Addendum to Product Assessment Report

**Product names:**

**Biopren 4 GR Plus larvicide granule** NL-0022257-0000

August 2021

Addendum to biocidal product assessment report related to product authorisation under Regulation (EU) 528/2012

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# Background

An application for a major change was received concerning the additation of a claim against litter beetle for Biopren 4 Plus larvicide granule (R4BP case number: BC-YD058340-42). The major change was applied for in the Netherlands.

Additionally, a minor change was applied for. The minor change includes:

* Change of colorant from Vynamon Blue to Irgalite rubine D 4240, where the concentration of the colorant within the product remains the same

Lastly, two administrative changes were applied for:

* Change of the product name from “Biopren 4 GR FLY Plus larvicide granule” to “Biopren 4 GR Plus larvicide granule”
* Additation of the trade name “BAYCIDAL GR4” in the Netherlands

The original assessment of Biopren 4 Plus Larvicide granule was also conducted by eCA NL and authorized under number NL-0022257-0000 and will expire on 31-01-2030.

### Section 2.1.1.1 Identifier of the product

| **Identifier** | **Country (if relevant)** |
| --- | --- |
| Biopren 4 GR Plus Larvicide granule | NL |

### Section 2.1.4 (authorised uses): add use description and instructions for use for the new use

### 2.14.1.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:  manure/litter in closed piggeries, cow and poultry houses, as well as in stables and other livestock breeding buildings.  Outdoor:  manure-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 evenly onto the manure’s surface by hand with a measuring cup or with an appropriate device, eg. hand held granule applicator according to the following instructions:  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 |

### 2.1.4.2.Use-specific instructions for use

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

### 2.1.4.3.Use-specific risk mitigation measures

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

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

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

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

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

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

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

Table 2. litter beetle 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)** | *Alphitobius diaperinus*  *litter beetle / Lesser mealworm*  *Larvae* |
| **Field of use** | Indoor: manure in closed poultry houses  Outdoor: poultry manure-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 evenly onto the manure surface by hand, with a measuring cup or with an appropriate device, eg. hand held granule applicator according to the following instructions:  Poultry Farms (professional users):  -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.  Only for general public, (non professional users): Apply the product after each cleaning event, on the top of the first new layer of manure / fresh litter.  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 will facilitate development of the larvicidal effect in the case of very dry environmental conditions.  The product can inhibit the development of litter beetle Lesser mealworm for a period of 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 |

### 2.1.4.7.Use-specific instructions for use

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

### 2.1.4.8.Use-specific risk mitigation measures

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

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

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

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

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

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

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

### Section 2.2.1 (intended uses): add use description for the new use

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

The uses below are the ones originally 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*  Lesser mealworm / litter beetle Larvae, *Alphitobius diaperinus* |
| Field of use | For fly:  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.  For Lesser mealworm / litter beetle:  Indoor  Apply the product to inhibit the transformation of litter beetle larvae into imagoes in poultry houses. |
| 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 and Lesser mealworm / litter beetle 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  Lesser mealworm / litter beetle Larvae, *Alphitobius diaperinus* |
| Field of use | For fly:  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.  For Lesser mealworm / litter beetle:  Indoor  Apply the product to inhibit the transformation of litter beetle larvae into imagoes in poultry houses. |
| 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 and Lesser mealworm / litter beetle 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) |

Section 2.2.5 (efficacy against target organisms): please update all required information fields in this section. This includes organisms to be controlled (2.2.5.2) and occurrence of resistance and resistance management (2.2.5.6). Also update the efficacy data table, the conclusion on efficacy of the product and the evaluation of label claims.

### 2.2.5.1.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 population (which represent more than 80 % of the full population) and larvae of litter beetle / Lesser mealworm, but has no effect on flies or beetles which have already reached the pupal or adult stage prior to treatment.

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.

### 2.2.5.2.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

*Alphitobius diaperinus* – litter beetle / Lesser mealworm - larvae

### 2.2.5.3.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.

### 2.2.5.4.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 and Coleoptera 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.

