EPA, 1996 | 0.41 %  batch No.: KI/100579 | Solid, particulate granules | xxxxxxx, Toxi-Coop, Zrt.,Study Report: Determination of the Appearance of BIOPREN 4GR fly larvicide granule,  Study no: 484-630-0566,April 21, 2015, Sponsor: Babolna Bio Ltd., |
| Colour at 20 °C and 101.3 kPa | OPPTS 830.6302 Color, US EPA, 1996 | 0.41 %  batch No.: KI/100579 | Blue-gray, light brown, heterogeneous | xxxxxxx, Toxi-Coop, Zrt.,Study Report: Determination of the Appearance of BIOPREN 4GR fly larvicide granule,  Study no: 484-630-0566,April 21, 2015, Sponsor: Babolna Bio Ltd., |
| Odour at 20 °C and 101.3 kPa | OPPTS 830.6304 Odor, US EPA, 1996 | 0.41 %  batch No.: KI/100579 | Odourless | xxxxxxx, Toxi-Coop, Zrt.,Study Report: Determination of the Appearance of BIOPREN 4GR fly larvicide granule,  Study no: 484-630-0566,April 21, 2015, Sponsor: Babolna Bio Ltd., |
| Acidity / alkalinity | CIPAC MT 75.3, Determination of pH Values  OECD No. 122,  Determination of pH, Acidity and Alkalinity, adopted July 26, 2013 | 0.41 %  batch No.: KI/100579 | pH:5.4 at 20 ± 1 °C ,  /1% (w/v) aqueous suspension  After storage at ambient temperature for 37 months:  pH: 6.4 at 20 ± 1 °C ,  /1% (w/v) aqueous suspension | xxxxxxx, Toxi-Coop Zrt.,Study Report: Determination of the pH of Aqueous Suspension of BIOPREN 4GR fly larvicide granule, Study no: 484-122-0608, April 01, 2015, Sponsor: Babolna Bio Ltd  xxxxxxx, Toxi-Coop Zrt.,Study Report: Determination of the pH values of BIOPREN 4GR fly larvicide granule (after storage), Study no: 484-122-4080, December 03, 2018, Sponsor: Babolna Bio Ltd |
| Relative density / bulk density | CIPAC MT 186, Bulk Density | 0.41 %  batch No.: KI/100579 | Pour density : 1.41 g/mL  Tap density :  1.53 g/mL | xxxxxxx, Toxi-Coop Zrt., Study Report: Determination of the Bulk Density of BIOPREN 4GR fly larvicide granule,Study no: 484-109-0609, March 31, 2015 Sponsor: Babolna Bio Ltd |
| Storage stability test – **accelerated storage** | CIPAC MT 46.3 | 0.41 %  batch No.: KI/100579 | The active substance content, appearance and packaging were evaluated before and after storage at 54±2°C for 14 days.  Packaging material was PP plastic bottle.  A.s content decreased from 0.404% to 0.390% (3.4% decrease), all other parameters remained the same. | xxxxxxx,Determination of the Accelerated Storage Stability of BIOPREN 4GR fly larvicide granule, TOXI-COOP ZRT., 2015 |
| eCA remark:  Acceptable.  The validated analytical method for active substance dertermination was used (see section 2.2.4).  The packaging material in the study report is only described as ‘plastic’. The applicant specified it as a PP plastic bottle.  According to the FAO manual, these physical properties should be tested after accelerated storage for GR formulations:  -acidity  -dustiness  -attrition resistance  Dustiness, pH and attrition resistance have not been tested after accelerated storage, but were tested after long-term storage for a different product. The composition of this product is provided below this Table. Read-across is acceptable. | | |
| Storage stability test – **long term storage at ambient temperature** | GIFAP Technical Monograph N°17, OPPTS 830.6303 OPPTS 830.6302 OPPTS 830.6304 | 0.41 %  batch No.: KI/100579 | The product was stored for 3 years at room temperature.  The active substance content, appearance and packaging were evaluated at 20±1°C at the start, after 6, 12, 18, 24, 30 and 36 months.  A.s content:  t = 0: 0.397 ± 0.006;  t = 6 months: 0.449 ± 0.005;\*  13% increase  t = 12 months: 0.418 ± 0.007;  5.3% increase  t=18 months 0.423±0.008  6.5% increase  t = 24 months: 0.419 ± 0.005;  5.5% increase  t = 30 months: 0.419 ± 0.009;  5.5% increase  t = 36 months 0.441± 0.008  11% increase  All other parameters remained the same.  \*the difference between the nominal and the measured value is slightly higher than 10%. The suspected reason is the inhomogenity of the sample. As the deviation was minor the study has been continued. Further measured values fulfilled the nominal AS content ± 10% range.  Results of pH, particle size distribution, dustiness, attrition resistance determination after storage studies can be found in this table at the relevant point | xxxxxxx,Determination of the Long Term Storage Stability of BIOPREN 4GR fly larvicide granule, Iterim Report TOXI-COOP ZRT., 2016 |
| eCA remark:  The validated analytical method for active substance determination was used (see section 2.2.4).  The active substance content was measured six times at different storage times. All measurements showed an increase in a.s. content of >5%, and an increase of >10% was measured twice (at t=6 months and t=36 months). The active substance cannot form upon storage and no trend in active substance content during storage is observed. The increase in apparent active substance content should be attributed to experimental errors. A more detailed explanation of the results should be provided by the applicant upon renewal of the authorization.  Packaging material is described as plastic box or commercial packaging. The applicant specified it as a PP plastic bottle. For extrapolations of packages, see ‘Effects on content of the active substance and technical characteristics of the biocidal product - reactivity towards container material’.  Data on dustiness, pH and attrition restistance after storage are summarized in this table under the different end points.  Lastly, it should be noted that no determination of free and encapsulated active substance was performed. If the product is considered to be a slow-release insecticide, such information should be made available for renewal of the authorization. This would also require an analytical method to be validated, able to distinguish between free and encapsulated S-methoprene. | | |
| Storage stability test – **low temperature stability test for liquids** | -- | -- | The product is solid therefore this is not applicable. | -- |
| Effects on content of the active substance and technical characteristics of the biocidal product - **light** |  |  | During the stability study the effects of light, humidity and higher temperature were not investigated as the packaging of the product is closed, water proof and ensure the protection from direct sunlight and other impacts of the environment. |  |
| Effects on content of the active substance and technical characteristics of the biocidal product – **temperature and humidity** | -- | -- | See " Effects on content of the active substance and technical characteristics of the biocidal product – **light"** results. | -- |
| **eCA remark**  The stability at elevated temperatures was addressed in the accelerated storage stability data, although the technical properties were not included. The CIPAC method was designed to mimic chemical stability, but not physical stability. Therefore, the eCA considers that sufficient data was provided, which allow the conclusion that the active substance is not sensitive to heating under the test conditions. The technical properties are addressed within the scope of the long-term storage stability data (shelf-life). | | |
| Effects on content of the active substance and technical characteristics of the biocidal product - **reactivity towards container material** |  |  | The accerelated stability study demonstrated that the plastic packaging material has not reacted with the product. Packaging material was PP plastic bottle.  No visible changes were observed in the appearance of the product and packing of the test item during the study.  PP plastic container is common used packaging. Referring to our more than 3 years marketing experience in several EU countries we can state that the product has no any effect on the packaging. Never was reported discoloration, corrosion or any other problem.  Effects of stacking in case of bag:  The main component of the product is the carrier (see confidential annex for more information). Based on our manufacturing experience, the carrier with the given particle size range is not compacting during the storage. The product also contains anticaking agent to prevent the compaction. Change of other phys-chem parameters is not relevant during the stacking. Therefore, further studies are not necessary. |  |
| eCA remark:  Acceptable  The effect of stacking must be investigated for solid formulations when extrapolating to more flexible packs. The applicant did not investigate this property, but provided an acceptable waiver. Therefore, besides PP, also HDPE and LDPE are acceptable. | | |
| Wettability |  |  | NA |  |
| Suspensibility, spontaneity and dispersion stability |  |  | NA: it is a ready to use granule, not intended for use in solution |  |
| Wet sieve analysis and dry sieve test | CIPAC MT 59.4 | 0.41 %  batch No.: KI/100579 | Particle size distribution is 0.5mm - 2mm (10%-90% w/w)  Particle size distribution after storage for 37 months at ambient temperatures:  0.5mm - 2mm (10%-90% w/w) | xxxxxxx, Toxi-Coop Zrt., Study Report: Sieve test of BIOPREN 4GR fly larvicide granule, 2015 Sponsor: Babolna Bio Ltd  xxxxxxx, Toxi-Coop Zrt.,Study Report: Determination of the Particle Size Distribution of BIOPREN 4GR fly larvicide granule (after storage), Study no: 484-110-4081, November 15, 2018, Sponsor: Babolna Bio Ltd |
| eCA remark:  Acceptable. 0.06% w/w of the particles are smaller than 125 µm prior to storage and 0.12% w/w of the particles are smaller than 125 µm after to storage. | | |
| Emulsifiability, re-emulsifiability and emulsion stability |  |  | NA |  |
| Disintegration time |  |  | NA |  |
| **Particle size distribution**, content of dust/fines, attrition, friability |  | eCA remark:  The dry sieve test (CIPAC MT 59.4) is used instead of CIPAC MT 170. This is acceptable. | | |
| Particle size distribution, **content of dust/fines**, attrition, friability | CIPAC Volume F, MT 171, Dustiness of Granular Products,  Gravimetric method | 0.41 %  batch No.: KI/100579  BIOPREN 4GR mosquito larvicide granule\*  Batch No.: KI/100580  AS %:0.44 % | The mean value is 13.6 +/- 1.0 mg (seven replicate samples of 30g)  Based on this result BIOPREN 4GR fly larvicide granule is categorized as essentially non dusty.  The mean value is 9.1 +/- 1.0 mg (five replicate samples of 30g) Based on this result BIOPREN 4GR mosquito larvicide granule is categorized as nearly dust-free. | xxxxxxx: Study Report  Determination of the Dustiness of BIOPREN 4GR Fly larvicide Granule, Toxi Coop Zrt, Sponsor: Babolna Bio Ltd  xxxxxxx: Study Report  Physico-Chemical Testing of BIOPREN 4GR Mosquito Larvicide Granule (After Storage) Sponsor: Babolna Bio Ltd |
| eCA remark:  Acceptable. Content of dust after storage was measured for a different product. The composition of this product is provided under this Table. Read-across is acceptable.  The storage period is not specifically mentioned in the study report. It can be deduced that the product was stored for 36 months. | | |
| Particle size distribution, content of dust/fines, **attrition**, friability | CIPAC Volume H, MT 178, Attrition Resistance of Granules | BIOPREN 4GR mosquito larvicide granule\*  Batch No.: 128548  AS%: 0.39 %  BIOPREN 4GR mosquito larvicide granule\*  Batch No.: KI/100580  AS %:0.44 % | Attrition resistance of BIOPREN 4GR mosquito larvicide granule was determined to be 99.9%  Attrition resistance of BIOPREN 4GR mosquito larvicide granule was determined to be 99.8% after 3 years storage | xxxxxxx: Study Report  Physico-Chemical Testing of BIOPREN 4GR Mosquito Larvicide Granule Sponsor: Babolna Bio Ltd  xxxxxxx: Study Report  Physico-Chemical Testing of BIOPREN 4GR Mosquito Larvicide Granule (After Storage) Sponsor: Babolna Bio Ltd |
| eCA remark:  Acceptable.  Attrition resistance after storage was measured for a different product. The composition of this product is provided under this Table. Read-across is acceptable.  The storage period is not specifically mentioned in the study report. It can be deduced that the product was stored for 33 months. | | |
| Persistent foaming | -- | -- | NA | -- |
| Flowability/Pourability/ Dustability | -- | -- | Flowability data are required for granular formulations applied through application equipment that would subject the granules to pressure and/or heat, to demonstrate that granular materials remain free flowing. Since the product does not undergo any pressure during application, testing according to CIPAC MT 172 is not required  Pourability is not required as the product is not a suspension.  Dustability data is not required as the product is not dusted (not a dustable powder). | -- |
| Burning rate — smoke generators | -- | -- | NA | -- |
| Burning completeness — smoke generators | -- | -- | NA | -- |
| Composition of smoke — smoke generators | -- | -- | NA | -- |
| Spraying pattern — aerosols | -- | -- | NA | -- |
| Physical compatibility | -- | -- | Ready to use granule, not intended for use with other products. | -- |
| Chemical compatibility | -- | -- | Ready to use granule, not intended for use with other products. | -- |
| Degree of dissolution and dilution stability | -- | -- | Ready to use granule, not intended to prepare solution. | -- |
| Surface tension | -- | -- | NA | -- |
| Viscosity | -- | -- | NA | -- |

\*Babolna Bio Ltd, the applicant propose read-across to the relevant GLP study of Biopren 4GR mosquito larvicide granule. This product is exactly identical to BIOPREN 4GR FLY LARVICIDE GRANULE, except for the colour, which is necessary to distinguish the two products. The difference between the two product is the following:

* + Biopren 4GR Fly larvicide granule: blue colour – contains Vynamon Blue (CAS 147-14-8) – 0.01%
  + Biopren 4GR Mosquito larvicide granule: no colouring agent present (the extra 0.01% in this product is sand)

eCA remark: Read-across from Biopren 4GR Mosquito larvicide granule to Biopren 4GR Fly larvicide granule is acceptable.

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| **Conclusion on the physical, chemical and technical properties of the product** |
| The product BIOPREN 4 GR FLY LARVICIDE GRANULE is a sand granule formulation containing S-methoprene IGR as active substance. The sand formulation with 4g/kg (0.4%w/w) contains 0.1 % free S-methoprene and the 0.3 % microencapsulated S-Methoprene.  The granule is a heterogeneous blue-gray, light brown, odourless, solid, particulate granule. The pH of 1% (w/v) aqueous suspension is 5.4, after storage pH is 6.4. Pour density is 1.41 g/mL and tap density is 1.53 g/mL. The product is not flammable and is not expected to have any explosive or oxidising properties due to the more than 95 % sand content.Based on the result of dustiness study the product is categorized as essentially non dusty. After storage the determination was repeated, the collected dust was 9.1 mg. Based on this result the granule is categorized as nearly dust-free.  Based on the sieve analysis, the particle size distribution of granule is [0.5 mm, 2 mm], repeated determination after storage is 0.5mm - 2mm (10%-90% w/w).  Attrition resistance was determined to be 99.9% and after storage the value was 99.8%.  Long-term stability study supports the three years shelf life.  For renewal of the product authorization, the follow data should be provided:   1. A shelf-life study including data on the active substance stability, free and encapsulated substance for the duration of the shelf-life claim (3y), with the recommendation to test all relevant parameters for a GR formulation as well (including particle size, attrition, dust content). The study should confirm that the free and encapsulated S-methoprene ratio is indeed 1:3. 2. An analytical method which distinguishes between free and encapsulated S-methoprene   Alternatively, the applicant should provide a justification that such information is not required or these studies are not feasible. |

eCA remark: The physical, chemical and technical characteristics of the product have been tested. The amount free and encapsulated S-methoprene was not provided. The ratio mentioned above is a calculation based on the manufacturing process. More information on free and encapsulated S-methoprene can be found in section 2.2.4 Methods for detection and identification.

The technical properties that should be measured after accelerated storage according to the FAO manual (version 1.3) have not been addressed. Instead, the properties were measured after long-term storage.   
PP was used during the storage stability studies. Other packaging materials, including more flexible packs, are applied for. Extrapolation to these more flexible packs is, based on a justification by the applicant, acceptable.

Shelf life is 3 years.

### Physical hazards and respective characteristics

| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **Reference** |
| --- | --- | --- | --- | --- |
| Explosives | -- | -- | Not explosive based on composition | -- |
| eCA remark: Acceptable | | |
| Flammable gases | -- | -- | NA | -- |
| Flammable aerosols | -- | -- | NA | -- |
| Oxidising gases | -- | -- | NA | -- |
| Gases under pressure | -- | -- | NA | -- |
| Flammable liquids | -- | -- | NA | -- |
| Flammable solids | -- | -- | Not flammable based on composition | -- |
| eCA remark: Acceptable | | |
| Self-reactive substances and mixtures | -- | -- | NA | -- |
| Pyrophoric liquids | -- | -- | NA | -- |
| Pyrophoric solids | -- | -- | NA | -- |
| Self-heating substances and mixtures | -- | -- | NA | -- |
| Substances and mixtures which in contact with water emit flammable gases | -- | -- | NA | -- |
| Oxidising liquids | -- | -- | NA | -- |
| Oxidising solids | -- | -- | Not oxidising based on composition | -- |
| eCA remark: Acceptable | | |
| Organic peroxides | -- | -- | Not present | -- |
| Corrosive to metals | -- | -- | NA | -- |
| eCA remark: Acceptable. The solid does not have a melting point <55°C. | | |
| Auto-ignition temperatures of products (liquids and gases) | -- | -- | NA | -- |
| Relative self-ignition temperature for solids | -- | -- | Not relevant | -- |
| eCA remark: Acceptable | | |
| Dust explosion hazard | -- | -- | The product is non dusty. | -- |

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| **Conclusion on the physical hazards and respective characteristics of the product** |
| Due to the composition we can state that the product has no any physical hazards characteristic. |

eCA remark: the product shows no physical hazard. Therefore, no classification according to Regulation 1272/2008 based on physical hazards is required.

