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

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

(submitted by the evaluating Competent Authority)



[MECDEET SOLUTION]

Product type(s) [19]

[DEET as included in the Union list of approved active substances]

Case Number in R4BP: [BC-DA018929-51]

Evaluating Competent Authority: [FR]

Date: [2021]

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**Note to the reader**

This PAR has been updated with the post-authorisation data provided by the applicant and is based on the PAR of the first authorisation.

In this consolidated PAR, the assessments related to the post authorisation data of the product are at the end of the concerned section and are highlighted in grey.

The SPC (in the first section of the PAR) corresponds to the currently authorised uses in France.

**History of the dossier**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Application type** | **refMS** | **Case number in the refMS** | **Decision date** | **Assessment carried out (i.e. first authorisation / amendment /renewal)** |
| NA-APP | FR | BC-DA018928-51 | 25.04.2018 | Initial assessment of the reference product |
| N.A | *FR* | BC-DA018928-51 |  | Post authorisation data assessment |

# CONCLUSION

**Conclusion on physico-chemical properties**

The product MECDEET SOLUTION is a micro emulsion ready-to-use (ME). All studies have been performed in accordance with the current requirements and the results are deemed to be acceptable except for the pending long term storage stability study.

The appearance of the product is white liquid with a slight fragrance. It is not explosive and has no oxidising properties. The product is not flammable. In aqueous solution (1 % dilution), it has a pH value of 6.93 at 20 °C.

There is no effect of high temperature on the stability of the formulation, since after 8 weeks at 40 °C, neither the active ingredient content nor the technical properties were changed. ‘The mention “Store away from frost” should be added.

Its technical characteristics are acceptable for micro emulsion ready-to-use (ME).

The formulation is not classified for the physico-chemical aspect.

No stability study at 54 °C during 14 days was submitted, a stability study at 40° was provided, the mitigation measure “do not store at more than 40 °C” was added. No stability study at 0°C during 7 days was submitted a mitigation measure “Store away from frost” has been added.

Some technical properties are missing in the storage studies. Consequently, the following data are required for confirmation and should be addressed in post-authorisation:

* Emulsion stability before and after long term storage and accelerated storage should be provided in post-authorisation.

**Post authorisation request 2021**

Emulsion stability before and after long term storage and accelerated storage was requested in post authorization. However, these results were not provided.

The mention “shake before use” is added as a mitigation measure to the SPC.

Analytical method for the determination of the active substance DEET in the formulation is available and validated. Analytical methods for DEET residues in soil, air and water are available in Assessment Report DEET Product-type 19 (March 2010).

**Conclusion on efficacy**

Data presented in the dossier demonstrate that the product MECDEET SOLUTION (DEET 19 % w/w) provides a protection time up to 5 hours when used on skin for human at the application rate of 1.67 µL/cm² against the tick *Ixodes ricinus*

It has to be noted that no claim has been made concerning efficacy on tropical tick species, so the use of this product against ticks in tropical areas is not demonstrated.

However, provided data are not sufficient to validate the efficacy on ticks for dog application.

Efficacy data have been submitted to demonstrate an efficacy of the product on mosquitoes. Nevertheless, important biases have been found in these tests. It is therefore concluded that the efficacy package for mosquitoes is insufficient, and then the claim against mosquitoes is not accepted

Considering the importance of this active substance in vector control, the authorisation holder has to monitor the resistance phenomenon toward the active substance DEET. Results of the resistance monitoring must be submitted to the Competent Authorities (CA) or other appointed bodies involved in resistance management every 5 years.

**Conclusion on human health**

Considering the intended uses on human skin of MECDEET SOLUTION, the human health risk is unacceptable for adults and children (between 6-11 years old) with one application per day.

Considering the intended uses on dog skin of MECDEET SOLUTION, the risk is not acceptable for dogs with one application per day.

Given the necessity to repel ticks in France to prevent Lyme disease, FR CA considers that MECDEET SOLUTION product could be authorized for application on humans, based on article 19(5), with appropriate risk mitigation measures that limit human exposure. The following RMMs are considered as applicable in France:

* For adult: “apply on the *face, neck, hands, ¾ arms, ½ legs and feet once a day”*
* For children: “*do not apply the product on hands of children” and “*“apply on the *face, neck, ¾ arms, ½ legs and feet once a day”*

With these additional RMMs, the risk for human health is acceptable for adult and children above 6 years old.

**Conclusion on indirect exposure via residues in food**

Regarding the intended use of the product MECDEET SOLUTION, a contamination of food cannot be excluded.

Considering the intended use on skin of MECDEET SOLUTION, an estimation of dietary exposure for toddler, children and adults was performed. These estimations are considered as a worst case using the assumption that all the active substance from the palm hands will be ingested. A rinsing factor of 3 is considered relevant regarding the label recommendation “Wash hands before handling food” (this factor is not considered appropriate for infant and toddler). According to use recommendations and risk mitigation measures, no dietary risk was identified for children and adults.