### 2.2.5.5.Efficacy data

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Experimental data on the efficacy of the biocidal product against target organism(s)** | | | | | | | |
| **Function** | **Field of use envisaged** | **Test substance** | **Test 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. | XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXx  XXXXXXXXXXXXXXXXXXXXXX  **XXXXXXXXXXXXXXXXXXXXXXXx** |
| 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. | XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXx  XXXXXXXXXXXXXXXXXXXXXX  **XXXXXXXXXXXXXXXXXXXXXXXx** |
| 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 | XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXx  XXXXXXXXXXXXXXXXXXXXXX  **XXXXXXXXXXXXXXXXXXXXXXXx** |
| 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* | XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXx  XXXXXXXXXXXXXXXXXXXXXX  **XXXXXXXXXXXXXXXXXXXXXXXx** |
| Insecticide | Indoor | Biopren 4 GR fly larvicide granule, 0.4 % 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. | XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXx  XXXXXXXXXXXXXXXXXXXXXX  **XXXXXXXXXXXXXXXXXXXXXXXx** |
| 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) | XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXx  XXXXXXXXXXXXXXXXXXXXXX  **XXXXXXXXXXXXXXXXXXXXXXXx** |
| Insecticide | Indoor | BIOPREN® 4 GR Larvicide Granule  S-methoprene (0.4 w/w%) | Lesser mealworm (*Alphitobius diaperinus*) larvae | Laboratory trial | Dosage: 25 g/m2 surface  Test Organisms: laboratory bred lesser mealworm (*Alphitobius diaperinus*)  larvae (size: ~9 mm; age: 40-50 days)  Number of Test Organisms: 50 larvae per replicate  Number of replicate tests: 5 (in separated test containers)  Untreated Control (UTC): Treatment  Control tests were performed the same way, with the same number of replicates,  with insect larvae from the same population, in the same medium as in the case  of Test Material treatments, but without using any biocides.  Study was performed in chicken manure with straw collected in poultry (laying hen) farms. 400 g prepared manure was measured out in individually marked plastic buckets (volume: 5 L) creating 6-8 cm thick manure layer at the bottom of the buckets. 50 healthy, motile *Alphitobius diaperinus* larvae were selected and placed on the  manure surface in each bucket. Following the 1-hour long acclimatization period  (after the larvae had buried themselves in the manure), the product was spread  evenly in a thin, smooth layer on the manure surface.  Survival of the larvae, and adult emergence rates were checked weekly until all  the larvae emerged into adults or died in all the replicate containers. Adult emergence inhibition efficiency of the product was calculated according  to Abbott’s corrected formula. | Adult  emergence inhibition efficiency: 97.77 %.  Adult emergence rate in the untreated control group: >85.0 % in all the  replicate containers (showing proper experimental conditions and adequate health  condition of the insect population used in the test) | XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXx  XXXXXXXXXXXXXXXXXXXXXX  **XXXXXXXXXXXXXXXXXXXXXXXx** |
| Insecticide | Indoor | BIOPREN® 4 GR Larvicide Granule  S-methoprene (0.4 w/w%) | Lesser mealworm *(Alphitobius diaperinus)* larvae | Field trial | Dose: 30 g/m².  The product was applied by a professional Pest Control Operator. The product was applied as a scatter granule in the empty buildings (no animals) on the litter.  The treatments were not repeated along the trial (only 1 application).  The trial was a field testing on naturally infested breeding premises. All were breeding of adult parentstock of hens *Gallus gallus* (the animals were not inside during the treatment).  5 treated + 5 control buildings were monitored.  Monitoring the effect: sticky traps were set into the building at a rate of 1 per 5 m², placed on the litter, near the preferred locations of the insects. The counts of the trapped insects were done 24 hours after setting. The counts of the insects trapped were done one and two weeks before and 4, 8 and 12 weeks after treatment.  The efficacy was calculated by the comparison of the monitoring of adult insects counts before and after treatment, in treated and untreated buildings: the efficacy was not assessed on larvae only but as a general effect on the global insects' populations. | Population reduction rate: 76.0% after 4 weeks, 92.2% after 8 weeks and 82.4% after 12 weeks after treatment.  Untreated control: 4 weeks, 7.4% increase, after 8 weeks 2.3% increase and after 12 weeks 1.3% population reduction. | XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXx  XXXXXXXXXXXXXXXXXXXXXX  **XXXXXXXXXXXXXXXXXXXXXXXx** |
| Insecticide | Indoor | BIOPREN® 4 GR Larvicide Granule  S-methoprene (0.4 w/w%) | Lesser mealworm *(Alphitobius diaperinus)* larvae | Field trial | Dose: 25 g/m².  The product was applied by a professional Pest Control Operator. The product was applied as a scatter granule in the empty buildings (no animals) on the litter.  The treatments were not repeated along the trial (only 1 application).  The trial was a field testing on naturally infested breeding premises. All were breeding of adult parentstock of hens *Gallus gallus* (the animals were not inside during the treatment).  5 treated + 5 control buildings were monitored.  Monitoring the effect: sticky traps were set into the building at a rate of 1 per 5 m², placed on the litter, near the preferred locations of the insects. The counts of the trapped insects were done 24 hours after setting. The counts of the insects trapped were done one and two weeks before and 4, 8 and 12 weeks after treatment.  The efficacy was calculated by the comparison of the monitoring of adult insects counts before and after treatment, in treated and untreated buildings: the efficacy was not assessed on larvae only but as a general effect on the global insects' populations. | Population reduction rate: 72.8% after 4 weeks, 91.4% after 8 weeks and 88.1% after 12 weeks after treatment.    Untreated control: 4 weeks, 10.5% reduction, after 8 weeks 8.5% increase and after 12 weeks 2.9% population increase. | XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXx  XXXXXXXXXXXXXXXXXXXXXX  **XXXXXXXXXXXXXXXXXXXXXXXx** |