### 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 | reverse phase HPLC method with UV detection on a Luna 3μ C18 (2) 100A column | 0.35 – 0.45%,  5 replicate determinations on both fortification level. | 6 - 10 μg/mL (0.3 – 0.5 %)  y = 105681x – 17400  R2 ≥ 0,9997 U/MPO, deze toevoeging weghalen?staande opmerking in IUCLID aan willen vullen met relevante info?worden in f-HDPE. | The specificity of the method for S-Methoprene in BIOPREN 4GR fly larvicide granule was examined by the analysis of control matrices Placebo Biopren 4GR fly larvicide granule. The chromatograms of the control solutions showed no interfering substances at the retention time (approx 5.4 min) of S-Methoprene. | 0.356 ± 0.013  0.457 ± 0.014 | 103%  103% | 2.  9  2.5 | Not applicable | Study Report,Validation of the Analytical Method (HPLC) for the determination of  S-Methoprene in BIOPREN 4GR fly larvicide granule, Study No.: 484-100-0565  Date of Final Report: April 01, 2015, xxxxxxx  Toxi-Coop Zrt. |

In the product BIOPREN GR FLY LARVICIDE GRANULE, the active ingredient is present in the form of a microencapsulated and free fraction. This type of formulation can achieve better residual efficacy than a product containing only free active substance.

The microencapsulated and free active substance fractions are added individually into the product during manufacturing. The development of an analytical method for the separate measurement of the microencapsulated and free fraction of active ingredient in the product is not possible for the following reasons.

During manufacturing of the product, the mechanical effect of the mixing during the coating of sand particles with active ingredient concentrate (friction between the sand particles and the particles and mixer tank wall) and the drying will open up at least partially some of the microcapsules, and their active substance content will leak out (this slow leakage is responsible for the residual effect on target organisms observed in the performed efficacy studies).

Analytical measurements were also performed to observe the separate effect of the different steps of sample preparation (see Analytical report attached in IUCLID, section 5, analytical method for active substance, Attached background material). These results show that even if the ultrasonic treatment or the drying step used for the opening of potentially closed microcapsules is omitted during the preparation step of the analytical measurement, approximately the same active ingredient content is found.

Consequently, it is clear that the two different fractions (free and microencapsulated) of active ingredient cannot be separately measured, due to the above mentioned reasons. Nevertheless, the storage stability study shows that the product is stable, and the efficacy studies ascertain that the product is effective. Further studies are not considered necessary.

**eCA remark:**

The method uses the following sample preparation procedure:

*0.5g of product is extracted in a 25mL volumetric flask with ethanol (20mL). The mixture is then sonicated three times for 10 minutes, left for 1 hour, sonicated again and ethanol was added to fill up the flask. Then, the sample is centrifuged, diluted with acetonitrile and analysed.*

The active substance is present in two fraction: free and encapsulated. The ratio in which encapsulated and free S-methoprene are mixed is 3:1.

The recovery samples are prepared by adding a spiking solution to a control sample, containing all co-formulants but no active substance. In the control sample, the capsules are formed prior to addition of S-methoprene, implying that all a.s. is free. Therefore, this is not an accurate representation of the product, in which part of the active substance is encapsulated.

No experimental method to separately determine the amount encapsulated and free S-methoprene in the product is provided. Given that the experimentally determined S-methoprene content in the repeatability measurements performed with the product resulted in the expected total S-methoprene content (both encapsulated and free), it can be concluded that all S-methoprene from the capsules is released during sample preparation.

As mentioned above, analytical measurements were performed to observe the separate effect of the different steps of sample preparation. Samples were either sonicated or not, and either dried for 24 h at 40°C or not. This resulted in four preparation methods. The measured S-methoprene content was similar in all four cases, suggesting that neither sonication nor drying is required to break the capsules. It should be noted that this information was not presented as study report, but rather as a summary of the results. This summary was not signed and the active substance content was determined using GC, which is not the validated test method.

Still, the method also requires centrifugation, which may break capsules. Alternatives like filtration were not tested. Also, the use of different extraction solvents was not investigated as ethanol may affect the integrity of the capsule walls.

Therefore, additional evidence is required that it is not possible to distinguish between free and encapsulated S-methoprene. The effects of the extraction solvent and alternatives for centrifugation (e.g. filtration) should be investigated. This data should be made available upon product renewal.

**Analytical methods for monitoring in 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.

**eCA remark**

Considering the applicant claims the product is based on slow release it may still be possible the environment is exposed to S-methoprene, even though its DT90 is <3 days. The effects of the encapsulation was not taken into account. This issue should be addressed at substance and product renewals.

**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.

**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 4GR fly larvicide granule was performed.  The procedure was found to be suitable for the analysis. |

eCA remark: The analytical method for S-methoprene determination in Biopren 4GR larvicide granule is validated. Analytical methods for monitoring are addressed sufficiently.

### Efficacy against target organisms

#### Function and field of use

BIOPREN 4 GR FLY LARVICIDE GRANULE is an S-methoprene-based insect growth regulator, a juvenile hormone analogue. The use of the product makes it possible to eliminate the less visible part of a fly populationwhich represent more than 80 % of the full population.

BIOPREN 4 GR FLY LARVICIDE GRANULE reduces the number of newly hatched adult flies for a period of 84 day after the larvicide treatment. Treated larvae continue to develop to the pupal stage after which they fail to emerge. Due to the slow release of the active ingredient, the formulation has a long lasting residuality.

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

BIOPREN 4 GR FLY LARVICIDE GRANULE is intended to control:

*Musca Domestica* – House fly larvae

*Stomoxys calcitrans* – Stable fly - larvae

*Eristalis tenax* – Drone fly – larvae

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

The product modulates ecdysteroid signalling during insect development and metamorphosis.

S-methoprene is an analogue to a unique insect-growth regulating hormone, which does not resemble any known mammalian hormones. Applied at very low rates, while insects are still in the egg or larval stage of their life cycle, S-methoprene prevents development to the adult reproductive stage so that insects die in arrested immaturity. S-methoprene is not toxic when applied to the adult stage of the target insects.

#### Mode of action, including time delay

S-methoprene is an insect growth regulator /juvenile hormone analogue.

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.

Treated larvae continue to develop to the pupal stage after which they fail to emerge. Expected time delay from the beginning of application to manifestation of the biocidal effect is 2-4 weeks (depending on severity of the infestation and life cycle of the target insect) based on the results of efficacy studies and life cycle of Diptera species.

S-methoprene is an invertebrate metabolic inhibitor which does not seem to cause direct toxic effects in mammals (IPCS INCHEM / WHO, No 47, Methoprene). S-methoprene is non-toxic to adult stages of the target insects. Since it interferes with the normal life cycle of insects and is not directly toxic to the pest, S-methoprene is considered as a biochemical pesticide.

#### 

#### Efficacy data

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **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 4GR (microencapsulated S-methoprene based sand granule) 0.4% S-methoprene – identical to BIOPREN 4GR FLY larvicide granule | *Musca domestica (larvae)* | Field test  in closed buildings (livestock breeding premises)  French Registration standard methodology C.E.B. No.:107 :"Method for testing the field efficacy of insecticides designed for the control of stable flies in stock-breeding premises" | 9 animal buildings were monitored:  -3 pigsties were treated with the test item (Biopren 4 GR), dosage: 30 g/m2  -3 pigsties were treated with a reference product SOLFAC dosage: 0.2 g/m2  -2 pigsities and a sheep-fold were used as untreated controls.  The treatments were done by Pest Control Operators. The Biopren 4 GR or SOLFAC was evenly scattered over the surface of the ground (including litters, pits, manure).  After the treatment the efficacy was monitored for a 90 days long period. Also the fly population was counted in the untreated buildings during the study period.  The trial was performed from July to November, 2011 in closed animal breeding sites | Biopren 4GR FLY 30 g/m2:  Mean of flies before treatment: 449 (531, 327 and 489).  Reduction: 59.4% after 14 days, 95.9% after 30 days, 91.1% after 90 days  Solfac:  Mean of flies before treatment: 503.7 (392,764 and 355).  Reduction: 98.0% after 14 days, 98.4% after 30 days, 97.5% after 90 days  Untreated control:  Mean of flies before treatment: 234 (271, 198 and 233).  Reduction: 2.9% after 14 days, 3.1% after 30 days, increase of 1.6% after 90 days. | Field Testing of Efficacy of an Insecticide Speciality to Control House Flies in Livestock Premises (Musca Domestica),  xxxxxxx, 2011,  xxxxxxx, 1453a/0611, 06/10/2011 | | | |
| Insecticide | Indoor | Biopren 4 GR house fly larvae granule (0.4% S-methoprene) – identical to BIOPREN 4GR FLY larvicide granule  . | *Musca domestica (larvae)* | Laboratory test  In-house trial protocol was followed | 3 replicate experiments were performed with two *Musca domestica* strains.  Substratum consisted of 60% chicken manure with straw, 20% grounded standard rodent food and 20% potabel water.  Dosage: 2 ppm (=30 g/m2)  Also 3 replicate controls were conducted with both strains.  100 L3 larvae per replicate  On day 0 the product was applied. After 4-8 days larvae pupated and were placed separately from substrate and each other.  Number of pupae and emerged imagos were counted and compared between controls and dosed replicates.  Total testduration:  24 days  Conditions: 24+/-1 °C, min 60% RH, continuous natural and artificial lighting period 12/12 hours, ventilation regime: continuous (the laboratory was ventilated by using commercial air conditioner). | The mortality of the pupae was 100 percent in case of all trials. Efficacy corrected by Abbott is also 100 percent.  The percentage of recovered pupae was 88-93 %. The percentage of hatched, viable imagoes was 0 % in all cases.  Control:  Hatching efficiency was 96.3% (mortality: 3.7 %) for strain A and 96.0% (mortality: 4.0%) for strain B in the control groups. | Laboratory bioassay study of Biopren 4 GR house fly larvae granule,  xxxxxxx, 2014, 143.001, 143.002, 143.003, 143.004,  xxxxxxx |
| Insecticide | Indoor | BIOPREN 4 GR fly larvicide granule - 0.4% (w/w) S-methoprene | *Eristalis tenax (larvae)*  *Stomoxys calcitrans (larvae)* | Field test  French Registration standard methodology C.E.B. No.:107 :"Method for testing the field efficacy of insecticides designed for the control of stable flies in stock-breeding premises"  Type of breeding premises monitored: cowsheds (11x), pigsties (5x), sheepfolds (8x) | To evaluate the fly populations by sticky trapping before and after  treatment of manure in breeding premises with natural fly infestations.  animal buildings were monitored in France:  -4 were treated with the test item in dosage 25g/m2 ,  4 were treated with the test item in dosage 40g/m2,  -4 buildings were used as untreated controls.  The counts of the flies trapped are done 7, 14, 21, 56 and 84 days after treatment.  Treated with a single dose. Test period from August to October, 2015. | 25 g/m2:  Mean of *S. calcitrans* before treatment: 43 (26, 37, 56 and 53).  Reduction: 66.9% after 14 days, 86.8% after 21 days , 94.9% after 56 days and 87.1% after 84 days.  Mean of *E.tenax* before treatment: 48.75 (69, 38, 46 and 42).  Reduction: 58.3% after 14 days, 89.6% after 21 days , 95.7% after 56 days and 97.6% after 84 days.  40g/m2:  Mean of *S. calcitrans* before treatment: 49.5 (41, 38, 55 and 64).  Reduction: 70.4% after 14 days, 92.7% after 21 days , 98.4% after 56 days and 96.7% after 84 days.  Mean of *E.tenax* before treatment: 43.5 (29, 48, 37 and 60).  Reduction: 69.8% after 14 days, 92.2% after 21 days , 95.3% after 56 days and 95.4% after 84 days.  Untreated control:  7.9% reduction of *Stomoxys calcitrans* and 9.7% of *Eristalis tenax* after 12 weeks | FIELD TESTING OF AN INSECTICIDE PRODUCT INTENDED TO  CONTROL FLIES IN BREEDING PREMISES TRIAL AGAINST THE STABLE FLY Stomoxys calcitrans AND THE DRONE FLY Eristalis  Tenax  xxxxxxx 2015  1931-FFT4GR/0515 |
| Insecticide | Indoor | BIOPREN 4 GR - Fly larvicide granule - 4 g/kg S-methopren | *Stomoxys calcitrans (larvae)*  *Eristalis tenax*  *(larvae)* | Laboratory test,  residual efficacy test  Manual for the Authorization of Pesticides - EU part – Biocides - Chapter 7 Efficacy - version 1.1; January 2013  NF T 72-320 | Dose: 25 g/m2 for both species:  25 last instar larvae (L3) from a colony breeding.  4 replicates per serie.  Substratum: cow manure + straw  Fresh treated substratum, aged substratum (treated 4, 8 or 12 weeks before) and untreated control  Conditions: 24+/-1 °C, 65 +/-5 % RH, light 1200 lux 8 hours + 16 hours darkness, no ventilation.  After 0, 4, 8 or 12 weeks, larvae were set onto the medium. The emerged adults were counted in the treated and the untreated series. | 25 g/m2:  Fresh and aged substratum (4, 8 or 12 weeks): hatching inhibition 100% of *Stomoxys calcitrans* and *Eristalis tenax* after 12 weeks  Untreated control:  92% emergence of *Stomoxys calcitrans* and 88 % emergence of *Eristalis tenax* | Laboratory measurement of the effectiveness of an IGR-insecticide speciality intended for the control of stable flies Stomoxys calcitrans and Eristalis tenax TEC Laboratoire,  xxxxxxx 2016  2069c/0416R |
| Insecticide | Indoor | Biopren 4 GR fly larvicide granule, 4 % S-Methoprene | *Musca domestica (larvae)* | Laboratory test  In-house trial protocol was followed. | Dosages:  25g/m2 and 30g/m2,  On day 0 the product was applied. After 4-7 days larvae pupated and were placed separately from substrate and each other.  During the pupation period (10 days) the larvae were checked regular. The evaluation of the trial took place following hatching and death of all fly imagos.  Total testduration: 20 days.  50 L3 larvae per replicate, 3 replicates per dosage.  Conditions: 24+/-1 °C, 65 +/-5 % RH, light natural/artificial, continuous ventilation. | Dosage 25g/m2:  pig slurry: hatching inhibition 100%  pig manure: hatching inhibition 100%  chicken manure: hatching inhibition 97.68%  chicken litter: hatching inhibition  85.44%  Dosage 30g/m2:  pig slurry: hatching inhibition 98.30%  pig manure: hatching inhibition 100%  chicken manure: hatching inhibition 97.52%  chicken litter: hatching inhibition  94.84%  Control mortalities were between 2.84 and 10.45% in the different substrates. | EFFICACY STUDY OF BIOPREN 4 GR FLY LARVICIDE GRANULE ON MUSCA DOMESTICA LARVAE IN FOUR DIFFERENT MANURES,  xxxxxxx, 2015, 153.041.-042.-045.  153.046.-047.-050.  153.051.-052.-055.  153.056.-057.-060 |
| Insecticide | Indoor | Biopren 4 GR microencapsulated S-methoprene based sand granule, (0.4% S-methoprene  identical to BIOPREN 4GR FLY larvicide granule | *Musca domestica (larvae)* | Laboratory test  In-house trial protocol was followed. | Dosages:  1 ppm (125 mg/500 g substrate – 91.56 cm2: 13.7 g/m2), 5 ppm (625 mg/500 g substrate – 91.56 cm2: 68.3 g/m2)and 10 ppm (1250 mg/500 g substrate – 91.56 cm2: 136.5 g/m2),  100L3 larvae per replicate, 2 replicates per dosage  On day 0 the product was applied. After 4-8 days larvae pupated and were placed separately from substrate and each other.  Total testduration:  20 days  Conditions:  23-25 C room temperature, 50-60% relative humidity.  Substratum:  40% manure, 30% ground granulated dry dog’s meat, 10% wet dog’s meat, 20% drinking water.  The evaluation of the trial took place following hatching and death of all fly imagos. | 1ppm: 89.6% hatching inhibition  5ppm: 98.88% hatching inhibition  10ppm: 100% hatching inhibition  Control hatching efficiency: 96.9 % (3.1% hatching inhibition) | Biological efficacy trial of Biopren 4GR microencapsulated S-methoprene based sand granule,  xxxxxxx, 2007, 073.047, 073.048, 073.049,  0.73.050 |

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| **Conclusion on the efficacy of the product** |
| Six efficacy study reports were provided in which efficacy of BIOPREN 4 GR FLY larvicide granules against house fly (*Musca domestica*), stable fly (*Stomoxys calcitrans*) and drone fly (*Eristalis tenax*) larvae was demonstrated in both laboratory and field tests, at a dose of 30 g/m2. All tests were performed with the product to be authorized. Test results proved sufficient efficacy under laboratory and field conditions with a residual efficacy of 12 weeks for all of the fly species claimed in the label. |

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#### Occurrence of resistance and resistance management

Some studies showed isolated population of mosquitoes and flies that have developed low level of resistance. Regarding flies, literature reference has been found (Kristensen M., and Jespersen J. B. (2003)).on the possible occurrence of resistance of these species to S-Methoprene. According to Marcombe et al. (2017), Monooxygenases (cytochrome P-450s) enzyme systems could be involved an IGR resistance.

Resistance management

To prevent the development of resistance it is advised to use insecticides with different mode of action as well in the pest control program. In the case of Biopren 4 GR fly larvicide granule it is advised to use adulticide product, sticky traps and UV lamps after a few application of the larvicide product. Sticky traps can also be used for monitoring purposes.

#### Known limitations

In the case of very dry substrates (e.g. chicken litter), effect of the product may develop slower. Adding 100-200 mL water/m2 to the substrate may facilitate development of larvicide effect in the case of very dry environmental conditions.