**Conclusion on ecotoxicology and environment**

For the environment, application on human skin leads to acceptable risks for all the environmental compartments whatever the tested scenario (for direct or indirect release). For application on dogs, the only unacceptable scenario is when the product is applied outdoor. Indoor application leads to acceptable levels of risk. The following risk mitigation measure shall be applied to limit the emission to the terrestrial compartment: “Applications on dogs shall be conducted indoor”.

**Overall conclusion**

**The efficacy of the product is demonstrated against ticks when applied on human skin. Risk for human health is however unacceptable based on standard application scenarios and conditions of article 19.1.b) iii) are not met for MECDEET SOLUTION product.**

**In France, given the need to repel tick from human to prevent Lyme disease, the product MECDEET SOLUTION will be authorized for use on humans against the tick *Ixodes ricinus* based on article 19(5) with appropriated risk mitigation measures. It has to be applied on adults and on children above 6 years old, only once per day, only uncovered parts of the body shall be treated, limited to head, arms, hands, lower legs.**

# ASSESSMENT REPORT

## Summary of the product assessment

### Administrative information

#### **Identifier of the product**

| **Identifier** | **Country (if relevant)** |
| --- | --- |
| MECDEET SOLUTION | France |

#### Considering that use against mosquitoes is not validated, the commercial names STOP TIQUES ET MOUSTIQUES and STOP MOUSTIQUE TIGRE cannot be authorized.

#### **Authorisation holder**

|  |  |  |
| --- | --- | --- |
| **Name and address of the authorisation holder** | **Name** | Beaphar B.V. |
| **Address** | Drostenkamp 3  8101 BX Raalte  Netherlands |
| **Authorisation number** |  | |
| **Date of the authorisation** |  | |
| **Expiry date of the authorisation** |  | |

#### **Manufacturer of the product**

|  |  |
| --- | --- |
| **Name of manufacturer** | Beaphar B.V. |
| **Address of manufacturer** | Drostenkamp 3  8101 BX Raalte  Netherlands |
| **Location of manufacturing sites** | Beaphar BV (site OLW)  Oude Linderteseweg  9 8102 EV Raalte  Netherlands |

#### **Manufacturerof the active substance**

|  |  |
| --- | --- |
| **Active substance** | N,N-diethyl-m-toluamide |
| **Name of manufacturer** | Vertellus Performance Materials Inc. |
| **Address of manufacturer** | 2110 High Point Road  Greensboro, NC 27403  USA |
| **Location of manufacturing sites** | 2110 High Point Road  Greensboro, NC 27403  USA |

### Product composition and formulation

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

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

Yes

No

#### **Identity of the active substance**

|  |  |
| --- | --- |
| **Main constituent(s)** | |
| **ISO name** | N,N-diethyl-m-toluamide (DEET) |
| **IUPAC or EC name** |  |
| **EC number** | 205-149-7 |
| **CAS number** | 134-62-3 |
| **Index number in Annex VI of CLP** |  |
| **Minimum purity / content** | 97% w/w |
| **Structural formula** |  |

#### **Candidate(s) for substitution**

The active substance contained in the biocidal product is not candidate for substitution in accordance with Article 10 of BPR.

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

| **Common name** | **IUPAC name** | **Function** | **CAS number** | **EC number** | **Content (%)** |
| --- | --- | --- | --- | --- | --- |
| DEET | N,N-diethyl-m-toluamide | Active substance | 134-62-3 | 205-149-7 | 19 |

Please see the confidential annex for further details.

#### **Information on technical equivalence**

Physical and chemical properties of the active substance and analytical methods for determination of active ingredients in the technical active ingredient have already been evaluated at EU level and are presented in the CAR of the active substance DEET. The notifier BeapharBV of the product MECDEET solution is not the applicant that supported the annex I inclusion dossier of the active substance but it has a letter of access to these data.

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

*Not relevant.*

#### **Type of formulation**

|  |
| --- |
| ME (microemulsion) |

### Hazard and precautionary statements

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

| **Classification** | |
| --- | --- |
| Hazard category | None |
| Hazard statement | None |
|  | |
| **Labelling** | |
| Signal words | None |
| Hazard statements | None |
| Precautionary statements |  |
|  | |
| Note | **-** |

### Authorised use(s)

**Based on standard application scenarios, conditions of article 19.1.b) iii) are not met.**

**In France, given the need to repel tick from human to prevent Lyme disease, the product MECDEET SOLUTION will be authorized for use on humans against the tick *Ixodes ricinus* based on article 19(5) and with appropriated risk mitigation measures.**

**The following SPC is therefore applicable in France.**

#### **Use description**

Table 1. Use # 1 – Human application

|  |  |
| --- | --- |
| **Product Type** | 19 |
| **Where relevant, an exact description of the authorised use** | Repellent |
| **Target organism (including development stage)** | *Ixodes ricinus* (common name : castor bean tick) |
| **Field of use** | Indoor, outdoor |
| **Application method(s)** | Spraying |
| **Application rate(s) and frequency** | 1.67 µL/cm²  Protection time: 5 hours  Adults and children (between 6-11 years old): apply once per day. |
| **Category(ies) of users** | General public (Non-professional) |
| **Pack sizes and packaging material** | Bottle and pump in HDPE with a spray dispenser of 125 mL, 200 mL. |