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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.  Three efficacy study reports were provided in which efficacy of BIOPREN 4 GR FLY larvicide granules against litter beetle / Lesser mealworm (*Alphitobius diaperinus*) was demonstrated in one laboratory and two field trials at a dose of 25-30 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 litter beetle / Lesser mealworm.  *Note*: BIOPREN 4 GR FLY Larvicide Granule used in the efficacy tests is equivalent to BIOPREN 4 GR PLUS Larvicide Granule. |

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2.2.5.6. **Occurrence of resistance and resistance management**

Some studies showed isolated populations of mosquitoes and flies that have developed low level of resistance against S-methoprene. Regarding flies, literature reference has been found XXXXXXXXXXXXXXXXXXXX XXXX on the possible occurrence of resistance of these species to S-Methoprene. Considering the possible biochemical mechanism of the development of IGR resistance in *Musca domestica*, it can not be excluded, that the same mechanism may be evolved in other *Diptera* species as well. However, up to now direct evidences were not reported for the presence of S-methoprene resistance in *Stomoxys calcitrans* and *Erystalis tenax*. Regarding litter beetle / Lesser mealworm, neither laboratory, nor field resistance against S-methoprene have been reported yet, however, it can not be excluded that resistance may occur in this species as well. According to XXXXXXXXXXXXXXXXXXXX XXXX and XXXXXXXXXX monooxygenase (cytochrome P-450s) enzyme systems could be involved in IGR resistance in mosquitoes and beetles. Thus, this is the presumed background of the development of S-methoprene resistance in other insects as well.

Resistance management

Observing the following rules while applying the product is recommended to prevent the development of insecticide resistance:

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

- It is advised to use insecticides with different mode of action in rotation during the pest control program, especially if an extended period of control is required.

- Where possible, chemical treatments should be recommended to be combined with application of non-chemical measures (e.g. sticky traps or fly traps with UV lamps).

- Sufficient elimination of pest insects should be attempted in infested areas. - Levels of effectiveness should be monitored, and cases of reduced effectiveness should be investigated for possible evidence of resistance in the frame of IPM programs.

It is advised to use adulticide products, sticky traps or UV traps after a few applications of the larvicide product or parallel with the larvicide treatment to achieve full population control (controlling larvae and adults simultaneously). Sticky traps can also be used for monitoring purposes in case of flies. For monitoring purposes or mechanical trapping of adult litter beetles, tube traps (described by XXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXX or CAPT7 pit-fall traps can be used.It is also important to keep good hygiene and proper disinfection and cleaning protocol in the empty buildings after removing old manure / litter, but before the installation of new livestock population to remove surviving adult beetles hiding in cracks and crevices and to prevent reinfestation.