#### Evaluation of the label claims

Target species of the product are fly species (house fly, stable fly and drone fly) inhabiting human environment and livestock units. Efficacy studies were performed on different substrates demonstrating proper fly larvicide effect in cow, pig and chicken manures.

Efficacy against *Musca domestica* (house fly):

- a laboratory test (xxxxxxx, 2014) demonstrated efficacy in chicken manure at an application rate of 30g/m2 (100% mortality of the pupae).

- a laboratory test (xxxxxxx, 2015) demonstrated efficacy in pig slurry, pig manure, chicken manure and chicken litter at 30g/m2 (all >95 % inhibition).

- a laboratory test (xxxxxxx, 2007) demonstrated efficacy in 3 dosages in a manure substratum. At 13.7 g/m2 89.6% inhibition was shown. At 68.3 g/m2 and 136.5 g/m2 inhibition was respectively 98.88% and 100%.

- a field test (xxxxxxx, 2011) demonstrated efficacy of Biopren 4GR in with a residual efficacy of 90 days at an application rate of 30 g/m2 in closed livestock breeding buildings (pigsties). After 30 days reduction of the fly population was 95.9% and after 90 days reduction was 91.1%.

Efficacy against *Eristalis tenax* (drone fly):

- a laboratory test (xxxxxxx, 2016) demonstrated efficacy in cow manure (100% mortality) after 12 weeks at an application rate of 25g/m2. The untreated control showed emergence of adult Eristalis tenax of 82%.

- a field test (xxxxxxx 2015) demonstrated efficacy in different types of manure (cow, pig and sheep) after 12 weeks at an application rate of 25 g/m2 and 40 g/m2 (97.6% and 95.4% reduction). Untreated control showed reduction of Eristalis tenax of 9.7 % after 12 weeks.

*Stomoxys calcitrans* (stable fly):

- a laboratory test (xxxxxxx, 2016) demonstrated efficacy in cow manure (100% mortality) after 12 weeks at an application rate of 25g/m2. The untreated control showed emergence of adult *Stomoxys calcitrans* of 91%.

- a fieldtest (xxxxxxx 2015) demonstrated efficacy in different types of manure (cow, pig and sheep) after 12 weeks at an application rate of 25 g/m2 and 40 g/m2 (87.1.6% and 96.7% reduction). Untreated control showed reduction of *Stomoxys calcitrans* of 7.9 % after 12 weeks.

Based on the provided efficacy data authorization can be granted for the control of larvae of *Musca domestica, Eristalis tenax* and *Stomoxys calcitrans* at an application rate of 30 g/m2 with a residual efficacy of 12 weeks (84 days). Expected time delay from the beginning of the application to manifestation of the biocidal effect is 2-4 weeks. The provided efficacy tests were conducted with cow manure, pig slurry and pig manure, with chicken manure and chicken litter and with sheepmanure.

For proper penetration and even distribution of the active substance in the whole quantity of the manure, it is important to treat every fresh manure layer accumulating on the top of previously treated layers. Since fly larvae usually live in the upper 5-15 cm of the manure, burying themselves from the top of the manure where the adults lay eggs, this is the thickness of fresh manure layer which should be treated from the top. Dosage were calculated based on these data to ensure that each set of new larvae receive the same active substance dose. This approach is in accordance with instructions of the WHO guideline (Vector control – Methods for Use by Individuals and Communities, 1997, Chapter 6: Houseflies): „Larvicides are applied with a sprayer or a watering can as emulsions, suspensions or solutions. The dosage has to be sufficient to wet the upper 10–15 cm of the substrate, i.e. 0.5–5 litres/m2.”

This product contains amorphous silicon dioxide (CAS 7631-86-9) which is approved for PT18. However, since it has a particle size of d50=18 μm (as indicated in its technical data sheet and safety data sheet) it can penetrate into the body of insects neither orally, nor topically. Therefore, it is not considered as an active substance of this product. Amorphous silicon dioxide used as an insecticide active substance is a nanomaterial with a much smaller particle size than het dimensions of our carrier (particle size distribution of the biologically active silicon dioxide (in mass) is: 90% below 4.8 μm; 50% below 3 μm and 1% below 1.9 μm).

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

BIOPREN 4 GR FLY larvicide granule is not intended to be used in combination with other biocidal products.

Risk assessment for human health

#### Assessment of effects on Human Health

Note NL CA: For all endpoints included below, the calculations method in line with CLP has been used. More information is included in the confidential annex to the PAR.

**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 4 GR FLY LARVICIDE GRANULE is considered not irritating to the skin.

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| **Conclusion used in Risk Assessment – Skin corrosion and irritation** | |
| Value/conclusion | BIOPREN 4 GR FLY LARVICIDE GRANULE is not a skin irritant |
| Justification for the value/conclusion | On the basis of the reactions observed in the S-methoprene skin irritation study, the active substance 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. |

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| **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 4 GR FLY LARVICIDE GRANULE is considered not irritating to the eye.

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| **Conclusion used in Risk Assessment – Eye irritation** | |
| Value/conclusion | BIOPREN 4 GR FLY LARVICIDE GRANULE is not an eye irritant |
| Justification for the value/conclusion | The active ingredient S-methoprene is not an eye irritant. The co-formulants are present in the biocidal product at concentrations insufficient to trigger the classification of the product. |
| Classification of the product according to CLP and DSD | No classification required according to CLP |

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| **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 4 GR FLY LARVICIDE GRANULE is considered not irritating to the respiratory tract.

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| **Conclusion used in the Risk Assessment – Respiratory tract irritation** | |
| Value/conclusion | No risk identified for BIOPREN 4 GR FLY LARVICIDE GRANULE in relation to respiratory tract irritation |
| 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 |

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| **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, EUH208 “Contains polyethyleneglycol-15-hydroxystearat. May produce an allergic reaction.” needs to be included in the labelling of BIOPREN 4 GR FLY LARVICIDE GRANULE.

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| **Conclusion used in Risk Assessment – Skin sensitisation** | |
| Value/conclusion | The product is not classified as a skin sensitiser. A component present in the product has the potential to cause allergic reaction. |
| Justification for the value/conclusion | The active ingredient S-methoprene is not senzitizing. The only co-formulant that has skin sensitization property is polyethylene-glycol-15-hydroxystearat. |
| Classification of the product according to CLP and DSD | EUH208 Contains polyethyleneglycol-15-hydroxystearat. May produce an allergic reaction. - according to CLP |

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| **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)***

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 does not have respiratory sensitizing properties. Furthermore, the co-formulants that are present in the biocidal product do not trigger classification of the product.

***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 4 GR FLY LARVICIDE GRANULE is considered not acute toxic via the oral route.

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| **Value used in the Risk Assessment – Acute oral toxicity** | |
| Value | No risk identified for BIOPREN 4 GR FLY LARVICIDE GRANULE in relation of 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 |

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| **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 4 GR FLY LARVICIDE GRANULE is considered not acute toxic via the inhalation route.

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| **Value used in the Risk Assessment – Acute inhalation toxicity** | |
| Value | No risk identified on BIOPREN 4 GR FLY LARVICIDE GRANULE in relation of 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 |

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| **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.

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| **Value used in the Risk Assessment – Acute dermal toxicity** | |
| Value | No risk identified on BIOPREN 4 GR FLY LARVICIDE GRANULE in relation of 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 |

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| **Data waiving** | |
| Information requirement | Acute dermal for 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***

Dermal absorption can be estimated on the basis of existing information that comes from the dossier of the active substance, S-methoprene, and from product characteristics.

In the CAR of S-methoprene the potential dermal absorption was investigated in an *in vitro* study using human volunteer skin (split-thickness skin mebranes) and radio-labelled S-methoprene (0.125% w/w) (Toner, 2009). Following topical application of the test substance to human skin *in vitro*, the absorbed dose of [14C]-S-methoprene was 0.04%. The dermal delivery of [14C]-S-methoprene was 1.61%. The majority of the applied dose was removed by washing the skin (the total dislodgeable dose was 94.16%). The dermal absorption of S-methoprene was therefore estimated to be 2.86% (dermal delivery and stratum corneum). An agreed dermal absorption rate of 3.50% was established from the estimated dermal absorption value of 2.86% based on the inclusion of tape strips (3-5) (0.58%) in the calculation (see also table below).

This value of 3.5% is considered valid for the current product as well. BIOPREN 4 GR FLY LARVICIDE GRANULE contains a higher concentration of active substance than the tested formulation (0.4% in product v.s. 0.125% in tested formulation). Furthermore, none of the co-formulants in the product are expected to enhance the dermal absorption of the active substance compared to the tested product in the dermal absorption study. Neither the tested formulation nor BIOPREN 4 GR FLY LARVICIDE GRANULE are classified as irritating or sensitizing. Therefore, the dermal absorption value based on the tested formulation can be considered relevant for BIOPREN 4 GR FLY LARVICIDE GRANULE. Consequently, for the risk assessment of BIOPREN 4 GR FLY LARVICIDE GRANULE the dermal absorption value of 3.5% is applied. See IUCLID section 8.6.

| **Summary table of in vitro studies on dermal absorption** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Method, Guideline,**  **GLP status, Reliability** | **Species, Number of skin samples tested per dose, Other relevant information about the study** | **Test substance, Doses** | **Absorption data for each compartment and final absorption value** | **Remarks** *(e.g. major deviations)* | **Reference** |
| OECD 428, GLP, Reliability 1 | Human skin, one dose, total of 10 skin samples | Test formulation: Biopren Pharaoh’s Ant Colony Eliminator with 0.5 % w/w labeled  S-methoprene,  Test preparation: 0.126 w/w% S-methoprene (actual) | Total dislogeable: 94.16 %  Dermal delivery: 1.61 %  Stratum corneum (tape strips 6-20): 1.21%  Strip 3-5: 0.58 %  Dermal absorption of [14C]-S-methoprene is 3.44 ≈ 3.5%. | none | xxxxxx, 2009. |

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| **Value(s) used in the Risk Assessment – Dermal absorption** | |
| Substance | S-methoprene |
| Value(s)\* | 3.5 % |
| Justification for the selected value(s) | An agreed dermal absorption rate of 3.50% was established in the AR based on an *in vitro* study using human volunteer skin. This value is considered relevant for BIOPREN 4 GR FLY LARVICIDE GRANULE based on its active substance content, composition and toxicological properties.  Note NL CA:  During the discussion phase of this dossier, it was pointed out that the product consists of several surfactants. Surfactants are known to enhance dermal penetration. Nevertheless, considering other factors i.e. the active substance concentration of 0.4% s-methoprene, microencapsulation and solid state, it was concluded that the dermal absorption value derived from the included study in the CAR is also representative for BIOPREN 4 GR FLY LARVICIDE GRANULE.  It is noted that the dermal absorption study referred to here is included in the CAR before any EFSA dermal absorption guidance was available. At substance renewal new guidance’s needs to be considered and therefore the value derived at active substance inclusion, i.e. 3.5% will be used for the risk assessment. It should be noted that applying the EFSA guidance on dermal absorption (2012), will result in a value of 5% (rounded) which does not influence the outcome of the risk assessment. |

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | Dermal absorption test on the product |
| Justification | Dermal absorption can be estimated on the basis of existing information that comes from the active substance dossier and from product characteristics. |

***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) were identified in the S-methoprene Assessment Report.

Furthermore, no substances of concern were identified using the guidance on Substances of Concern (CA-Nov14-Doc.5.11), considering all 5 criteria.

***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. Based on the calculation method described in Annex I of Regulation 1272/2008/EC, EUH208 “Contains polyethyleneglycol-15-hydroxystearat. May produce an allergic reaction.” needs to be included in the labelling of BIOPREN 4 GR FLY LARVICIDE GRANULE.

***Others***

**Endocrine disruption activity**

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.

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.

No toxicological studies are available for the product BIOPREN 4 GR FLY LARVICIDE GRANULE. The product was not tested for potential endocrine disruption properties.

In the CAR for S-methoprene (Dec 2013) it has been agreed that S-methoprene should be further assessed with regards to its endocrine disruptor propersies once further guidance is available, which should be harmonised at the EU level.

To examine if any of the co-formulants contained in the product may possess ED properties a screening using the databases listed in the ECHA/EFSA ED guidance (2018) was conducted by the CA NL. From the screening 3 co-formulants (X, Y, Z) triggered an alert for ED properties.

Regarding co-formulant X a concern has been raised by a member state to include this substance in the CoRAP (Community rolling action plan) list due to its ED potency. No further ED assessment was considered necessary for this PAR because the discussion should be coordinated at the EU level. The ED assessment for this co-formulant X should await the outcome of the discussions at EU level.

The applicant was requested to provide additional information for two of the co-formulants (Y, Z) and it was concluded that these two substances do not fulfil the ED criteria c) as indicated above, and therefore, have no ED concern.

More information about the ED screening of the co-formulants including identity of the co-formulant X Y and Z and ED assessment provided by the applicant on co-formulant Y and Z are found in Confidential Annex 3.6.

#### Exposure assessment

The active substance, S-methoprene and the product BIOPREN 4 GR FLY LARVICIDE GRANULE are manufactured and formulated in Hungary. Production and formulation of the biocidal product is covered by other legislation.

Potential exposure to S-methoprene from BIOPREN 4 GR FLY LARVICIDE GRANULE will occur through use of the product. Exposure assessment for use of this product is undertaken below. In addition, there is negligible indirect human exposure to BIOPREN 4 GR FLY LARVICIDE GRANULE expected via the environment therefore, human exposure assessment via the environment for use of this product is not undertaken.

**Inhalation exposure**

S-methoprene is not volatile (0.623 mPa at 20oC and 1.08 mPa at 25oC) and so the risk of inhalation exposure to S-methoprene for professional or amateur users during use is considered to be negligible, which is also supported by the result of the dustiness test on the BIOPREN 4 GR FLY LARVICIDE GRANULE, showing that the product is essentially non-dusty, and by the particle size distribution of 0.5-2 mm. Similarly, for non-users, the risk of inhalation exposure to residues during or after application via the environment is considered to be negligible.

**Dermal exposure**

BIOPREN 4 GR FLY LARVICIDE GRANULE is loaded by hand. The main route of exposure is dermal exposure of users during loading and application. Exposure of other parts of the body can be counted as negligible, but is included in the exposure calculation. After application, non-users are not likely to come into contact with BIOPREN 4 GR FLY LARVICIDE GRANULE used in manure treatment. However as a worst case, secondary exposure calculation is also included.

**Oral exposure**

BIOPREN 4 GR FLY LARVICIDE GRANULE is not likely to directly reach the mouth of professional or amateur users. Therefore, the risk during use 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. Similarly, for non-users, risk of oral exposure to residues during or after application is considered to be negligible. Infants and children are not present in animal houses. However school children may visit animal farms.

**Identification Of Main Paths Of Human Exposure Towards S-Methoprene From Its Uses In Biocidal Products**

The preparation has to be spread onto the manure’s surface either with a measuring cup, or with an appropriate device, e.g. hand-held granule applicator at a dose of 30 g/m2. Slatted floor: it is necessary to repeat treatment after each removal of dung. Deep litter: on every new layer of litter and after every 8 - 10 cm increase the treatment has to be repeated with the product.

The vapour pressure of the active substance is very low. Evaporation of substance will be so minor that the inhalation exposure is considered to be negligible. Also the granular product will not produce significant amount of dust to get into the air. According to the result of the dustiness test on BIOPREN 4 GR FLY LARVICIDE GRANULE, the product is essentially non-dusty. The particle size distribution is 0.5-2 mm.

Some dermal exposure could occur when loading and during application of the product. There are no EU harmonised exposure calclulation models for application of a granular biocide product. Therefore default values were taken from the US EPA Occupational Pesticide Handler Unit Exposure Surrogate Reference Table (June 2018, hereafter referred to as US EPA Guide).

The product is recommended for use 1 time per 8 weeks. Therefore, short/medium-term exposure (same AEL value) is used for the risk assessment.

| **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. | negligible | negligible | n.a. | negligible | negligible | n.a. |
| Dermal | n.a. | yes | yes | n.a. | yes | 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  US EPA Occupational Pesticide Handler Unit Exposure Surrogate Reference Table:  Scenario ”Mixing / Loading Granules” | Professional, non-professional |
| 2. | Application / handheld granule applicator | Primary exposure  US EPA Occupational Pesticide Handler Unit Exposure Surrogate Reference Table:  Scenario ”Applicator, Open Cab Solid Broadcast Spreader” | Professional |
| 3. | Granular bait dispersed by hand | Primary exposure  US EPA Occupational Pesticide Handler Unit Exposure Surrogate Reference Table:  Scenario ”Applicator, Granules by Hand” | Professional |
| 4 | Granular bait dispersed by hand | Primary exposure  US EPA Occupational Pesticide Handler Unit Exposure Surrogate Reference Table:  Scenario ”Applicator, Granules by Hand” | Non-Professional |
| 5 | Children touching treated surfaces | Secondary exposure  Children may be dermally exposed by touching treated surfaces when visiting animal farms or when the product is used by non-professionals | Children |
| 6 | Dietary exposure | Secondary exposure  The general public could be exposed to residues via eating food from animal origin | General public |

The exposure from cleaning of application equipment is considered not to be higher than the loading opearation, thus covered by scenario 1 for professional and non-professionals.

***Industrial exposure***

The active substance, S-methoprene and the product BIOPREN 4 GR FLY LARVICIDE GRANULE are manufactured and formulated in Hungary. Production and formulation of the biocidal product is covered by other legislation.