#### **Use-specific instructions for use**

|  |
| --- |
|  |

#### **Use-specific risk mitigation measures**

|  |
| --- |
|  |

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

|  |
| --- |
| - |

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

|  |
| --- |
| - |

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

|  |
| --- |
| - |

### General directions for use

#### **Instructions for use**

|  |
| --- |
| * Always read the label or leaflet before use and follow all the instructions provided. * Respect the recommended application doses. * The user should inform the registration holder if the treatment is ineffective. * In case of a concomitant use of the product with sunscreen), first apply the sunscreen and wait 20 minutes before the application of the product. * The use of the product with other repellent products is not recommended. * The protection time is only indicative. Environmental factors (e.g. high temperature, wind velocity) can modify it. * The product is not intended to be used in tropical areas. * The product cannot be used on children < 6 years of age. * Spray onto adult´s hand and apply sparingly onto adult´s or child´s face, avoiding eyes and mouth. * Do not use under clothing. * Children 6-11 years old: apply 4 sprays per arm, 6 sprays per leg, 5 for the face and neck, once a day. * Adult and children above 12 years old: apply 8 sprays per arm, 12 sprays per leg, 10 for the face and neck, 4 per hand, once a day. * Shake before use. |

#### **Risk mitigation measures**

|  |
| --- |
| * Do not apply more than once a day. * Apply only on head, arms, hands, lower legs. * Cover untreated parts of the body by clothing. * For children of 6 to 12 years: The repellent must be applied by adults. * Do not apply on children hands. * Wash hands before handling food. * Do not apply directly on or near food, feed or drinks, or on surfaces or utensils likely to be in direct contact with food, feed and drinks. * To prevent contamination of food, avoid contact of treated skin with food. * Keep out of reach of children. The product is not intended for use on animals/pets. |

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

|  |
| --- |
| * Eye contact: Immediately flush with plenty of water, occasionally lifting the upper and lower eyelids. Check for and remove any contact lenses if easy to do. Continue to rinse with warm water for at least 10 minutes. Get medical attention if irritation or vision impairment occurs. * Skin contact: in case of skin reaction, contact poison treatment specialist or get medical attention if irritation occurs. * Inhalation of large quantities: keep at rest in a half-sitting position. Seek medical advice immediately if symptoms occur. * Mouth contact: Wash out mouth with water. Contact poison treatment specialist immediately if symptoms occur and/or in case of mouth contact with large quantities. * Do not give fluids or induce vomiting in case of impaired consciousness; place in recovery position and seek medical advice immediately. * Keep the container or label available. |

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

|  |
| --- |
| * Do not discharge the product on the ground, into water courses, into pipes (sink, toilets…) nor down the drains. * The packaging must not be reused. * Dispose of unused product, its packaging and all other waste in accordance with local regulations. |

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

|  |
| --- |
| * Store away from frost. * Do not store at more than 40°C. * Shelf-life : 2 years |

### Other information

|  |
| --- |
| * Considering the importance of this active substance in vector control, the authorisation holder has to implement a monitoring of scientific literature toward the active substance DEET. Results of this assessment must be submitted to the Competent Authorities (CA) or other appointed bodies involved in resistance management every 5 years. |

### Packaging of the biocidal product

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Type of packaging** | **Size/volume of the packaging** | **Material of the packaging** | **Type and material of closure(s)** | **Intended user (e.g. professional, non-professional)** | **Compatibility of the product with the proposed packaging materials (Yes/No)** |
| bottle | 125 mL, 200 mL | HDPE | pump with a spray dispenser | Non professional | Yes |

### Documentation

#### **Data submitted in relation to product application**

**Identity, physicochemical and analytical method data**

Physico-chemical properties studies and analytical methods on the biocidal product MECDEET solution were provided by BeapharBV.

**Efficacy data**

* An arm-in-cage study conducted with 5 human volunteers with the product MECDEET SOLUTION (19% w/w DEET) on two mosquito species *(Aedes aegypti, and Culex quinquefasciatus).*
* An arm-in-cage study conducted with 10 human volunteers with the product MECDEET SOLUTION (19% w/w DEET) on *Aedes albopictus.*
* An arm-in-cage study conducted with 5 human volunteers with the product MECDEET SOLUTION (19% w/w DEET) on one mosquito species *(Culex quinquefasciatus).*
* A laboratory study conducted with 10 human volunteers with the product MECDEET SOLUTION (19% w/w DEET) on the nymph stage of *Ixodes ricinus.*
* A laboratory study conducted with 6 dogs with the product MECDEET SOLUTION (19% w/w DEET) on the adult stage of *Ixodes ricinus.*

**Toxicology data**

4 studies were performed with MecDEET solution: acute dermal irritation test, acute ocular irritation test, skin sensitisation test, acute oral toxicity (limit test), and acute dermal toxicity test. For other toxicology points, please refer to the CAR.

**Residus data**

No new data provided.

**Ecotoxicology data**

No new data provided, please refer to the CAR.

#### **Access to documentation**

BEAPHAR BV has access on data of the active substance DEET with a Letter of Access of Vertellus.