### 2.2.5.8.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 and litter beetles in poultry farms. Efficacy studies were performed on different substrates demonstrating proper fly larvicide effect in cow, pig and chicken manures and larvicide effect in chicken manure for litter beetles.

Efficacy against *Musca domestica* (house fly):

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

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

- a laboratory test (XXXXXXXXXXXX) 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 (XXXXXXXXXXXX) 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 (XXXXXXXXXXXX) 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 (XXXXXXXXXXXX) 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.

Efficacy against *Stomoxys calcitrans* (stable fly):

- a laboratory test (XXXXXXXXXXXX) 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 (XXXXXXXXXXXX) 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.

Efficacy against *Alphitobius diaperinus* (litter beetle / Lesser mealworm):

- a laboratory test (XXXXXXXXXXXX) demonstrated efficacy in chicken manure at an application rate of 25g/m2 (adult emergence inhibition efficiency: 97.77 %). The untreated control showed an 89.6% emergence rate of adults.

- a field test (XXXXXXXXXXXX) demonstrated efficacy in closed, naturally infested breeding premises of adult parentstock of hens (*Gallus gallus*) with a residual efficacy of 12 weeks at an application rate of 30 g/m2. Population reduction rate: 76.0% after 4 weeks, 92.2% after 8 weeks and 82.4% after 12 weeks after treatment.Untreated control showed a population reduction of 1.3% after 12 weeks.

- a field test (XXXXXXXXXXXX) demonstrated efficacy in closed, naturally infested breeding premises of adult parentstock of chicken (*Gallus gallus*) with a residual efficacy of 12 weeks at an application rate of 25 g/m2. Population reduction rate: 72.8% after 4 weeks, 91.4% after 8 weeks and 88.1% after 12 weeks after treatment. Untreated control showed a population increase of 2.9 % after 12 weeks.

For tests laboratory and simulated use tests with an insect growth regulator against *Alphitobius diaperinus* >90% mortality should be achieved. For field studies no specific criteria are mentioned in the Guidance. The laboratory test showed 97.77% adult emergence inhibition. The field tests both showed >70% adult population reduction after 4 weeks and >80% after 8 and 12 weeks. Although no specific criteria are mentioned in the Guidance, the eCA considers the measured population reduction sufficient for authorisation of this product. The adult litter beetles are not targeted by this product and can live for 60-400 days. After 4, 8 and even 12 weeks some of the litter beetles caught in the sticky traps will therefore be the adult litter beetles which were already present during time of of the application of the product.

Based on the provided efficacy data authorization can be granted for the control of larvae of *Musca domestica, Eristalis tenax* and *Stomoxys calcitrans,* as well as larvae of *Alphitobius diaperinus* 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 for flies were conducted with cow manure, pig slurry and pig manure, with chicken manure and chicken litter and with sheep manure. The provided efficacy tests for litter beetles were conducted with chicken manure.

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 insect 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. Dosages 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 (XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXxx xxxxxxXXXXXXXXX): „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).

# Decision

The authorisation holder has applied for a major change: adding litter beetle as new target organism. The efficacy data provided against litter beetles is sufficient to authorise this target organisms, following the application method and application rate mentioned in the authorised use.

As the field of use, the application method(s), and the application rate(s) and frequency is not affected by the addition of the new target organism, the risk assessment for human health, for animals and for the environment are covered by the original authorisation and no new assessment was therefore made.

Addtionally, some minor changes were applied for. The minor changes include:

* Changes of colorant (more information included in the confidential Annex)
* Changes of the product name (change included in section 2.1.1.1).

The change of colorant does not affect the classification nor the risk assessment of the product and is therefore considered acceptable.

The change of the trade name of the product is also considered acceptable.

# Confidential Annex 3.6

See separate document ‘20210806\_NL-0022257-0000\_Confidential\_Addendum’