No industrial use of BIOPREN 4 GR FLY LARVICIDE GRANULE is foreseen.

***Professional exposure***

Professional exposure refers to professional users such as a Pest Control Operators (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 professional user is expected to use gloves, however, the Tier 1 evaluation does not include any PPE.

According to the use instruction the product has to be spread onto the manure or deep litter’s surface either with a measuring cup, or with an appropriate device, e.g. hand held granule applicator. The US EPA Occupational Pesticide Handler Unit Exposure Surrogate Reference Table (June 2018) was used for the estimation of exposure data, as there are no EU harmonised exposure calclulation models for application of a granular biocide product. The scenarios presented in the EPA guide cover the most closely the foreseen application scenarios: loading of granules into a treatment device, application with a solid broadcast spreader or application of granules by hand.

Animal housing treatment:

As a worst case the estimated exposure (and risk) was calculated on the basis of the US EPA Guide scenarios “Mixing/Loading Granules” and “Applicator, Open Cab Solid Broadcast Spreader”.

As a worst case it was assumed that one worker will treat the whole animal housing area. Calculation was made with the ESD scenario: Laying hens in battery cages with aeration (belt drying), where the total treated area is: 2560 m2.

Manure treatment:

For manure treatment the US EPA Guide Scenario “Applicator, Granules by Hand” was used. Based on the treatment of 200 m2, a total of 6 kg/day needs to be scattered containing 6\*0.004 = 0.024 kg active substance.

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

| **Description of Scenario 1:** Professional user, US EPA Occupational Pesticide Handler Unit Exposure Surrogate Reference Table, Scenario “Mixing / Loading Granules” | | |
| --- | --- | --- |
| **Professional user** The product packaging includes bags and boxes up to 25 kg. Before the application small portion of product from such a big bag or box may be transferred to another container such as hand-held granule applicator. For this operation only dermal exposure is included as inhalation exposure is considered negligible (see above the paragraph on inhalation exposure).  Defaults from US EPA Surrogate Exposure Guide: total dermal exposure (single layer clothes, no gloves): 23.6 µg/lb ai. handled = 0.0520 mg/kg ai. | | |
|  | Parameters | Value |
| Tier 1/No PPE | estimated dermal exposure  (based on US EPA Guide) | 23.6 µg/lb ai. = 0.0520 mg/kg ai. |
| dose | 30 g/m2 product |
| Concentration of the active substance | 0.4% |
| dermal absorption | 3.5 % |
| Inhalation absorption | 100 % |
| User body weight | 60 kg\* |
| Treated area | 2560 m2\*\* |
| Conversion lb to kg | /0.45359237 |

\*: HEEG paper No 17, Default human factor values

\*\*: OECD ESD No.14: Laying hens in battery cages with aeration (belt drying)

Calculations are included in Annex 3.2.

*Scenario 2:* Professional user, Application / handheld granule applicator

| **Description of Scenario 2:** Professional user, US EPA Occupational Pesticide Handler Unit Exposure Surrogate Reference Table, Scenario “Applicator, Open Cab Solid Broadcast Spreader” | | |
| --- | --- | --- |
| **Professional user** applying the product with a handheld granule applicator. Therefore, for the assessment US EPA Surrogate Exposure Guide: Scenario “Applicator, Open Cab Solid Broadcast Spreader” was considered to be the most appropriate. Only dermal exposure is included and inhalation exposure is considered negligible (see above the paragraph on inhalation exposure).  Defaults from US EPA Surrogate Exposure Guide: total dermal exposure (single layer clothes, no gloves): 9.9 µg/lb ai. handled = 0.0218 mg/kg ai. | | |
|  | Parameters | Value |
| Tier 1/No PPE | estimated dermal exposure  (based on US EPA Guide) | 9.9 µg/lb ai. = 0.0218 mg/kg ai. |
| dose | 30 g/m2 product |
| Concentration of the active substance | 0.4% |
| dermal absorption | 3.5 % |
| Inhalation absorption | 100 % |
| User body weight | 60 kg\* |
| Treated area | 2560 m2\*\* |
| Conversion lb to kg | /0.45359237 |

\*: HEEG paper No 17, Default human factor values

\*\*: OECD ESD 14: Laing hens in battery cages with aeration (belt drying)

Calculations are included in Annex 3.2.

*Scenario 3:* Professional user, Granular bait dispersed by hand

| **Description of Scenario 3:** Professional user, US EPA Occupational Pesticide Handler Unit Exposure Surrogate Reference Table, Scenario “Applicator, Granules by Hand” | | |
| --- | --- | --- |
| **Professional user:** applying the product by hand. Only dermal exposure is included as inhalation exposure is considered negligible (see above the paragraph on inhalation exposure).  Defaults from US EPA Surrogate Exposure Guide: total dermal exposure (single layer clothes, no gloves): 104000 µg/lb ai. handled = 229.28 mg/kg ai. | | |
|  | Parameters | Value |
| Tier 1/No PPE | estimated dermal exposure  (based on US EPA Guide) | 104000 µg/lb ai. = 229.28 mg/kg ai. |
| dose | 30 g/m2 product |
| Concentration of the active substance | 0.4% |
| dermal absorption | 3.5 % |
| Inhalation absorption | 100 % |
| User body weight | 60 kg\* |
| Treated area | 200 m2\*\* |
| Conversion lb to kg | /0.45359237 |

\*: HEEG paper No 17, Default human factor values

\*\*: Estimated worst case for manual manure treatment

Calculations are included in Annex 3.2.

**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, loading | Tier 1/No PPE | negligible | 9.32 x 10-6 mg/kg bw/d | n.a. | 9.32 x 10-6 mg/kg bw/d |
| Scenario 2 Professional user, open cab | Tier 1/No PPE | negligible | 3.91 x 10-6 mg/kg bw/d | n.a. | 3.91 x 10-6 mg/kg bw/d |
| Scenario 3  Professional user, bait dispersed by hand | Tier 1/No PPE | negligible | 3.21 x 10-3 mg/kg bw/d | n.a. | 3.21 x 10-3 mg/kg bw/d |

**Further information and considerations on scenarios [1-3]**

none

*Combined scenarios*

For professional users it is foreseen that the same person performs the loading into a hand-held applicator and application with the device or into a smaller container before manual application, therefore a combined scenario is considered relevant for scenarios 1+2 and for scenario 1+3. The exposure for the loading step was calculated with the product amount to be used during 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]  Tier 1  (no PPE) | negligible | 1.32 x 10-5 mg/kg bw/d | n.a. | 1.32 x 10-5 mg/kg bw/d |
| Scenarios [1+3]  Tier 1  (no PPE) | negligible | 3.21 x 10-3 mg/kg bw/d | n.a. | 3.21 x 10-3 mg/kg bw/d |

***Non-professional exposure***

For non-professional users the estimated exposure (and risk) was calculated based on the US EPA Occupational Pesticide Handler Unit Exposure Surrogate Reference Table (June 2018), Scenario “Applicator, Granules by Hand”. For non-professional users the worst case animal housing size is assumed to be 88 m2. The value was derived based on the available area for walking, feeding and resting for dairy cows of 8.8 m2 per animal described in OECD ESD No. 14, Emission Scenario Document for Insecticides for Stables and Manure Storage Systems, and an arbital number of 10 animals as a realistic worst case scenario for non-professional users.

For non-professional users the packaging will contain a measuring cup, which is also used for spreading the product, therefore the hand may be exposed to the product. As it concerns non-professional use, only exposure to the unprotected skin is included for the risk assessment. PPE is not relevant.

*Scenario 1: Non-p*rofessional use, Open mixing and loading

| **Description of Scenario 1:** Non-professional user, US EPA Occupational Pesticide Handler Unit Exposure Surrogate Reference Table, Scenario “Mixing / Loading Granules” |
| --- |
| **Non-Professional user** The product packaging includes buckets and boxes up to 5 kg. Before the application small portion of product from such a big box may be transferred to a smaller container. For this operation only dermal exposure is included as inhalation exposure is considered negligible (see above the paragraph on inhalation exposure).  The exposure level is lower than the Mixing and loading scenario for professionals as the amount of product handled will be less for the non-professionals. Parameters and the calculation are presented in scenario 1 for professionals and will not be repeated here. |

*Scenario 4:* Non-Professional, Granular bait dispersed by hand

| **Description of Scenario 4:** Non-professional user, US EPA Occupational Pesticide Handler Unit Exposure Surrogate Reference Table, Scenario “Applicator, Granules by Hand” | | |
| --- | --- | --- |
| **Non-Professional user** The product is applied by hand. Only dermal exposure is included as inhalation exposure is considered negligible (see above the paragraph on inhalation exposure).  Defaults from US EPA Surrogate Exposure Guide: Total dermal exposure (single layer clothes, no gloves): 104000 µg/lb ai. handled = 229.28 mg/kg ai. | | |
|  | Parameters | Value |
| Tier 1/No PPE | estimated dermal exposure  (based on US EPA Guide) | 104000 µg/lb ai. handled = 229.28 mg/kg ai. |
| dose | 30 g/m2 product |
| Concentration of the active substance | 0.4% |
| dermal absorption | 3.5 % |
|  |  |
| User body weight | 60 kg\* |
| Treated area | 88 m2\*\* |
| Conversion lb to kg | /0.45359237 |

\*: HEEG paper No 17, Default human factor values

\*\*: FAO Cattle housing > Housing for the Small Herd

Calculations are included in Annex 3.2.

**Calculations for Scenario 4, non-professional uses**

| **Summary table: systemic exposure from non-professional uses** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake** | **Estimated dermal uptake** | **Estimated oral uptake** | **Estimated total uptake** |
| Scenario 1, non-professional user, loading | Tier 1/No PPE | negligible | <9.32 x 10-6 mg/kg bw/d | n.a. | <9.32 x 10-6 mg/kg bw/d |
| Scenario 4  Non-professional user, bait dispersed by hand | Tier 1/ No PPE | negligible | 1.41 x 10-3 mg/kg bw/d | n.a. | 1.41 x 10-3 mg/kg bw/d |

*Combined scenarios*

For non-professional users it is foreseen that the same person performs the loading into another smaller container before application by using measuring cup, therefore a combined scenario is considered relevant for scenarios 1+4.

| **Summary table: combined systemic exposure from non-professional uses** | | | | |
| --- | --- | --- | --- | --- |
| **Scenarios combined** | **Estimated inhalation uptake** | **Estimated dermal uptake** | **Estimated oral uptake** | **Estimated total uptake** |
| Scenarios [1+4]  Tier 1  (no PPE) | negligible | 1.41 x 10-3 mg/kg bw/d | n.a. | 1.41 x 10-3 mg/kg bw/d |

***Exposure of the general public***

Considering the product is applied on manure or deep litter surface, secondary exposure of adults by touching treated surfaces is considered to be only accidental. Such exposue of children may be possible when they visit animal farms or housing, or when the product is applied by non-professionals.

*Scenario 5:* Secondary exposure, children

Palms of a child may be exposed dermally touching the treated floor. Hand-to-mouth exposure is a behaviour normally included for the exposure of children, however, as the product is spread directly on the manure, therefore there is no direct contact without touching the manure . oral exposure due to hand-to mouth behaviour by touching treated manure is not considered a realistic exposure. Subsequently, only dermal exposure is considered.

Although, the presence of a toddler is not very likely in such animal housing, as a worst case the exposure of a toddler is assessed.

| **Description of Scenario [5]** Secondary exposure, toddler (1-2 years old) visit animal farms | | |
| --- | --- | --- |
|  | Parameters | Value |
| Tier 1 | Dose | 30 g/m2 product |
| fraction of active substance on indoor surface that is available for transfer | 100% (worst case)\* |
| Surface area (both palms) |  |
| Concentration of the active substance | 0.4% |
| Dermal absorption | 3.5% |
| Surface area (both palms) | 115.2 cm2/event |
| Body weight child (HEAdhoc Recommendation No. 14) | 10 kg |

\* The treated surface that is touched may be wet. As there are no appropriate parameter available the worst case (100% transfer) is considered.

Dermal exposure is calculated as following:Dose x fraction available for transfer x concentration of the a.s. x dermal absorption x surface area (both palms) /body weight

= 30 g/m2 product x 100% transfer x 0.4% a.i. x 3.5% dermal absorption x 115.2 cm2 /10 kg bw

= 0.0048 mg/kg bw

**Calculations for Scenario 5**

| **Summary table: secondary exposure scenarios** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake** | **Estimated dermal uptake** | **Estimated oral uptake** | **Estimated total uptake** |
| Scenario [5], children indirect exposure | Tier 1, no PPE | negligible | 0.0048 mg/kg bw/day | negligible | **0.0048 mg/kg bw/d** |

***Monitoring data***

No monitoring data is available.

***Dietary exposure***

A risk mitigation measure is included stating “Keep away from food, drink and animal feedingstuffs”, “Do not disperse the granules in the immediate surroundings of feeding and watering places or where the animals may consume the product. In the event that the animal’s feed or drinking water might be contaminated, empty or cover the feeder and the water dispenser before treating the area” and “DO NOT store with food, feedstuffs, seed and fertilisers”. During the storage, mixing & loading and the application no food, drinking water are exposed to the product. Therefore as no food is contaminated no Dietary Risk Assesment (DRA) is required.

Furthermore, indirect consumer exposure is discussed below in: *Estimating Livestock Exposure to Active Substances used in Biocidal Products* and in *Estimating residues in edible crops via fertilizer.*

*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 (scenario 6)*

Livestock are not present when the litter or manure is treated. The only possible exposure is via secondary exposure.

Indirect exposure after treatment of the floors with BIOPREN 4 GR FLY LARVICIDE GRANULE may be possible, as livestock may lick/eat from the floor. When animals lay down also dermal contact is possible. The amount of BIOPREN 4 GR FLY LARVICIDE GRANULE on the floor is indicated to be up to 30 g/m2 according to the label. This leads to a worst case of 30 x 0.004 = 0.12 g/m2 S-methoprene. The dislodgable fraction from a smooth floor is 2-6% according to TNsG (2007, p 102) for a powder. However, the treated surface that is touched may be wet and thus this value is not applicable. As there are no appropriate parameter available 100% transfer is considered as the worst case, resulting in 0.12 g/m2 dislodgable residue. The realistic worst-case external exposure calculation for a calf as the representative animal is performed according to the DRAWG Draft proposal guidance on Estimating Livestock Exposure to Biocidal Active Substances (2010), included in p.344 of the BPR guidance (Vol III, Part P+C). Livestock exposure estimates should be performed for all representative livestock species (beef and dairy cattle, pigs, chicken). As the biocidal product is intended to be applied in pig, cow and poultry stables an assessment, using the BfR calculator for estimating external exposure of livestock animals is included (Excel document is included in Annex 3.2).

For the calculation three scenarios were considered, Tier 1 based on 100% oral and dermal absorption and in Tier2 including an refinement factor of 35% for dermal and oral absorption:

1) oral-animals licking surfaces

2) dermal-rubbing against surfaces

3) oral- ingestion of dead insects

More detailed justification for the use of 35% for oral and dermal absorption of livestock is included in the confidential Annex to the PAR.

|  |  |  |  |
| --- | --- | --- | --- |
| Total Estimated Livestock Exposure (mg a.s./kg bw/d)Animal Species |  | Sum of  all routes of exposure,  Tier 1 | Sum of  all routes of exposure,  Tier 2 |
| Beef cattle |  | 0.3648 | 0.1277 |
| Dairy cattle |  | 0.3249 | 0.1137 |
| Calf |  | 0.5700 | 0.1995 |
| Fattening pig |  | 0.6360 | 0.2226 |
| Breeding pig\* |  | 0.4246 | 0.1486 |
| Breeding pig\* | individual housing | 0.0000 | 0.0000 |
| Breeding pig\* | group housing | 0.0000 | 0.0000 |
| Sheep |  | 0.1280 | 0.0448 |
| Lamb |  | 0.2400 | 0.0840 |
| Slaughter goat (= goat kids) |  | 2.1231 | 0.7431 |
| Lactating goat |  | 0.9086 | 0.3180 |
| Broilers\* |  | 0.0824 | 0.0288 |
| Broilers\* | free range, litter floor | 0.0000 | 0.0000 |
| Broilers\* | parent broilers, free range (grating floor) | 0.0000 | 0.0000 |
| Broilers\* | parent broilers in rearing, free range (grating floor) | 0.0000 | 0.0000 |
| Laying hen\* |  | 0.0737 | 0.0258 |
| Laying hen\* | battery | 0.0000 | 0.0000 |
| Laying hen\* | free range (litter floor) | 0.0000 | 0.0000 |
| Laying hen\* | free range (grating floor) | 0.0000 | 0.0000 |
| Turkey |  | 0.0200 | 0.0070 |
| Horse |  | 0.4860 | 0.1701 |
| Rabbit |  | 0.0000 | 0.0000 |
| \*Please note that some scenarios for chicken and pigs distinguish between several housing conditions. | | |  |

For consumer exposure, the standard food basket as defined in Commission Regulation (EU) 2018/782 is considered.

According to the standard food basket the theoretical maximum daily intake for animal origin product for an adult is:

2.0 kg for mammals (0.3 kg muscle, 0.05 kg fat, 0.1 kg liver, 0.05 kg kidney 1.5 kg milk), and 0.6 kg for poultry (0.3 kg muscle, 0.09 kg fat and skin in natural portions, 0.1 kg liver, 0.01 kg kidney, 0.1 kg egg).