## Assessment of the biocidal product

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

Table 1. Intended use # 1 – Human application

|  |  |
| --- | --- |
| Product Type(s) | 19 |
| Where relevant, an exact description of the authorised use | Repellents and attractants (Pest control) |
| Target organism (including development stage) | Culicidae: House mosquitoes - Adults  Culicidae: Aedes mosquitoes - Adults  Ixodidae: Ticks - Nymphs |
| Field of use | Indoor, Outdoor |
| Application method(s) | Spraying  Spray lightly on the areas of skin to be protected and then evenly spread by hand (avoid facial areas such as eyes, ears, nose and mouth and damaged areas of  skin). When applying to facial areas, spray the product onto the palm of your hand and spread sparingly over the face. On a surface like the arm, apply 3 sprays. |
| Application rate(s) and frequency | 3 sprays for a surface like the arm.  For children above 12 years old and adults: Do not spray more than twice per day.  For children below 12 years old: Do not spray more than once per day. |
| Category(ies) of user(s) | Non-professional |
| Pack sizes and packaging material | Plastic Bottle: HDPE 125 and 200 mL with a pumpspray |

Table 2. Intended use # 2 – Dog application

|  |  |
| --- | --- |
| Product Type(s) | 19 |
| Where relevant, an exact description of the authorised use | Repellents and attractants (Pest control) |
| Target organism (including development stage) | Ixodidae: Ticks - Nymphs |
| Field of use | Indoor, Outdoor |
| Application method(s) | Spraying on dogs (aged 12 weeks or older) for up to 5 hours against ticks. |
| Application rate(s) and frequency | For small dogs: apply 5-7 sprays on the fur  For medium dogs: apply 8-11 sprays on the fur  For large dogs: apply 13-18 sprays on the fur  frequency: once per day |
| Category(ies) of user(s) | Non-professional |
| Pack sizes and packaging material | Plastic Bottle: HDPE 125 and 200 mL with a pumpspray |

Table 3. Intended use # 3 – Dog application

|  |  |
| --- | --- |
| Product Type(s) | 19 |
| Where relevant, an exact description of the authorised use | Repellents and attractants (Pest control) |
| Target organism (including development stage) | Ixodidae: Ticks - Adults |
| Field of use | Indoor, Outdoor |
| Application method(s) | Spraying on dogs (aged 12 weeks or older) for up to 5 hours against ticks. |
| Application rate(s) and frequency | For medium dogs: apply 1-2 sprays on the fur  For large dogs: apply 2-3 sprays on the fur  frequency: once per day |
| Category(ies) of user(s) | Non-professional |
| Pack sizes and packaging material | Plastic Bottle: HDPE 250 and 500 mL with a pumpspray |

### Physical, chemical and technical properties

#### **Active ingredient**

##### Identity, origin of active ingredient

DEET: N,N-diethyl-m-toluamide

Vertellus Performance Materials Inc.

2110 High Point Road

Greensboro, NC 27403

USA

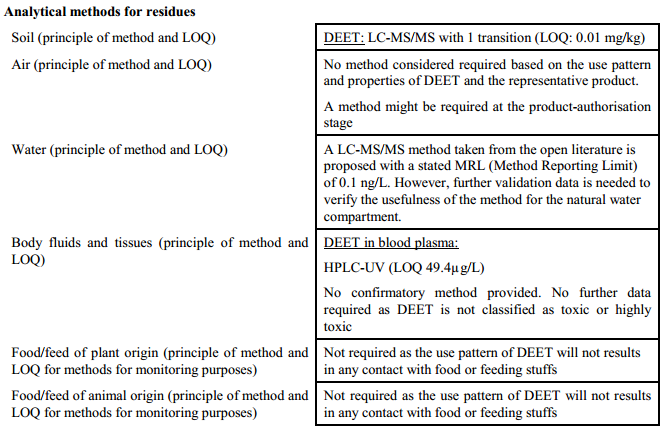
##### Physico-chemical properties and Analytical method for determination of active ingredient and impurities in the technical active ingredient

Physical and chemical properties of the active substance and analytical methods for determination of active ingredients in the technical active ingredient have already been evaluated at EU level and are presented in the CAR of the active substance DEET. The notifier BeapharBV of the product MECDEET solution is not the applicant that supported the annex I inclusion dossier of the active substance but it has a letter of access to these data.

**Summary for DEET:**

|  |  |
| --- | --- |
|  | Principle of method |
| Technical active substance as manufactured: | GC-FID |
| Impurities in technical active substance: | GC-FID with GC-MS for confirmation of identities |

**Summary**



#### **Biocidal product**

##### Identity, composition of the biocidal product, packaging

The biocidal product is not the same as the one assessed for the inclusion of the active substances in annex 1 of directive 98/8/EC. The composition of the product is confidential and is presented in a confidential annex. The product contains 19 % w/w of DEET.