The theoretical maximum consumption of the substance is therefore calculated as following using Tier 1 calculations (100% oral and dermal absorption:

(0.6360 mg/kg bw (based on fattening pig, worst case mammal, see table above) x 2.0 kg) + (0.0824 mg/kg bw (worst case poultry, see table above) x 0.6 kg) x 35% oral absorption

= (1.272 + 0.04944) mg/person x 35%

= 0.4625 mg/person

= 0.0077 mg/kg bw/d based on a 60 kg person.

For S-methoprene, no ADI is set in EU. The AEL long-term was derived from the NOAEL of 21.7 mg/kg bw/d from the 2-yr rat study, using an assessment factor of 100 and corrected for oral absorption, resulting in a value of 0.08 mg/kg bw/day. For the derivation of an ADI, the NOAEL of 21.7 mg/kg bw/d from the 2-yr rat study is applicable and including an assessment factor of 100, a value of 0.217 mg/kg bw/ day is derived.

Therefore, the maximal theoretical maximum consumption of 0.00289 mg/kg bw/d is 1.3% of the derived ADI.

Therefore no concern has been identified from the consumption of animal products.

**Conclusion**

Based on the calculation of the dermal and oral dose of the livestock it is expected that the product BIOPREN 4 GR FLY LARVICIDE GRANULE does not pose a concern for consumers. Furthermore taking into account the low toxicity of S-methoprene (acute as well as chronic toxicity) and the result of the toxicokinetic results (rapid elimination from the body, no accumulation in the body), no adverse effect on the livestock is expected.

However, as the trigger value of 0.004 mg/kg bw/d is exceeded for the representative animal species the issue of potential residues in food of animal origin must be further addressed and this will be included in section 2.2.6.3 Risk characterision for Human Health when discussing MRLs.

*Estimating residues in edible crops via fertilizer (scenario 6b)*

As manure is commonly spread onto agricultural land as fertilizer, biocidal residues contained in manure may be transferred into crops grown on this land.

For this, the concentration in plant roots due to the absorption of the s-methoprene via roots is calculated, based on the model used for environmental risk assessment for REACH. According to the EUSES background document,

cid:image002.png@01D51081.49953B00

Fwaterplant: volume fraction of water in plant tissue [m3.m-3]

Flipidplant: volume fraction of lipids in plant tissue [m3.m-3]

Kow: octanol-water partition coefficient [m3.m-3]

b: Correction for differences between plant lipids and octanol [-]

Kplant-water: partition coeff. between plant tissue and water [m3.m-3]

Kplant-water: = 0.65 + 0.01 x 6.34 L/kgx0.95 = 0.71 m3/m3

cid:image003.png@01D51081.49953B00

Kplant-water

partition coeff. between plant tissue and water [m3.m-3]

Cagric,porew: in pore water of agricultural soil [kgc.m-3] (PEC value in groundwater)

RHOplant: bulk density of plant tissue (wet weight) [kgwwt.m-3]

Croot: concentration in root tissue of plant [kgc.kgwwt-1]

Croot: = (0.71 x 5.17 E-7 kg/m3)/700 = 5.24 E-10 kg a.s./kgwwt = 5.24E-4 mg/ kgwwt = 0.00052 mg/ kgwwt

The half-life of S-methoprene in the soil is 1.55 days, and the a.s. will rapidly decompose in field. Also, the instruction not to use treated manure earlier than 2 months after treatment is included. The decomposition of the a.s. during this two months in manure is not taken into account in the calculation for PECground water. The calculated concentration represents therefore the theoretical worst case and in practice the concentration should be much lower

**Conclusion**

Based on the CA document for an interim approach for the establishment of MRL (CA-March17-Doc.7.6.c-final), the question of residues should be further explored only when active substances can lead to measurable residue levels in food (sec 2.2). The calculated S-methoprene level of 0.00052 mg/kg bw is below the default MRL of 0.01 mg/kg, which is set at the LOD, thus not measurable.

In addition, MRLs for S-methoprene are set to be 0.02-5 mg/kg for different food categories for both plants and animal origin, based on EU No 396/2005.

Altogether, S-methoprene concentration in crop is considered not to be measurable, and is below the MRLs. Therefore no adverse effects on consumers via dietary exposure to food of plant origin of land fertilized with treated manure is expected.

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

Dietary exposure by consuming animal products is considered in the section “Estimating Livestock Exposure to Active Substances used in Biocidal Products” above. Further no food contamination would occur during the use of BIOPREN 4 GR FLY LARVICIDE GRANULE. The product is used for manure treatment in animal stables and manure pits.

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

Dietary exposure by consuming animal products is considered in the section “Estimating Livestock Exposure to Active Substances used in Biocidal Products” above. Further no food contamination would occur during the use of the product. BIOPREN 4 GR FLY LARVICIDE GRANULE is used for manure treatment in animal stables and manure pits.

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

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

Exposure during formulation of the product BIOPREN 4 GR FLY LARVICIDE GRANULE is expected to be minimal due to operating in a closed system with a ventilation system of the premises. Measurement and mixing of components is automated and controlled by computer. During the production every worker must wear protective glasses, plastic gloves, mask and overall.

Therefore no hazard is identified during manufacturing, and no risk assessment is needed.

There is no guide for calculation of the exposure associated with waste disposal. However based on the toxicological profile and fast photo- and biodegradation of S-methoprene in the environment no significant exposure is expected during the waste disposal of the product.

***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**  **(mg/kg bw)** |
| 1. | Professional user | Tier 1, No PPE | **9.32 x 10-6 mg/kg bw/d** |
| 2. | Professional user | Tier 1, No PPE | **3.91 x 10-6 mg/kg bw/d** |
| 3. | Professional user | Tier 1, No PPE | **3.21 x 10-3 mg/kg bw/d** |
| 1. | Non-professional user | Tier 1, No PPE | **<9.32 x 10-6 mg/kg bw/d** |
| 4. | Non-professional user | Tier 1, No PPE | **1.41 x 10-3 mg/kg bw/d** |
| 5. | Children, secondary exposure | Tier 1, No PPE | **0.0048 mg/kg bw/d** |
| 1+2 | Professional user | Tier 1, No PPE | **1.32 x 10-5 mg/kg bw/d** |
| 1+3 | Professional user | Tier 1, No PPE | **3.21 x 10-3 mg/kg bw/d** |
| 1+4 | Non-professional user | Tier 1, No PPE | **1.41 x 10-3 mg/kg bw/d** |
| 6a | General public | Tier 1, dietary exposure | **0.0077 mg/kg bw/d** |

#### 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 repeated 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). However an ARfD for S-methoprene was not established.

AELmedium-term:

In the dog 90-day repeated 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 300 mg/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 was 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 21.7 mg/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 AELshort-term reference value of: AELshort-term 0.35 mg/kg bw/day.

**Maximum residue limits or equivalent**

In the Approval Regulation of S-methoprene PT18 (in force on 1-9-2015) 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.

For the purpose of dietary risk assessment, and to establish the need to derive a MRL, and in absence of an EU harmonised ADI, an ADI was derived based on the information included in the S-Methoprene dossier. The AEL long-term was derived from the NOAEL of 21.7 mg/kg bw/d from the 2-yr rat study, using an assessment factor of 100 and corrected for oral absorption (35%). For the derivation of an ADI, the NOAEL of 21.7 mg/kg bw/d from the 2-yr rat study is applicable and including an assessment factor of 100, a value of 0.217 mg/kg bw/ day is derived.

The dietary exposure assessment concluded no concern as the theoretical maximum consumption of 0.0077 mg/kg bw/d using the food basket which includes exposure of an adult to 2.6 kg of meat and this is 3.6% of the derived ADI. According to BPR guidance, no MRL needs to be derived if the dietary exposure is below 30% of the ADI.

The CA-March17-Doc.7.6.c-final (An interim approach for the establishment of maximum residue limits for residues of active substances contained in biocidal products for food and feed and specific migration limits in food contact materials), states at section 2.3: Likely consumer exposure via food with the potential for appreciable risk: the question of the need of setting a limit for residues should be further explored

As the dietary exposure results in 1.3% of the derived ADI based on very worst case consumer exposure assessment, no appreciable risk is identified. However, in the referred to sections active substances are discussed that fall under food contact material (FCM), veterinary use (VMP) and plant protection products (PPP).

S-methoprene is used for veterinary medicine. No MRL is derived. However, medicine containing s-methoprene only includes use in cats and dogs. However, based on EMA Guideline on risk characterisation and assessment of MRLs for biocides, no MRL needs to be derived, as the included dietary risk assessment based on calculation is lower than the limit of 30%ADI based on the calculated theoretical maximum consumption using the standard food basket as defined in Commission Regulation (EU) 2018/782 (i.e. which resulted in 1.3% ADI).

Furthermore, S-Methoprene is an active substance formerly used as Plant Protection Products, for which 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 (included in Annex I to Reg. 396/2005). Although S-Methoprene is not approved under PPP, as is included in Reg. 396/2005 the statutory limit set under PPP applies.

S-methoprene concentration in crop is considered not to be measurable and therefore is below the MRLs.

Lifestock exposure assessment (see table below) shows that values exceed the MRL based on the lower limit of analytical determinations.

|  |  |  |  |
| --- | --- | --- | --- |
| Total Estimated Livestock Exposure (mg a.s./kg bw/d)Animal Species |  | Sum of  all routes of exposure,  Tier 1 | Sum of  all routes of exposure,  Tier 2 |
| Beef cattle |  | 0.3648 | 0.1277 |
| Dairy cattle |  | 0.3249 | 0.1137 |
| Calf |  | 0.5700 | 0.1995 |
| Fattening pig |  | 0.6360 | 0.2226 |
| Breeding pig\* |  | 0.4246 | 0.1486 |
| Breeding pig\* | individual housing | 0.0000 | 0.0000 |
| Breeding pig\* | group housing | 0.0000 | 0.0000 |
| Sheep |  | 0.1280 | 0.0448 |
| Lamb |  | 0.2400 | 0.0840 |
| Slaughter goat (= goat kids) |  | 2.1231 | 0.7431 |
| Lactating goat |  | 0.9086 | 0.3180 |
| Broilers\* |  | 0.0824 | 0.0288 |
| Broilers\* | free range, litter floor | 0.0000 | 0.0000 |
| Broilers\* | parent broilers, free range (grating floor) | 0.0000 | 0.0000 |
| Broilers\* | parent broilers in rearing, free range (grating floor) | 0.0000 | 0.0000 |
| Laying hen\* |  | 0.0737 | 0.0258 |
| Laying hen\* | battery | 0.0000 | 0.0000 |
| Laying hen\* | free range (litter floor) | 0.0000 | 0.0000 |
| Laying hen\* | free range (grating floor) | 0.0000 | 0.0000 |
| Turkey |  | 0.0200 | 0.0070 |
| Horse |  | 0.4860 | 0.1701 |
| Rabbit |  | 0.0000 | 0.0000 |
| \*Please note that some scenarios for chicken and pigs distinguish between several housing conditions. | | |  |

The CA-March17-Doc.7.6.c-final documents includes at point 42 the following:

*In such cases a specific MRL can be established by Regulation (EC) No 396/2005 for the active substance, based on information submitted by stakeholders and authorities. The MRL should sufficiently protect consumers on the possible exposure to residues due to the use of the substance in biocidal products, as low as reasonable possible and based on good practice for the use of the specific biocidal product(s).*

However, it should be noted that exceedance of the MRL (i.e. residues compared to lowest MRL of 0.05 mg/kg considering Tier 1: 1.6-12.7 or Tier2 assessment: 0.5-4.5) are concluded based on worst case calculations due to rubbing or licking/eating dead insects with 100% transfer and no metabolism in the animal. If the applicant can provide monitoring data showing that concentrations remain below the lower limit of analytical determinations as included in Annex I to Reg. 396/2005, no specific MRLs need to be set.

Although the assessment shows that MRLs are exceeded, safe use is identified for use of BIOPREN 4 GR FLY LARVICIDE GRANULE based on the risk assessment for consumers and animals. As safe use is concluded, BIOPREN 4 GR FLY LARVICIDE GRANULE complies with the Conditions for granting an authorisation (Article 19) and therefore the product can be authorised.

***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** | **AEL**  **mg/kg bw/d** | **Estimated uptake**  **mg/kg bw/d** | **Estimated uptake/ AEL**  **(%)** | **Acceptable**  **(yes/no)** |
| Scenario 1, Open mixing& loading, no PPE | Tier 1 | 0.076 | 9.32 x 10-6 mg/kg bw/d | 0.012% | yes |
| Scenario 2, Application / open cab, no PPE | Tier 1 | 0.076 | 3.91 x 10-6 mg/kg bw/d | 0.005% | yes |
| Scenario 3 dispersed by hand, no PPE | Tier 1 | 0.076 | 3.21 x 10-3 mg/kg bw/d | 4% | yes |

For use by professional users the exposure is maximally 0.9% of the AELlong-term, and therefore, safe use can be concluded for the professional use of BIOPREN 4 GR FLY LARVICIDE GRANULE, even without the use of any PPE.

**Combined scenarios (professional use)**

The combination of Scenarios 1+2 and 1+3 were considered relevant for professional users:

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Scenarios combined** | **Tier** | **Systemic NOAEL**  **mg/kg bw/d** | **AEL**  **mg/kg bw/d** | **Estimated uptake**  **mg/kg bw/d** | **Estimated uptake/ AEL**  **(%)** | **Acceptable**  **(yes/no)** |
| Scenarios 1 + 2 | Tier 1, no PPE | 100 mg/kg bw/d | 0.076 mg/kg bw/d | 1.32 x 10-5 mg/kg bw/d | 0.017% | yes |
| Scenarios 1 + 3 | Tier 1, no PPE | 100 mg/kg bw/d | 0.076 mg/kg bw/d | 3.21 x 10-3 mg/kg bw/d | 4% | yes |

When considering the relevant combined scenarios for the professional use of the product, risks were found to be acceptable at Tier 1. Thus, safe use was established for all presented scenarios for unprotected professional users.

**Local effects:**

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

**Conclusion**

No primary risk to professional users was identified.

***Risk for non-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 | Tier 1 | 100 mg/kg bw/d | 0.35 mg/kg bw/d | <9.32 x 10-6 mg/kg bw/d | <0.0027% | yes |
| Scenario 4  Non-professional user | Tier 1 | 100 mg/kg bw/d | 0.35 mg/kg bw/d | 1.41 x 10-3 mg/kg bw/d | 0.4035% | yes |

For use by non-professional users the exposure was up to 0.4035% of the AELshort/medium-term and therefore safe use can be concluded for non-professional use of BIOPREN 4 GR FLY LARVICIDE GRANULE.

**Combined scenarios**

The combination of Scenarios 1+4 was considered relevant for non-professional users:

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Scenarios combined** | **Tier** | **Systemic NOAEL**  **mg/kg bw/d** | **AEL**  **mg/kg bw/d** | **Estimated uptake**  **mg/kg bw/d** | **Estimated uptake/ AEL**  **(%)** | **Acceptable**  **(yes/no)** |
| Scenarios 1 + 4 | Tier 1, no PPE | 100 mg/kg bw/d | 0.35 mg/kg bw/d | 1.41 x 10-3 mg/kg bw/d | 0.4035% | yes |

When considering the relevant combined scenarios for the professional use of the product, risks were found to be acceptable. Thus, safe use was established for all presented scenarios for unprotected non-professional users.

**Local effects:**

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

**Conclusion**

No risk for non-professional users as primary exposure was identified.

***Risk for the general public***

**Systemic effects**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Task/**  **Scenario** | **Tier** | **AEL**  **mg/kg bw/d** | **Estimated uptake**  **mg/kg bw/d** | **Estimated uptake/ AEL**  **(%)** | **Acceptable**  **(yes/no)** |
| Scenario 5, children indirect exposure | Tier 1 | 0.35 | 0.0048 mg/kg bw/day | 1.4% | yes |

From the above risk characterization it can be concluded that the BIOPREN 4 GR FLY LARVICIDE GRANULE is safe for children entering the treated area.

**Combined scenarios** Not relevant. No secondary exposure of adult by touching treated surface is expected as the product is applied on manure or deep litter surface.

**Local effects:**

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

**Conclusion**

No secondary risk to workers and school children was identified.

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

**Systemic effects**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Task/**  **Scenario** | **Tier** | **ADI\***  **mg/kg bw/d** | **Estimated uptake**  **mg/kg bw/d** | **Estimated uptake/ ADI**  **(%)** | **Acceptable**  **(yes/no)** |
| Scenario 6a, dietary exposure, eating food from animal origin | Tier 1 | 0.217 | 0.0077 mg/kg bw/d | 3.6% | yes |

\* For S-methoprene, no ADI is set in EU. The AEL long-term was derived from the NOAEL of 21.7 mg/kg bw/d from the 2-yr rat study, using an assessment factor of 100 and corrected for oral absorption. For the derivation of an ADI, the NOAEL of 21.7 mg/kg bw/d from the 2-yr rat study is applicable and including an assessment factor of 100, a value of 0.217 mg/kg bw/ day is derived.

From the above risk characterization not adverse health effects are expected for people eating products from animals which were exposure to BIOPREN 4 GR FLY LARVICIDE GRANULE treated manure.

The calculated exposure levels via diet is far below 30% of the derived ADI (0.22 x 30% = 0.066 mg/kg bw/d) for a child and an adult. Therefore no concern has been identified from the consumption of animal products. See section “Estimating Livestock Exposure to Active Substances used in Biocidal Products” for more details. However, MRLs are available, see discussion included under section MRL.

During the mixing & loading and the application scenarios, no food, drinking water are exposed to the product. Therefore as no food is contaminated no Dietary Risk Assesment (DRA) is required.

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

The product contains one active substance. Furthermore, no sunbstances of concern were identified using the guidance on Substances of Concern (CA-Nov14-Doc.5.11). Therefore, no combined exposure assessment needs to be performed.

### Risk assessment for animal health

The following RMMs/instructions are included in the use: “Keep away from food, drink and animal feedingstuffs”, “Do not disperse the granules in the immediate surroundings of feeding and watering places or where the animals may consume the product. In the event that the animal’s feed or drinking water might be contaminated, empty or cover the feeder and the water dispenser before treating the area”and “DO NOT store with food, feedstuffs, seed and fertilisers”.

Therefore, livestock exposure is only possible exposure via secondary exposure.

Indirect exposure after treatment of the floors with BIOPREN 4 GR FLY LARVICIDE GRANULE may be possible, as livestock may lick/eat from the floor. When animals lay down also dermal contact is possible. The amount of BIOPREN 4 GR FLY LARVICIDE GRANULE on the floor is indicated to be up to 30 g/m2 according to the label. This leads to a worst case of 30 x 0.004 = 0.12 g/m2 S-methoprene. The dislodgable fraction from a smooth floor is 2-6% according to TNsG (2007, p 102) for a powder. However, the treated surface that is touched may be wet and thus this value is not applicable. As there are no appropriate parameter available 100% transfer is considered as the worst case, resulting in 0.12 g/m2 dislodgable residue. The realistic worst-case external exposure calculation for a calf as the representative animal is performed according to the DRAWG Draft proposal guidance on Estimating Livestock Exposure to Biocidal Active Substances (2010), included in p.344 of the BPR guidance (Vol III, Part P+C). Livestock exposure estimates should be performed for all representative livestock species (beef and dairy cattle, pigs, chicken). As the biocidal product is intended to be applied in pig, cow and poultry stables an assessment, using the BfR calculator for estimating exernal exposure of livestock animals is included (Excel document is included in Annex 3.2).

For the calculation three scenarios were considered, including an refinement factor of 35% for dermal and oral absorption:

1) oral-animals licking surfaces

2) dermal-rubbing against surfaces

3) oral- ingestion of dead insects

More detailed justification for the use of 35% for oral and dermal absorption is included in the confidential Annex to the PAR.

|  |  |  |  |
| --- | --- | --- | --- |
| Animal Species |  | Sum of  all routes of exposure,  Tier 1 | Sum of  all routes of exposure,  Tier 2 |
| Beef cattle |  | 0.3648 | 0.1277 |
| Dairy cattle |  | 0.3249 | 0.1137 |
| Calf |  | 0.5700 | 0.1995 |
| Fattening pig |  | 0.6360 | 0.2226 |
| Breeding pig\* |  | 0.4246 | 0.1486 |
| Breeding pig\* | individual housing | 0.0000 | 0.0000 |
| Breeding pig\* | group housing | 0.0000 | 0.0000 |
| Sheep |  | 0.1280 | 0.0448 |
| Lamb |  | 0.2400 | 0.0840 |
| Slaughter goat (= goat kids) |  | 2.1231 | 0.7431 |
| Lactating goat |  | 0.9086 | 0.3180 |
| Broilers\* |  | 0.0824 | 0.0288 |
| Broilers\* | free range, litter floor | 0.0000 | 0.0000 |
| Broilers\* | parent broilers, free range (grating floor) | 0.0000 | 0.0000 |
| Broilers\* | parent broilers in rearing, free range (grating floor) | 0.0000 | 0.0000 |
| Laying hen\* |  | 0.0737 | 0.0258 |
| Laying hen\* | battery | 0.0000 | 0.0000 |
| Laying hen\* | free range (litter floor) | 0.0000 | 0.0000 |
| Laying hen\* | free range (grating floor) | 0.0000 | 0.0000 |
| Turkey |  | 0.0200 | 0.0070 |
| Horse |  | 0.4860 | 0.1701 |
| Rabbit |  | 0.0000 | 0.0000 |
| \*Please note that some scenarios for chicken and pigs distinguish between several housing conditions. | | |  |

To derive an AEL for animals, an assessment factor of 5 (for human 100 is used) can be applied according to the EFSA guidance on birds and mammals (2009). From the NOAEL 21.7 mg/kg bw, by applying correction for oral absorption (0.35) and the assessment factor of 5, the AEL of 1.52 mg/kg bw can be derived for animals. As the exposure levels calculated above are all below this AEL for animal, the risk for livestock is considered acceptable.

### Risk assessment for the environment

The environmental exposure of S-methoprene, formulated as a sand granule insecticide, is assessed. The insecticide function for this assessment is for the control of house fly (*Musca domestica*), drone fly (*Eristalis tenax*) and stable fly (*Stomoxys calcitrans*) through disruption of the development and metamorphosis of fly larvae and ultimately to prevent egg production. The trade name for the S-methoprene product is BIOPREN 4 GR FLY LARVICIDE GRANULE. The nature of the preparation is granular (GR) and contains 0.4% w/w S-methoprene. The preparation is proposed as a ready-to-use sand granule for indoor (stables) and outdoor (manure pit, dunghill) use by professional and non-professional users.

BIOPREN 4 GR FLY LARVICIDE GRANULE is an S-methoprene based insect growth regulator, a juvenile hormone analogue. BIOPREN 4 GR FLY LARVICIDE GRANULE prevents the emergence of adult flies, but has no effect on flies which have reached the pupal or adult stage prior to treatment.

The preparation has to be spread onto the manure’s surface either with a measuring cup, or with an appropriate device, eg. hand held granule applicator according to the following dosing: 30 g/m2.

For presenting the risk assessment of BIOPREN 4 GR FLY LARVICIDE GRANULE on the environment all representative uses (animal-housing scenarios) were selected for the exposure (and hazard) assessment.

The environmental exposure of S-methoprene was assessed in accordance with the Guidance on the Biocidal Product Regulation, Volume IV: Environment - Part B+C: Risk Assessment (Active Substances), European Chemicals Agency, Report no. ECHA-15-G-01-EN, Helsinki, Finland (2017), hereafter referred to as guidance, and the OECD ESD for Insecticides for Stables and Manure Storage Systems No.14 (2006). Concentrations for micro-organisms in a STP and the STP’s effluent were calculated with the model SimpleTreat version 3.0 by using the default values for parameters, unless otherwise noted. Release of active substance during the waste phase of the end-products is not assessed, because it is assumed that end-products to which the active substance is added are disposed as solid waste and usually incinerated. Possible pH effects on the environment were not considered, because the STP and receiving compartments are expected to have sufficient buffering.

In accordance with the Biocide Regulation, the life cycle of the product is incorporated into the risk assessment.

The risk characterisation is performed by comparing the predicted no effect concentration (PNEC), with the predicted environmental concentration (PEC). Considering the different ingredients in the product, only the active ingredient S-methoprene will cause risk for the environment and the risk characterization is therefore only performed for the active ingredient S-methoprene.

It has to be highlighted that there is no guideline available for testing the biodegradation in manure therefore all calculations are made without degradation of S-methoprene in manure as a worst case. However S-methoprene proved to degrade rapidly in the environment in the biodegradation study in soil (geometric mean DT50 0.83 days) and in water-sediment of pond and river systems (geometric mean DT50 in total system: 1.07 days, geometric mean DT50 in water: 0.65 days, geometric mean DT50 in sediment: 5.01 days). The relevant metabolites are also degrading fast (in the water sediment study metabolite M2 2.85 and 5.21 days; metabolite M3 1.21 and 1.91 days in the river and the pond system respectively).

#### 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 |

|  |  |
| --- | --- |
| **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 4 GR FLY LARVICIDE GRANULE 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), 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)***

|  |  |
| --- | --- |
| **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 4 GR FLY LARVICIDE GRANULE. The product was not tested for potential endocrine disruption properties. BIOPREN 4 GR FLY LARVICIDE GRANULE 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 4 GR FLY LARVICIDE GRANULE needs to be re-evaluated.

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

No significant direct release into the environment is expected from indoor professional use of BIOPREN 4GR FLY LARVICIDE GRANULE as a larvicide in animal housing.

Emissions can occur from spreading treated manure on agricultural land, and from the potential release to municipal sewage treatment plants from cleaning of certain types of animal housing. Considering that most farms are not connected to the municipal sewer, waste water is often released to the manure depot instead. If present, residues may be released to individual sewage treatment plants. In all other cases release to the municipal sewer and subsequently to a sewage treatment plant (STP) is likely.

During outdoor use, also surface water can be directly exposed by transport of insecticide residues via runoff and/or via agricultural drainage systems.

***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 | xxxxxxx (2014); Inherent Biodegradability of S-Methoprene In Modified MITI Test (II). TOXI-COOP ZRT, 8230 Balatonfüred, Arácsi út 97, Hungary , 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 | xxxxxxx (2015), Degradation and Metabolism in Four Soils of [14C] S-methoprene Incubated under Aerobic Conditions. xxxxxxx,  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

|  |  |
| --- | --- |
| **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***

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **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 | xxxxxxx (2015), Route and Rate of Degradation of [14C]S-Methoprene in Aerobic Aquatic Sediment Systems. xxxxxxx, 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. The BIOPREN 4 GR FLY LARVICIDE GRANULE is a solid sand granule 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. The BIOPREN 4 GR FLY LARVICIDE GRANULE is a solid sand granule therefore an overspray study is not required. The nature of the formulation (sand granule with 95.99 % sand content) and use pattern (used in stables and manure pits) of the biocidal product BIOPREN 4 GR FLY LARVICIDE GRANULE is unlikely to generate significant levels of particulates to the air. According to the result of the dustiness test on the BIOPREN 4 GR FLY LARVICIDE GRANULE product is essentially non-dusty.

#### Exposure assessment

**General information**

|  |  |
| --- | --- |
| Assessed PT | PT 18 |
| Assessed scenarios | Scenario 1: Stable litter treatment  Scenario 2: Manure pit treatment |
| ESD(s) used | OECD Emission Scenario Document for Insecticides for Stables and Manure Storage Systems. OECD report ENV/JM/MONO(2006)4. |
| Approach | Scenario 1: Average consumption  Scenario 2: Average consumption |
| Distribution in the environment | Calculated based on Guidance on BPR Vol IV Part B+C (2017) and SimpleTreat version 3 |
| Groundwater simulation | Simulation for leaching with FOCUS PEARL 4.4.4 |
| Further higher tier simulation | FOCUS SWASH 5.3 is used to calculate the PECs in surface water and sediment after STP sludge and manure application to agricultural soil. |
| Confidential Annexes | No |
| Life cycle steps assessed | Scenario 1 and 2:  Production: No  Formulation: No  Use: Yes  Service life: Yes |
| Remarks | PECs after ten years of successive manure application were calculated according to:   * Recommendation of the BPC Ad hoc Working Group on Environmental Exposure. An Addendum to OECD SERIES ON EMISSION SCENARIO DOCUMENTS, Number 14: Emission Scenario Document for Insecticides for Stables and Manure Storage Systems ENV/JM/MONO(2006)4. (Agreed at the Environment session of WG-V-2015 on 27 November 2015). * Item 7.7: Consultation of the BPC Working Group Environment. Proposal for revision of AHEE Recom WG V 2015 PT18. Calculation of PIECsoil\_grassland after 10 year. (Agreed at the WG-I-2018, January 2018). |

The environmental exposure of S-methoprene was assessed in accordance with the Guidance on BPR Vol IV Part B+C (2017) and the OECD ESD for Insecticides for Stables and Manure Storage Systems No.14. In accordance with the Biocides Regulation, the life cycle of the product is incorporated into the risk assessment. Degradation in manure was not taken into account. FOCUS PEARL 4.4.4. was used to estimate concentrations for S-methoprene in shallow groundwater. The physical-chemical parameters applied in the assessment for the different compartments (STP, water, sediment, soils and groundwater) are presented elsewhere.

The ESD distinguishes 18 types of farms (i1=1-18), which were in this risk assessment grouped in dairy cattle (i1=1), beef cattle (i1=2-3), pig farming (i1=4-6), and poultry (i1=7-18). The final conclusion was based on the worst-case for each category as presented in the PAR, i.e. the stable type that results in the highest PECs. This is not necessarily the stable with the highest surface as the PECs are determined by nitrogen production as well. The worst-case stable types for each category are:

* Dairy cows dairy cows (i1=1);
* Beef cattle veal calves (i1=3);
* Pig farming Sows in groups (i1=5);
* Poultry Free range laying hens on litter (i1=11) for application in stables and turkeys (i1=16) for direct application on manure.

Note that battery cages are not allowed in Europe ([Regulation No 1999/74/EC) of the European Parliament](http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:286:0001:0030:EN:PDF)) and therefore stable types i1=7-10 are not considered relevant. Nevertheless, none of these stable types are worst-case and therefore covered by the risk assessment for free range hens. The full risk assessment for all stable types is presented in the annex of the current PAR.

The granules have to be spread onto the manure’s surface either with a measuring cup, or with an appropriate device, eg. hand held granule applicator according to the following dosing: 30 g/m2.

Aquatic compartment (incl. sediment) and STP

*Indoor use – STP route*

There is no direct exposure of surface water (including sediment) for the proposed use as insecticide in stables in case applied indoors. Indirect exposure of surface water and sediment is expected from indoor applications of the product in animal housings after wet cleaning of residues present on the stable floor and emission to the STP (certain poultry houses).

According to the ESD, only the animal species kept in poultry houses within certain types of housing are considered (relevant subcategories: 8, 11, 12, 16, 17, 18) and the assumption has been made that a discontinuous process is involved with one occurrence every month. This means a peak release from one application at the time reaching the STP. According to the ESD, table 5.4, the fraction of the insecticide, i.e. the active ingredient, reaching the waste water is 0.1 for all categories-subcategories if applied by sprinkling.

The Simpletreat v.3.0 model is used to calculate distribution and degradation in the STP and to derive the PEC for the effluent. The distribution and degree of removal of S-methoprene in the STP is determined by the processes of biodegradation, adsorption onto sludge, removal due to sludge removal and volatilisation. Distribution and final PECs for water, sediment, and soils are subsequently calculated according to the guidance.

*Indoor and outdoor use – manure/slurry route*

It may be expected that the majority of the active substance is released to the manure storage when manure and bedding materials are collected and/or stables are cleaned. Soils are therefore polluted when manure is applied as a fertiliser. The active substance may subsequently enter surface water in adjacent ditches when S-methoprene-enriched manure is applied as a soil fertiliser for agricultural land due to run-off or drainage. This route is assessed with FOCUS SWASH 5.5.3.

The scenario in SWASH is similar to the PT18 groundwater assessment. As a worst-case for both arable land and grassland, the crop setting used is grassland. The application scheme is a distribution of the manure over 4 equal events. Application depth is 5 cm with soil incorporation and the application method is application to soil, linear. The application dates are determined by an application scheme, which starts at March the 1st and ends September the 6th, with an interval of 53 days (and taking the 30 day SWASH requirement into account). All FOCUS scenarios are included.

The application rate is set to the worst-case value of 1 kg/ha, covering spreading of manure on arable land and grassland, and sludge distribution on agricultural soils with a large margin of safety.

Soil compartment

The PECs were calculated according to the ESD for insecticides for stables and manure storage systems. The exposure for application in stables was assessed according to the parameters for the application ‘larvicides in stables’ where the emission to the manure or slurry was based on the total surface of slatted areas, other areas, and manure areas inside (Table 5.3 of the ESD). In line with the TAB (ENV-168) the fractions to slurry and manure were summed for poultry. PECs resulting from application in manure were based on the default parameters as presented in Appendix 5 of the ESD. For application in slurry emission was only calculated for rectangular storage tanks being the realistic worst-case. Application on slurry stored in lagoons was not considered as such storage systems are unlikely in Europe to prevent distribution of pathogens, odour, and unacceptable emissions to the environment. Although the applicant has stated that the product is efficacious for twelve weeks, emission to the environment was still based on six applications during the fly season (ESD default) as repetitive treatment may be necessary. Degradation of the active compounds in manure or slurry during storage was not considered as no information is available. Degradation in soils between two successive manure or slurry applications was considered by applying the active substance’s half-life (DT50) in soils.

According to the ESD for PT18, the deposition of active substances onto agricultural land (grassland) by manure/ slurry is estimated on the basis of emission standards for nitrogen or phosphor. Depending on the amount of nitrogen or phosphor in manure and the type of soil to which it is applied, these emission standards define the maximum amount of manure/slurry that can be applied per hectare and per year. The concentration in soil after manure/slurry application at maximum permissible rate (170 kg N/ha for both grassland and arable land and 110 kg P/ha for grassland and 85 kg P/ha for arable land) is calculated using the equations as proposed in the ESD for PT18. According to ENV 124 in the TAB (2017), it was decided to use the nitrogen immission standards from the EC Nitrates Directive (91/676/EC) of 170 kg N ha-1 yr-1 for all soils (arable land and grassland). Therefore, only the predicted environmental concentrations (PECs) based on the nitrogen emission standards are presented in the current PAR.

The PEC’s as calculated with the ESD represent the concentration after one manure application on arable land and one on grassland (Predicted Initial Environmental Concentrations, PIEC). However, agricultural soils are fertilised repeatedly and the active substance may consequently accumulate in soils after successive years of manure applications. Therefore, the concentrations presented in the current assessment report are the concentrations after ten years, i.e. ten manure applications on arable land and forty on grassland. Concentrations in soils after ten years were calculated according to the addendum for PT18 (insecticide in stables), although the no-manure time was increased from 206 to 365 days (agreed at WG-I-2018).