Owner of the biocidal product:

Beaphar BV

Drostenkamp 3

8101 BX Raalte

Netherlands

##### Physico-chemical properties

The biocidal product MECDEET is a white liquid with a slight fragrance. The pH of the pure product is about 6.93 at 20°C and its relative density is about 1.003. The product is a Microemulsion (ME) type formulation.

|  |  |  |
| --- | --- | --- |
| Trade Name | MECDEET | |
| Manufacturer’s development code number | 300153 | |
| Ingredient of preparation | Function | Content (% w/w) |
| DEET 134-62-3 | Active substance | 19 |
| Formulants | Details on confidential PAR | |
| Physical state of preparation | Liquid | |
| Nature of the preparation | ME (microemulsion) | |

There are no preservatives in the biocidal product.

The tested product is MECDEET, 19 % w/w DEET.

The preparation is a ME (microemulsion), ready to use.

The used batch is 2026921.

### Physical hazards and respectives characteristics

| **(Sub)Section (Annex point)** | | **Method** | **Purity/specifications** | **Results** | **Reference** | **FR evaluation** |
| --- | --- | --- | --- | --- | --- | --- |
| **B3.1** | **Appearance (IIB, III 3.1)** | | | | |  |
|  | Physical state and nature |  |  |  |  |  |
|  | Colour | visual method | Test item: MecDEET  Batch n°: 2026921 | White liquid with a slight fragrance | Lanata M. 2014, final report No. 2012/1671AMi | Acceptable |
| **B3.5** | **Acidity / alkalinity (IIB, III 3.5)** | | | | |  |
|  | pH value | CIPAC MT 75.3 | Test item: MecDEET  Batch n°: 2026921 | pH of the test item : 6.93 at 20°C | Meluso A. 2012, report 2012/1667AMi Cert-1 | Acceptable |
|  | Acidity / Alkalinity | - | - | Not required since pH of the test item is > 4 and < 10 | - | Not required. |
| **B3.6** | **Relative density (IIB, III 3.6)** | | | | |  |
|  | Relative density | EEC A.3  Calculation | Test item: MecDEET  Batch n°: 2026921 | 1.003 at 20°C and 101.3kPa | Meluso A. 2012, report 2012/1667AMi Cert-1 | Acceptable |
|  | Bulk density | - | - |  | - | - |
| **B3.7** | **Storage stability-stability and shelf life (IIB, III 3.7)** | | | | |  |
|  | Stability after accelerated storage for 8 weeks at 40 °C | Method for quantitation of AS is validated in method 2012/1669AM-MdP.  CIPAC MT 46.3  CIPAC MT 75.3  CIPAC MT 36.3 | Test item: MecDEET  Batch n°: 2026921 | |  |  |  | | --- | --- | --- | |  | Initial | After 8 weeks at 40°C | | Appearance | White liquid with a slight fragrance | No change | | Appearance of packaging | White plastic botlle with spray dispenser in HDPE | No change | | Content of DEET (% w/w) | 18.17 | 18.82 | | % variation | / | 3.6% | | Weight | 1743 g | 1742 g | | Variation of weight | / | -0.05% |  |  |  |  | | --- | --- | --- | | Emulsion stability of the test item  initially  after 30 minutes  after 2 hours  after 24 hours  after re-emulsification after 24 h  30 minutes after the  re-emulsification |  |  | | Meluso A. 2012, report 2012/1670 | The biocidal product is stable after 8 weeks at 40°C except emulsion stability which is not provided.  The emulsion stability before and after accelerated storage should be provided in post-authorisation within 2 years.  No stability study at 54°C during 14 days was submitted, the mention “the mitigation measure “do not store at more than 40°C” should be added. |
|  | Stability after storage at low temperatures | - | - | No data submitted.  The mention “Store away from frost” should be added to the label. | - | The mention “Store away from frost” should be added. |
|  | Shelf life following storage at ambient temperature | Method for quantitation of AS is validated in method 2012/1669AM-MdP. | Test item: MecDEET  Batch n°: 2026921 | |  |  |  |  |  | | --- | --- | --- | --- | --- | |  | Initial | After 1 year | After 18 months | After 2 years | | Appearance | White liquid with a slight fragrance | No change | No change | No change | | Appearance of packaging | White plastic botlle with spray dispenser in HDPE | No change | No change | No change | | pH at 20°C | 6.96 | 7.01 | 6.86 | 6.97 | | Content of DEET (% w/w) | 18.23 | 18.98 | 19.03 | 18.80 | | % variation | / | 4.1% | 4.4 | 3.1 | | Density at 20°C | 1.008 | 1.004 | 1.000 | 1.004 | | Variation of weight | / | -0.24% | -0.40% | -0.55% |   Storage in commercial packaging material (plastic bottle with a white spray dispenser). | Lanata M. 2014, final report No. 2012/1671AMi | The biocidal product is stable 2 years at ambient temperature but physico-chemical properties are lacking.  Emulsion stability should be provided before and after long term storage in post-authorisation within 2 years. |
|  | **Post authorisation request 2021**  Emulsion stability before and after long term storage was requested in post authorization. However, these studies were not provided.  The stability of the product has not been fully demonstrated. A doubt remains on the stability of the emulsion after storage.  Therefore, the mitigation measure is added to the SPC: “shake before use”. | | | | | |