The active substance disappears from soils between two subsequent manure events due to degradation, leaching, and evaporation. The leaching rate constants and resulting PECs were calculated according to the guidance based on the active substance’s physical-chemical parameters as presented elsewhere. The corresponding half-lives for leaching from the topsoil layer are 7648 d in arable land (20 cm) and 3842 d in grassland (5 cm). Evaporation was not considerd as the active substance does not easily evaporates from soil to air (low Henry’s law constant).

As the amount of treatments per year and the surfaces to be treated strongly depend on the type of animal housed, emission to soils due to treatment of stables varies among the different farm industries.

Not that the product concerns granules from which slowly release the active substance. No information is available on the release rate. Emission was therefore based on the assumption that all substance was lost from the granules once released to the environment. Considering that the PEC:PNEC ratios are based on initial concentration, i.e. after the last manure application, the risk assessment can be considered as worst-case. When granules are release to the environment, the PECs will be considerably lower as the concentration hardly increases due to slow release and fast degradation.

Groundwater compartment

For refinement FOCUS PEARL (PEARL model © RIVM/Alterra, FOCUS v. 4.4.4) was used to estimate concentrations in shallow groundwater. The exposure scenario to soil did not include degradation of the active substance in manure. PEARL calculations do include aerobic degradation of active substance in soil.

The worst-case concentrations in soil were recalculated to kg/ha for manure spread on grassland and on arable land in order to be entered in PEARL. It was assumed that this concentration is equally distributed over 1 ha, in a soil layer with an incorporation depth of 0.2 m for arable land and of 0.05 m for grassland and a density of 1700 kg wwt/m3. From these parameters, application rates expressed in kg /ha in manure in arable land or in grassland were calculated and used in PEARL.

For arable land, a single land application to maize 20 days before crop emergence takes place. For grassland, four land applications to grassland/alfalfa at 1st of March, 23rd of April, 15th of June and 7th of August take place with an interval of 53 days take place each year. Anaerobic degradation in manure was not taken into account for the substance during manure storage. PEARL does include degradation in soil. The plant uptake factor was set at 0. The Q10 was set at 2.2. The activation energy was set at 54 kJ/mol. A simulation period of 20 years was chosen. The Freundlich exponent was set at 1.

***Emission estimation***

Three different emission pathways are described in the ESD for PT18 (2006):

* Release via sewage treatment plant;
* Release via slurry/manure;
* Release via run off.

These pathways are all relevant for the environmental exposure assessment of BIOPREN 4 GR FLY LARVICIDE GRANULE.

**Scenario [1] Stable litter treatment**

|  |  |  |  |
| --- | --- | --- | --- |
| **Input parameters for calculating the local emission** | | | |
| **Input** | **Value** | **Unit** | **Remarks** |
| Scenario:Stable litter treatment | | | |
| Type of insecticide | Flies | - | i2=1 |
| Application rate of biocidal product (Qprod-uins) | 30 | g/m² | - |
| Concentration of active substance in the product (Fbioc) | 4 | g/kg | - |
| Type of application | Sprinkling |  | i3=4 |
| Maximum number of application days per year (Napp-bio) | 6 | d | ESD worst case |
| Biocide application interval (Tbioc-int) | 28 | d | ESD default value |
| Surface | see remark | m² | The product is distributed over the stable’s floor. Emission is therefore based on the default total floor area as specified in the ESD |

**Scenario [2] Manure pit treatment**

| **Input parameters for calculating the local emission** | | | |
| --- | --- | --- | --- |
| **Input** | **Value** | **Unit** | **Remarks** |
| Scenario:Manure pit treatment | | | |
| Application rate of biocidal product (Qprod-uins) | 30 | g/m² | - |
| Concentration of active substance in the product (Fbioc) | 4 | g/kg | - |
| Maximum number of application days per year (Napp-bio) | 6 | d | ESD worst case |
| Biocide application interval (Tbioc-int) | 28 | d | According to use instructions |
| Surface | see remark | m² | Emission is based on the default areas for rectangular storage tanks |

***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: Stable litter treatment | yes | yes | yes | yes | yes | no | yes | yes | no |
| Scenario 2: Manure pit treatment | yes | yes | yes | yes | no | no | yes | yes | no |

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** |
| Molecular weight of S-methoprene | 310.48 | g/mol | - |
| Melting point | 53.8 | °C | calculated with Epiweb 4.1. Active substance is a solid at 12°C. |
| Vapour pressure (20°C) | 6.23E-04 | Pa | - |
| Experimental solubility (20°C) | 6.85 | mg/L | - |
| Molar enthalpy of vaporisation | 95 | kj/mol | - |
| Molar enthalpy of dissolution | 27 | kj/mol | - |
| Henry’s Law Constant (20 °C) | 0.0306 | Pa/m3/mol | calculated |
| Organic carbon-water partitioning coefficient (Koc) | 8.76E+02 | L/kg | - |
| Organic organic matter-water partitioning coefficient (Kom) | 5.08E+02 | L/kg | Koc / 1.724 |
| Freundlich sorption exponent | 1.0 |  | default worst-case |
| 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 | - |
| Half-life for biodegradation in water (Geometric mean, 12 °C) | 2.5 | day | Whole system DT50 river system, AR (2016) |
| Half-life for biodegradation in sediment (Geometric mean, 12 °C) | 1000 | day | Default worst-case when whole system value is for water. |
| Half-life on crop canopy | 10 | d | Default worst-case |
| TSCF | 0.0 | - | Plant uptake factor worst-case |

Other SWASH parameters were copied from the EXSW0 substance in SPIN.

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 |
| Air | n.r. | - |
| Water | 90.2 |
| Sludge | 9.8 |
| Degraded in STP | 0 |

**Calculations**

***Calculated PEC values***

The PECs are presented below. All PECs are based after ten years of successive sewage sludge or manure application. Concentrations are based on the nitrogen emission standards for emission to the manure.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Summary table on calculated PEC values** | | | | | | | |
|  | **PECSTP** | **PECwater** | **PECsed** | **PECseawater** | **PECseased** | **PECsoil** | **PECGW** | **PECair** |
| [mg/L] | [mg/L] | [mg/kgwwt] | [mg/L] | [mg/kgwwt] | [mg/kg wwt] | [μg/L] | [mg/m3] |
| **stable litter treatment** | | | | | | | | |
| via STP - (poultry)\* | | | | | | | | |
|  | 6.22E-03 | 6.21E-04 | 1.23E-02 | -- | -- | 2.52E-03 | 1.20E-02 | -- |
| via slurry/manure to grassland | | | | | | | | |
| Diary cattle | -- | 4.28E-05 | 8.50E-04 | - | - | 6.68E-03 | 4.29E-01 | -- |
| Beef cattle | -- | 1.04E-04 | 2.07E-03 | - | - | 1.63E-02 | 1.04E+00 | -- |
| Pig farming | -- | 9.39E-05 | 1.86E-03 | - | - | 1.47E-02 | 9.41E-01 | -- |
| Poultry | -- | 9.23E-05 | 1.83E-03 | - | - | 1.62E-02 | 1.04E+00 | -- |
| via slurry/manure to arable land - | | | | | | | | |
| Diary cattle | -- | 1.96E-05 | 3.90E-04 | - | - | 3.06E-03 | 1.97E-01 | -- |
| Beef cattle | -- | 4.78E-05 | 9.47E-04 | - | - | 7.45E-03 | 4.78E-01 | -- |
| Pig farming | -- | 4.31E-05 | 8.54E-04 | - | - | 6.72E-03 | 4.31E-01 | -- |
| Poultry | -- | 4.23E-05 | 8.39E-04 | - | - | 7.42E-03 | 4.77E-01 | -- |
| **manure treatment** | | | | | | | | |
| via slurry/manure to grassland | | | | | | | | |
| Diary cattle | -- | 6.16E-05 | 1.22E-03 | - | - | 9.62E-03 | 6.17E-01 | -- |
| Beef cattle | -- | 2.31E-04 | 4.58E-03 | - | - | 3.60E-02 | 2.31E+00 | -- |
| Pig farming | -- | 5.43E-05 | 1.08E-03 | - | - | 8.46E-03 | 5.43E-01 | -- |
| Poultry | -- | 2.72E-05 | 5.39E-04 | - | - | 4.24E-03 | 2.72E-01 | -- |
| via slurry/manure to arable land | | | | | | | | |
| Diary cattle | -- | 2.83E-05 | 5.60E-04 | - | - | 4.41E-03 | 2.83E-01 | -- |
| Beef cattle | -- | 1.06E-04 | 2.10E-03 | - | - | 1.65E-02 | 1.06E+00 | -- |
| Pig farming | -- | 2.49E-05 | 4.93E-04 | - | - | 3.88E-03 | 2.49E-01 | -- |
| Poultry | -- | 1.25E-05 | 2.47E-04 | - | - | 1.94E-03 | 1.25E-01 | -- |

A more realistic approach to calculate the sediment concentrations has been performed by using higher tier FOCUS SWASH modelling applying the input parameters as previously mentioned. PECwater and PECsed following applications to grassland from all SWASH scenarios available for grass/alfafa are presented in the table below.

|  |  |  |
| --- | --- | --- |
| **Results for s-methoprene using FOCUS SWASH modelling for grassland** | | |
| **Scenario** | **PECwater** | **PECsed #** |
|  | [mg/L] | [mg/kg dwt] |
| D1\_ditch | 1.00E-09 | 1.00E-09 |
| D1\_stream | 1.00E-09 | 1.00E-09 |
| D2\_ditch | 1.00E-09 | 1.00E-09 |
| D2\_stream | 1.00E-09 | 1.00E-09 |
| D3\_ditch | 1.00E-09 | 1.00E-09 |
| D4\_pond | 1.00E-09 | 1.00E-09 |
| D4\_stream | 1.00E-09 | 1.00E-09 |
| D5\_pond | 1.00E-09 | 1.00E-09 |
| D5\_stream | 1.00E-09 | 1.00E-09 |
| D6\_ditch | na | na |
| R1\_pond | na | na |
| R1\_stream | na | na |
| R2\_stream | 4.60E-06 | 1.56E-06 |
| R3\_stream | 3.48E-07 | 3.48E-07 |
| R4\_stream | na | na |

na – scenario not available

# In line with the agreed approach (WG ENV IV 2016) for the refinement of PECsed, the PECsw value should be converted to PECsed with the BPR guidance default distribution (see equation 53). This is due to differences in the suspended matter characteristics[[1]](#footnote-2) between the BPR guidance and the FOCUS guidance. Therefore, the reported FOCUS TOXSWA (SWASH) PECsed values are not the correct values for biocidal product risk assessment, because the distribution between water and sediment was calculated differently. However, because FOCUS TOXSWA already included a distribution between water and sediment, thereby reducing the PECwater concentration, the direct conversion from the reported PECwater to PECsed would underestimate the actual PECsed value. Ideally, FOCUS TOXSWA should be recalculated with the BPR suspended matter characteristics. However, based on the reported risk values, it can be seen that a large margin of safety (see risk section) is available for both the water and sediment compartment. Therefore a recalculation of the distribution is not deemed necessary, because the outcome would remain the same.

The PEC values in groundwater presented in the above table were calculated in line with the approach of the Guidance on the BPR Volume IV Environment - Part B+C (2017) using the pore water concentration in soil as indication for the groundwater level. Resulting PECporewater concentrations exceed the 0.1 µg/L criterion for emission via manure or stable litter spread on grassland or arable land. Therefore it was concluded that a potential risk for groundwater exists and this needed to be assessed using higher tier methods, i.e. PEARL.

The worst-case concentrations in soil for beef cattle in scenario 1 and 2 were recalculated to 3.06E-02 kg/ha for manure spread on grassland and 5.61E-02 kg/ha for manure spread on arable land in order to be entered in PEARL. It was assumed that these concentrations are equally distributed over 1 ha, in a soil layer with an incorporation depth of 0.2 m for arable land and of 0.05 m for grassland and a density of 1700 kg wwt/m3.

For arable land, a single land application to maize 20 days before crop emergence takes place. For grassland, four land applications to grassland/alfalfa at 1st of March, 23rd of April, 15th of June and 7th of August take place with an interval of 53 days take place each year. Anaerobic degradation in manure was not taken into account for the substance during manure storage. PEARL does include degradation in soil. The plant uptake factor was set at 0. The Q10 was set at 2.2. The activation energy was set at 54 kJ/mol. A simulation period of 20 years was chosen. The Freundlich exponent was set at 1.

The resulting 80th percentile of average annual groundwater concentrations at 1 m depth were < 0.001 µg/L at all nine PEARL locations.

***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. It is furthermore not expected that birds and mammals are directly exposed to granulates or contaminated larvae as stables, manure storages, and slurry tanks are no common foraging areas. Hence the product meets the standards for the risk to birds and mammals. Primary and secondary poisoning is not expected for the intended uses.

#### 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 live 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** | |
|  | **PEC/PNECSTP** |
| Scenario 1, stable litter treatment (poultry)\* | < 0.001 |

\* worst-case PEC/PNECs for poultry are calculated for animal category 11 (laying hens in free range with litter floor (partly litter floor, partly slatted)). PEC/PNECs calculated for poultry in battery cages were excluded.

Conclusion: The worst-case PEC/PNEC value for treatment of poultry stables is well below 1. From this PEC/PNEC value it can be concluded that no risk is identified for micro-organisms in the STP when poultry stables are treated with BIOPREN 4GR FLY LARVICIDE GRANULE.

***Aquatic compartment***

Emission of the active substance to surface water and sediment after application in animal housing occurs mainly via manure and waste water (STP), the latter only in some types of poultry houses.

|  | **Summary table on calculated PEC/PNEC values** | |
| --- | --- | --- |
|  | **PEC/PNECwater** | **PEC/PNECsediment** |
| **Stable litter treatment** | | |
| via STP - (poultry)\* | | |
| Scenario 1, stable litter treatment (poultry)\* | **3.3** | **32.4** |
| via slurry/manure to grassland | | |
| Diary cattle | 0.226 | **2.24** |
| Beef cattle | 0.548 | **5.44** |
| Pig farming | 0.494 | **4.9** |
| Poultry, including battery cages | 0.546 | **5.42** |
| Poultry, excluding battery cages | 0.486 | **4.81** |
| via slurry/manure to arable land | | |
| Diary cattle | 0.103 | **1.03** |
| Beef cattle | 0.252 | **2.49** |
| Pig farming | 0.227 | **2.25** |
| Poultry, including battery cages | 0.25 | **2.48** |
| Poultry, excluding battery cages | 0.223 | **2.21** |
| **Manure treatment** | | |
| via slurry/manure to grassland | | |
| Diary cattle | 0.324 | **3.22** |
| Beef cattle | **1.22** | **12** |
| Pig farming | 0.286 | **2.83** |
| Poultry, including battery cages | 0.143 | **1.42** |
| Poultry, excluding battery cages | 0.143 | **1.42** |
| via slurry/manure to arable land | | |
| Diary cattle | 0.149 | **1.47** |
| Beef cattle | 0.557 | **5.52** |
| Pig farming | 0.131 | **1.3** |
| Poultry, including battery cages | 0.066 | 0.65 |
| Poultry, excluding battery cages | 0.066 | 0.65 |

\* worst-case PEC/PNECs for poultry are calculated for animal category 11 (laying hens in free range with litter floor (partly litter floor, partly slatted)). PEC/PNECs calculated for poultry in battery cages were excluded.

Conclusion: From these PEC/PNEC values it can be concluded that a risk is identified for water and sediment organisms when poultry stables are treated with BIOPREN 4GR FLY LARVICIDE GRANULE when discharged to the sewer. The load to the STP for the worst-case animal category 11 (laying hens in free range with litter floor (partly litter floor, partly slatted) is 0.0138 kg a.s./d, while for the best-case animal categories 16,17 and 18 (turkeys, ducks and geese in free range with litter floor) the load to the STP is 0.00072 kg/d which is a factor 19 lower. Despite this lower load to the STP the PEC/PNEC for sediment is still exceeded (32.4/19 = 1.7). However, it is considered that there is acceptable risk for the STP in case the following risk mitigation measure is included in the proposed label:

*” it is forbidden to use* BIOPREN 4GR FLY LARVICIDE GRANULE *in case effluent/wastewater of the stable and/or manure deposit can directly leach into the sewer.”*

The first tier assessment for runoff from fertilised soils results in unacceptable risks for the aquatic environment. No risks for the sediment and surface water are identified considering higher tier modelling using FOCUS SWASH 5.3, see table below.

|  | **Summary table on calculated PEC/PNEC values** | |
| --- | --- | --- |
|  | **PEC/PNECwater** | **PEC/PNECsediment** |
| **Manure treatment** | | |
| via slurry/manure to grassland | | |
| D1\_ditch | < 0.001 | < 0.001 |
| D1\_stream | < 0.001 | < 0.001 |
| D2\_ditch | < 0.001 | < 0.001 |
| D2\_stream | < 0.001 | < 0.001 |
| D3\_ditch | < 0.001 | < 0.001 |
| D4\_pond | < 0.001 | < 0.001 |
| D4\_stream | < 0.001 | < 0.001 |
| D5\_pond | < 0.001 | < 0.001 |
| D5\_stream | < 0.001 | < 0.001 |
| D6\_ditch | na | na |
| R1\_pond | na | na |
| R1\_stream | na | na |
| R2\_stream | < 0.001 | < 0.001 |
| R3\_stream | < 0.001 | < 0.001 |
| R4\_stream | na | na |

na – scenario not available

***T******errestrial compartment***

| **Calculated PEC/PNEC values** | |
| --- | --- |
|  | **PEC\*\*/PNECsoil** |
| via STP - Scenario 1, stable litter treatment (poultry)\* | |
|  | 0.017 |
| via slurry/manure to grassland - Scenario 1, stable litter treatment | |
| Dairy cattle | 0.045 |
| Beef cattle | 0.11 |
| Pig farming | 0.099 |
| Poultry | 0.109 |
| via slurry/manure to arable land - Scenario 1, stable litter treatment | |
| Dairy cattle | 0.021 |
| Beef cattle | 0.05 |
| Pig farming | 0.045 |
| Poultry | 0.050 |
| via slurry/manure to grassland - Scenario 2, manure treatment | |
| Dairy cattle | 0.065 |
| Beef cattle | 0.243 |
| Pig farming | 0.057 |
| Poultry | 0.029 |
| via slurry/manure to arable land - Scenario 2, manure treatment | |
| Dairy cattle | 0.03 |
| Beef cattle | 0.112 |
| Pig farming | 0.026 |
| Poultry | 0.013 |

\* worst-case PEC/PNECs for poultry are calculated for animal category 11 (laying hens in free range with litter floor (partly litter floor, partly slatted)). PEC/PNECs calculated for poultry in battery cages were excluded.

Conclusion: No risks are expected due to the distribution of sewage sludge or manure as all PECs are below the PNEC. Therefore, the standards for the terrestrial environment are met. No additional risk mitigations are required.

***Non-target arthropods (including bees)***

The exposure 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. Primary exposure to bees cannot be expected as well as the product is applied as granules in areas where bees are likely absent. Hence, the risk for bees is considered acceptable for the active substance.

***Groundwater***

|  |  |
| --- | --- |
| **Calculated PEC values** | |
|  | **PEC\*\* (µg/L)** |
| via STP - Scenario 1, stable litter treatment (poultry)\* | |
|  | 1.20E-02 |
| via slurry/manure to grassland - Scenario 1 and , stable litter or manure treatment | |
| Chateaudun | < 0.001 |
| Jokioinen | < 0.001 |
| Hamburg | < 0.001 |
| Kremsmuenster | < 0.001 |
| Okehampton | < 0.001 |
| Piacenza | < 0.001 |
| Porto | < 0.001 |
| Sevilla | < 0.001 |
| Thiva | < 0.001 |
| via slurry/manure to arable land - Scenario 1 and , stable litter or manure treatment | |
| Chateaudun | < 0.001 |
| Jokioinen | < 0.001 |
| Hamburg | < 0.001 |
| Kremsmuenster | < 0.001 |
| Okehampton | < 0.001 |
| Piacenza | < 0.001 |
| Porto | < 0.001 |
| Sevilla | < 0.001 |
| Thiva | < 0.001 |

Conclusion: After performing refined PECgroundwater calculations (using PEARL v. 4.4.4) for S-methoprene, it is concluded that the 0.1 µg/L criterion is not exceeded for STP sludge spread on land or manure or stable litter spread on grassland or arable land for all nine PEARL locations.

***Primary and secondary poisoning***

Conclusion:

Primary poisoning is not expected for the intended uses.

Although the BCF values suggest a high potential for bioaccumulation, 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 not expected that birds and mammals are directly exposed to granulates or contaminated larvae as stables, manure storages, and slurry tanks are no normal foraging areas. Hence the product meets the standards for the risk to birds and mammals.

***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.

*Tiered approach*

No relevant component except the active ingredient that has an environmental toxicity was identified, therefore mixture risk assessment is covered by the risk assessment of the active ingredient S-methoprene.

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 in animal housings.

***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 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** |
| When used in accordance with the label instructions for use, BIOPREN 4 GR FLY LARVICIDE GRANULE complies with the environmental standards and will not cause unacceptable effects to the environment provided that the following risk mitigation measure is included in the proposed label:  *” it is forbidden to use* BIOPREN 4GR FLY LARVICIDE GRANULE *in case effluent/wastewater of the stable and/or manure deposit can directly leach into the sewer.”* |

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

The product is used in animal housing on litter and manure to control house fly, drone fly and stable fly larvae. 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 4 GR fly larvicide granule is recommended for use by professional pest control operators and by non-professionals. Specific training is not required for the use of Biopren 4 GR fly larvicide granule. |
| ***Methods and precautions concerning handling and use*** |
| Eye protection: Not necessary  Respiratory protection: Not necessary  Other protective equipment:  Other protective equipment: Not necessary  The usual precautionary measures for handling chemicals should be observed. |
| ***Methods and precautions concerning storage*** |
| Store at room temperature in areas that dry. Store away from heat, ignition sources and sunlight. Read and follow all precautions and instructions on the product label. |
| ***Methods and precautions concerning transport*** |
| Biopren 4 GR fly larvicide granule is NOT classified as “Dangerous goods for transport”.  Proper shipping name: NON HAZARDOUS - not restricted |
| ***Methods and precautions concerning fire*** |
| Extinguishing media: Water, carbon dioxide  Fire fighting procedures: In case of fire no special measures are needed for fire fighting. |

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

|  |
| --- |
| **Specific treatment in case of an accident, e.g. first-aid measures, antidotes, medical treatment if available** |
| |  |  |  | | --- | --- | --- | | Eyes | No known adverse effects | Flush with water for a few minutes | | Skin | No known adverse effects | Wash affected area with soap and water. | | Inhalation |  | Inhalation exposure not likely | | Ingestion | No known adverse effects | Rinse mouth, drink some water | |
| ***Emergency measures to protect the environment*** |
| If spillageoccurssweep and transfer 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: Wastes resulting from this product may be disposed of on site (household waste) or at an approved waste disposal facility. 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 as a granular formulation indoor (stables) and outdoor (manure pit) in controlled way. The product contains 95.99 % sand and essentially not dusty. 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 (stables) and outdoor (manure pit) 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 95.99 % sand ingredients and the active ingredient S-Methoprene is rapidly degrading in water. |
| **Possibility of destruction or decontamination following release in or on soil** |
| Direct application on soil of the product is not expected. Release to soil is via fertilizing the soil with manure considering the use pattern of the product: indoor (stables) and outdoor (manure pit) 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 95.99 % sand ingredients and the active ingredient S-Methoprene is rapidly degrading in water. |

**Controlled incineration:**

Not applicable

**Measures to protect animals:**

The product is used in animal housing on litter and manure therefore pets and wild animals are not expected to get in contact with the product. No risk mitigation is necessary.

**Measures to protect the environment**

When used in accordance with the label instructions for Use, BIOPREN 4 GR FLY LARVICIDE GRANULE complies with the environmental standards and will not cause unacceptable effects to the environment provided that the following risk mitigation measure is included in the proposed label:

*” it is forbidden to use* BIOPREN 4GR FLY LARVICIDE GRANULE *in case effluent/wastewater of the stable and/or manure deposit can directly leach into the sewer.”*

### Assessment of a combination of biocidal products

BIOPREN 4 GR FLY LARVICIDE GRANULE 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[[2]](#footnote-3)

## 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. | xxxxxxx | 2015 | Determination of the Appearance of BIOPREN 4GR fly larvicide granule, TOXI-COOP ZRT., Unpublished | Y | Babolna Bio Ltd |
| IUCLID  3.2. | xxxxxxx | 2015 | Determination of the pH of Aqueous Suspension of BIOPREN 4GR fly larvicide granule, TOXI-COOP ZRT., Unpublished | Y | Babolna Bio Ltd |
| IUCLID  3.2. | xxxxxxx | 2018 | Determination of the pH values of BIOPREN 4GR fly larvicide granule (after storage), unpublished | Y | Babolna Bio Ltd |
| IUCLID  3.2. | xxxxxxx | 2015 | Determination of the Acidity/Alkalinity of BIOPREN 4GR fly larvicide granule, Toxi-Coop Zrt., Unpublished | Y | Babolna Bio Ltd |
| IUCLID  3.3. | xxxxxxx | 2015 | Determination of the Bulk Density of BIOPREN 4GR fly larvicide granule, Toxi-Coop Zrt., Unpublished | Y | Babolna Bio Ltd |
| IUCLID 3.4.1. | xxxxxxx | 2015 | Determination of the Accelerated Storage Stability of BIOPREN 4GR fly larvicide granule, TOXI-COOP ZRT., Unpublished | Y | Babolna Bio Ltd |
| IUCLID 3.4.1. | xxxxxxx | 2015 | Determination of the Long-term Storage Stability of BIOPREN 4GR fly larvicide granule, TOXI-COOP ZRT., Unpublished | Y | Babolna Bio Ltd |
| IUCLID  3.5. | xxxxxxx | 2015 | Determination of the Dustiness of BIOPREN 4GR fly larvicide granule, TOXI-COOP ZRT., Unpublished | Y | Babolna Bio Ltd |
| IUCLID  3.5. | xxxxxxx | 2015 | Sieve test of BIOPREN 4GR fly larvicide granule, Toxi-Coop Zrt., Unpublished | Y | Babolna Bio Ltd |
| IUCLID  3.5. | xxxxxxx | 2018 | Determination of the Particle Size Distribution of BIOPREN 4GR fly larvicide granule (after storage), | Y | Babolna Bio Ltd |
|  | xxxxxxx | 2018 | Physico-Chemical Testing of BIOPREN 4GR Mosquito Larvicide Granule /  CIPAC Handbook Volume H, MT 178, Attrition Resistance of Granules, Toxi-Coop Zrt., Unpublished | Y | Babolna Bio Ltd |
|  | xxxxxxx | 2018 | Physico-Chemical Testing of BIOPREN 4GR Mosquito Larvicide Granule (After Storage) /  CIPAC Handbook Volume H, MT 178, Attrition Resistance of Granules, /  CIPAC Handbook Volume F, MT 171, Dustiness of Granular Products Toxi-Coop Zrt., Unpublished | Y | Babolna Bio Ltd |
| IUCLID  5. 484-100-0565 | xxxxxxx | 2015 | Validation of the Analytical Method (HPLC) for the determination of S-Methoprene in BIOPREN 4GR fly larvicide granule ,TOXI-COOP ZRT., Unpublished | Y | Babolna Bio Ltd |
| IUCLID  5.  CRA119111 | xxxxxxx | 2007 | S-methoprene Technical Residue Analytical Method for Determination in Tap Water, Surface Water and Ground Water, DR.U.NOACK-LABORATORIEN | Y | Babolna Bio Ltd |
| IULID  5  484.102.3618 | xxxxxxx | 2012 | Validation of the Analytical Method for the Determination of S-methoprene in Aquatic Formulations, Toxi-Coop Zrt., Unpublished | Y | Babolna Bio Ltd |
| IUCLID  5  484-100-0737 | xxxxxxx | 2015 | Validation of the Analytical Method for the determination of S-Methoprene in Edible Meat Matrices, Toxi-Coop Zrt., Unpublished | Y | Babolna Bio Ltd |
| IUCLID  6.7. | xxxxxxx | 2011 | Field Testing of Efficacy of an Insecticide Speciality to Control House Flies in Livestock Premises (Musca Domestica), T.E.C. Laboratory, Study No: 1453a/0611, Unpublished | Y | Lodi SAS |
| IUCLID  6.7. | xxxxxxx | 2014 | Laboratory bioassay study of Biopren 4 GR house fly larvae granule, Babolna Bio Ltd, Babolna Bio Biological Laboratory, Study No: 143.001, 143.002, 143.003, 143.004, Unpublished | Y | Babolna Bio Ltd |
| IUCLID  6.7. | xxxxxxx | 2007 | Biological efficacy trial of Biopren 4 GR micrencapculated S-methopren based sand granule, Babolna Bio Ltd, Babolna Bio Biological Laboratory, Study No: 073.047, 073.048,073.049,073.50, Unpublished | Y | Babolna Bio Ltd |
| IUCLID  6.7. | xxxxxxx | 2015 | TRIAL AGAINST THE STABLE FLY Stomoxys calcitrans AND THE DRONE FLY Eristalis tenax, T.E.C. LABORATORY, Study No: 1931-FFT4GR/0515, Unpublished | Y | Babolna Bio Ltd |
| IUCLID  6.7. | xxxxxxx | 2015 | EFFICACY STUDY OF BIOPREN 4 GR FLY LARVICIDE GRANULE ON MUSCA DOMESTICA LARVAE IN FOUR DIFFERENT MANURES, Babolna Bio Ltd, Babolna Bio Biological Laboratory, Study No: 153.041.-042.-045. 153.046.-047.-050. 153.051.-052.-055. 153.056.-057.-060., Unpublished | Y | Babolna Bio Ltd |
| IUCLID  6.7. | xxxxxxx | 2016 | LABORATORY MEASUREMENT OF THE EFFECTIVENESS OF AN IGR-INSECTICIDE SPECIALITY INTENDED FOR THE CONTROL OF THE STABLE FLIES STOMOXYS CALCITRANS AND ERISTALIS TENAX, TEC Laboratory, 2069c/0416R, Unpublished | Y | Babolna Bio Ltd |
| IUCLID 9.2.2.2 | xxxxxxx | 2015 | Effects of S-methoprene technical on earthworm (*Eisenia fetida*) reproduction in a chronic toxicity test, Toxi-Coop Zrt., Study no. 484-222-0675, Unpublished | Y | Babolna Bio Ltd |
| IUCLID 9.2.5. | xxxxxxx | 2015 | COLLEMBOLAN REPRODUCTION TEST IN SOIL WITH S-METHOPRENE TECHNICAL, Toxi-Coop Zrt., Study No: 484-232-0676, Unpublished | Y | Babolna Bio Ltd |
| IUCLID 10.1. | xxxxxxx | 2011 | Environmental distribution of S-Methoprene (Level 1 Fugacity Calculator ver1.2 by Karl Nieman), Rivendell Consulting Limited, Study No: RIV2011/03/08, Unpublished | Y | Babolna Bio Ltd |
| IUCLID 10.2. | xxxxxxx | 2015 | S-Methoprene: Route and Rate of Degradation of [14C]S-Methoprene in Aerobic Aquatic Sediment Systems, Harlan Laboratories Ltd., Study No: D93728, Unpublished | Y | Babolna Bio Ltd |
| IUCLID 10.2. | xxxxxxx | 2015 | S-methoprene: Degradation and Metabolism in Four Soils of [14C]S-methoprene Incubated under Aerobic Conditions, Harlan Laboratories Ltd. Study No: D93717, Unpublished | Y | Babolna Bio Ltd |
| IUCLID 10.2. | xxxxxxx | 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 1: Professional user, Open mixing&loading**

**Dermal exposure (no protective clothing, without gloves):**

Conversion from US EPA Guide: 23.6 µg/lb a.i. handled = 0.0236 mg/lb a.i. = 0.0520 mg/kg a.i. (conversion factor: /0.45359237)

Dermal external exposure: 0.0520 mg/kg a.i. handled x 2560 m2 (treated area) x 0.03 kg/m2 (dose) x 0.004 (0.4% a.i.) = 0.01598 mg a.i./day

Dermal systemic exposure:

0.01598 mg a.i./day x 0.035 (3.5% dermal absorption)/60 kg (bw) = 9.3236 x 10-6 mg/kg bw/day

**Scenario 2: Professional user, Application / open cab**

**Dermal exposure (no protective clothing, without gloves):**

Conversion from US EPA Guide: 9.9 µg/lb a.i. handled = 0.0099 mg/lb a.i. = 0.0218 mg/kg a.i. (conversion factor: /0.45359237)

Dermal external exposure: 0.0218 mg/kg a.i. handled x 2560 m2 (treated area) x 0.03 kg/m2 (dose) x 0.004 (0.4% a.i.) = 0.006705 mg a.i./day

Dermal systemic exposure:

0.006705 mg a.i./day x 0.035 (3.5% dermal absorption)/60 kg (bw) = 3.9112 x 10-6 mg/kg bw/day

**Scenario 3: Professional user, Granular bait dispersed by hand**

**Dermal exposure (single layer clothing, without gloves):**

Conversion from US EPA Guide: 104000 µg/lb a.i. handled = 104 mg/lb a.i. = 229.2808 mg/kg a.i. (conversion factor: /0.45359237)

Dermal external exposure: 229.2808 mg/kg a.i. handled x 200 m2 (treated area) x 0.03 kg/m2 (dose) x 0.004 (0.4% a.i.) = 5.5027 mg a.i./day

Dermal systemic exposure:

5.5027 mg a.i./day x 0.035 (3.5% dermal absorption)/60 kg (bw) = 3.2099 x 10-3 mg/kg bw/day

**Scenario 4: Non-professional user, Granular bait dispersed by hand**

**Dermal exposure (single layer clothing, without gloves):**

Conversion from US EPA Guide: 104000 µg/lb a.i. handled = 104 mg/lb a.i. = 229.2808 mg/kg a.i. (conversion factor: /0.45359237)

Dermal external exposure: 229.2808 mg/kg a.i. handled x 88 m2 (treated area) x 0.03 kg/m2 (dose) x 0.004 (0.4% a.i.) = 2.4212 mg a.i./day

Dermal systemic exposure:

2.4212 mg a.i./day x 0.035 (3.5% dermal absorption)/60 kg (bw) = 1.4124 x 10-3 mg/kg bw/day

********

## 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 species 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)[[3]](#footnote-4)

All efficacy studies were included into the submitted IUCLID file.

See IUCLID section 6.7

## Confidential annex

## 3.7 Environmental risk assessment



1. Bulk density, volume, concentration [↑](#footnote-ref-2)
2. 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-3)
3. If an IUCLID file is not available, please indicate here the summaries of the efficacy studies. [↑](#footnote-ref-4)