| **B3.8** | **Technical characteristics (IIB, III 3.8)** | | | | |  |
|  | Wettability | - | - | - | - | - |
|  | Persistent foaming | - | - | Justification of the notifier: applicable only to products to be diluted | - | Acceptable. |
|  | Suspensibility | - | - | - | - | - |
|  | Spontaneity of dispersion | - | - | - | - | - |
|  | Dilution stability | - | - | - | - | - |
|  | Dry sieve test | - | - | - | - | - |
|  | Wet sieve test | - | - | - | - | - |
|  | Dust content / Particle size of dust |  |  |  |  | - |
|  | Friability and attrition characteristics of granules |  |  |  |  | - |
|  | Bulk or tap density |  |  |  |  | - |
|  | Emulsifiability / Emulsion stability / Re-emulsifiability | CIPAC MT 36.3  (visual method) |  | Justification of the notifier: not applicable to ready-to-use product |  | An emulsion stability study should be provided in post-authorisation because the stability of micro emulsion must be demonstrated. |
|  | **Post authorisation request 2021**  The emulsion stability of the product has not been demonstrated.  Therefore, the mitigation measure is added to the SPC: “shake before use”. | | | | | |
|  |
|  | Stability of dilute emulsions | - | - | - | - | - |
|  | Flowability | - | - | - | - | - |
|  | Pourability (including rinsed residue) | - | - | - | - | - |
|  | Dustability following accelerated storage | - | - | - | - | - |
| **B3.9** | **Compatibility with other products (IIB, III 3.9)** | - | - | - | - | - |
| **B3.10** | **Surface tension and viscosity (-)** | | | | |  |
|  | Surface tension | OECD Guideline 115 (Surface Tension of Aqueous Solutions) | Test item: MecDEET  Batch n° 2121511 | Surface tension: 43,1 mN/m at 20°C.The biocidal product is active surface. | Mazzei A. 2015, Report 201504109 | Acceptable  The biocidal product is active surface. |
|  | Kinematic viscosity | OECD Test Guideline 114 | Test item: MecDEET  Batch n° 2121511 | Kinematic viscosity at 20°C: 25.66 cSt  Dynamic viscosity at 20°C 25.71 mPa\*s  Kinematic viscosity at 40°C: 6.6 cSt  Dynamic viscosity at 40°C 6.56 mPa\*s | Meluso a., 2016, final report S-2015-03393 AM | Acceptable |
| **B 3.11** | **Particle size distribution (-)** | CIPAC MT 187 | test item: MecDEET 19%  Batch n°621475 (bottle 125 mL) | Considering the similarity of spray output and the spray pattern of the 125 and 200 mL bottle, results of particule size distribution for 125 mL bottle can be extrapolated to the 200 mL bottle (same nozzle).   |  |  |  |  | | --- | --- | --- | --- | | Test item n° | Dv (10%) (µm) | Dv (50%) (µm) | Dv (90%) (µm) | | 1 | 29.46 | 58.79 | 110.02 | | 2 | 36.02 | 64.05 | 114.98 | | 3 | 34.45 | 61.77 | 112.44 | | **Mean** | **33** | **62** | **112** | | Matyssek F. 2018, Report AQ018-18-2 | A study has been provided by the applicant only for 125 bottle. Results for 250 and 500 mL bottles are not necessary as these packagings are not authorised. |
| **B3.12** | **Spray pattern** |  | Test item: MecDEET  Batch n°: 2026921  34 months aged sample | |  |  |  |  | | --- | --- | --- | --- | |  | Bottle 1 200 mL(full 150 mL MecDEET ) | Bottle 2 200 mL (filled for 30%) | Bottle 3 200 mL (full 150 mL) | | Spray output (g/spray) | 0.1880 | 0.1837 | 0.1834 | | Range | 0.1886-0.1909 | 0.1852-0.1886 | 0.1842-0.1872 | | Mean (5 single sprays) | 0.1898 | 0.1859 | 0.1857 | | Standard deviation | 0.0009 | 0.0006 | 0.0015 | | Grootkarzijn, A.2014, report n°: 347 | Spray pattern was tested with an aged sample of 8 months and 34 months, we can consider that it is acceptable.  There is an important difference between the distributed quantities in different sizes of bottles. An explanation was request and was not submitted.  However the rate is expressed into mL/cm², therefore the packaging does not have an impact on the authorised rate.  This explanation is not necessary anymore. |
|  |  |  | Test item: Mec DEET  *Batch n°: 2121511*  8 months aged sample | |  |  |  |  | | --- | --- | --- | --- | |  | Bottle 1 (90 %full 125 mL) | Bottle 2 (filled for 50%) | Bottle 3 (filled for 30%) | | Spray output (g/spray) | 0.185 | 0.183 | 0.189 | | Range | 0.182-0.186 | 0.181-0.185 | 0.189-0.191 | | Mean (5 single sprays) | 0.184 | 0.183 | 0.190 | | Standard deviation | 0.002 | 0.002 | 0.001 |  |  |  |  |  | | --- | --- | --- | --- | |  | Bottle 1 (90% full 250 mL) | Bottle 2 (filled for 50%) | Bottle 3 (filled for 30%) | | Spray output (g/spray) | 1.038 | 1.038 | 1.037 | | Range | 1.029-1.048 | 1.035-1.046 | 1.025-1.037 | | Mean (5 single sprays) | 1.038 | 1.040 | 1.032 | | Standard deviation | 0.008 | 0.005 | 0.005 |  |  |  |  |  | | --- | --- | --- | --- | |  | Bottle 1 (90% full 500 mL) | Bottle 2 (filled for 50%) | Bottle 3 (filled for 30%) | | Spray output (g/spray) | 1.229 | 1.224 | 1.221 | | Range | 1.215-1.230 | 1.222-1.241 | 1.217-1.230 | | Mean (5 single sprays) | 1.226 | 1.227 | 1.221 | | Standard deviation | 0.006 | 0.008 | 0.005 | | report n°: 347 v2, 2015 |  |

| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **Reference** |
| --- | --- | --- | --- | --- |
| Explosives | Statement | - | As MecDEET contains ≈80% w/w water and as no ingredient classified as explosive.  The product has no explosive properties. | - |
| Flammable gases | - | - | Not required as the product is a liquid product. | - |
| Flammable aerosols | - | - | Not required as the product is a liquid product and the spray is not under pressure.. | - |
| Oxidising gases | - | - | Not required as the product is a liquid product. | - |
| Gases under pressure | - | - | Not required as the product is a liquid product and the spray is not under pressure. | - |
| Flammable liquids | Statement | - | As MecDEET contains ≈80% w/w water and as no ingredient classified as flammable.  Flashpoint > 100°C.  The preparation is not flammable. | Wo C., 2013  Study number 35443 |
| Flammable solids | - | - | Not required as the product is a liquid product. | - |
| Self-reactive substances and mixtures | - | - | Not required as no self-reactive substance is present in the biocidal product. | - |
| Pyrophoric liquids | - | - | As MecDEET contains ≈80% w/w water and as no ingredient classified as pyrophoric. The preparation is not pyrophoric. | - |
| Pyrophoric solids | - | - | Not required as the product is a liquid product. | - |
| Self-heating substances and mixtures | - | - | Not required as the product is a liquid product. | - |
| Substances and mixtures which in contact with water emit flammable gases | - | - | Not required as the product contains water. | - |
| Oxidising liquids | Statement | - | As MecDEET contains ≈80% w/w water and as no ingredient is classified as oxidising liquid or solid.  The product has no oxidizing properties. | Statement |
| Oxidising solids | - | - | Not required as the product is a liquid product. | - |
| Organic peroxides | - | - | No peroxide is present in biocidal product. | - |
| Corrosive to metals | Statement | - | As MecDEET contains ≈80% w/w water and as no ingredient classified as corrosive to metal. The preparation is not corrosive to metal. |  |
| Auto-ignition temperatures of products (liquids and gases) | Statement | - | The product MecDEET is not expected to present a significant hazard for auto-flammability. Test is not required as MecDEET contains contains ≈80% w/w water and as no ingredient is considered to be auto-flammable based on available data found in safety data sheets. | Statement |
| Relative self-ignition temperature for solids | - | - | Not required as the product is a liquid product. | - |
| Dust explosion hazard | - | - | Not required as the product is a liquid product. | - |

### Methods for detection and identification

#### **Analytical method for determining the active substance and relevant component in the biocidal product**

The tested product is MECDEET, 19 % w/w DEET.

The used batch is 2026921.

The preparation is a ME (microemulsion), ready to use.

**Analytical method validation for the identification and quantification of active ingredient N, N-diethyl-meta-toludamide (DEET) in the test item 'MECDEET' (A. Meluso, 2012, rapport 2012/1669 AMi, Eurofins Biolab S.r.l Via Bruno Buozzi, 2 20090 Vimodrone (MI) Italia.**

Principle of the method:

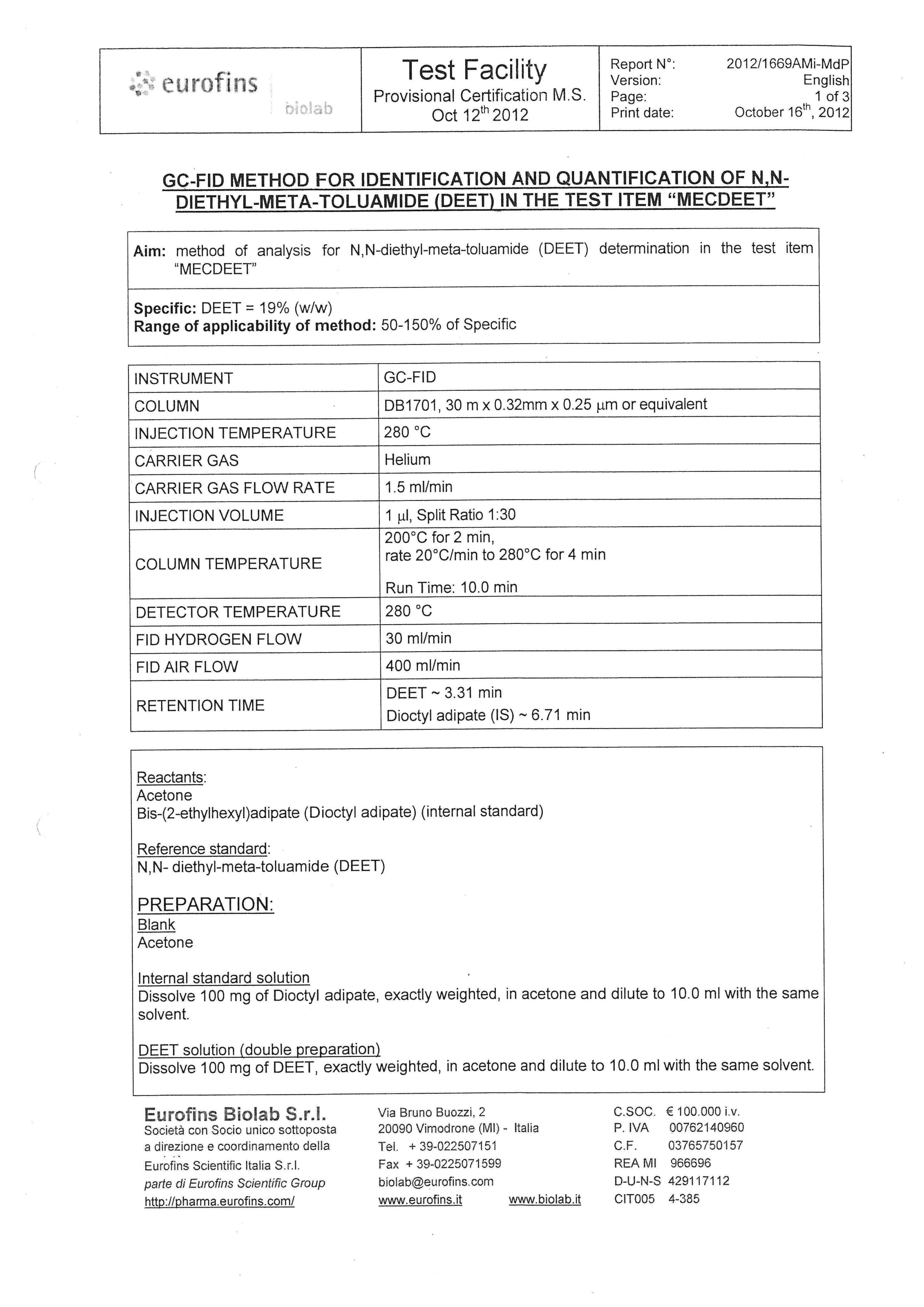
The method was performed by GC-FID and the instrumental conditions were optimised in order not to saturate the system and obtain a good repeatability of the data. The use of internal standard has levelled the variations in the chromatographic response.

As part of the development of the method, it was necessary to confirm the identity of compounds and provide that there were no interferences ≥3%.

The standards, the internal standard, the placebo and the test sample solution were diluted in acetone. Rt DEET= 3.31 min.

Sample preparation consist to: dissolve 105 mg of test sample and 2.0 mL of internal standard solution in 20 mL volumetric flask with acetone and brought to volume with the same solvent.

Method conditions:



Batch number reference active substance: 113394

GLP: Yes

Results

Specificity:

The chromatograms of blank, standard, internal standard, blank matrix, and sample were provided, and there is no interference.

Linearity:

A calibration curve was realised (6 levels of concentrations: 0.487-1.462 mg/mL, with n=1), R²=0.9999 and it was linear.

Recovery:

The accuracy was tested at 3 levels with n=2, the mean recovery is 101.3%.

Repeatability:

The repeatability was tested with 6 different preparations of sample performed in the same analytical session, with a RSD of 0.7%. The repeatability is acceptable.

Conclusion:

The analytical method is validated.

#### **Analytical methods for determining relevant components and/or residues in different matrices**

Analytical methods for DEET residues in soil, air and water are available in Assessment Report DEET Product-type 19 (March 2010). A letter of access from Vertellus has been provided.

**Analytical methods for the active substance**

|  |  |
| --- | --- |
| Technical active substance (principle of method) | GC-FID |
| Impurities in technical active substance (principle of method) | GC-FID with GC-MS for confirmation of identities |

**Analytical methods for residues**

|  |  |
| --- | --- |
| Soil (principle of method and LOQ) | DEET: LC-MS/MS with 1 transition (LOQ: 0.01 mg/kg) |
| Air (principle of method and LOQ) | No method considered required based on the use pattern and properties of DEET and the representative product.  A method might be required at the product-authorisation stage |
| Water (principle of method and LOQ) | A LC-MS/MS method taken from the open literature is proposed with a stated MRL (Method Reporting Limit) of 0.1 ng/L. However, further validation data is needed to verify the usefulness of the method for the natural water compartment. |
| Body fluids and tissues (principle of method and LOQ) | DEET in blood plasma:  HPLC-UV (LOQ 49.4µg/L)  No confirmatory method provided. No further data required as DEET is not classified as toxic or highly toxic |
| Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) | Not required as the use pattern of DEET will not results in any contact with food or feeding stuffs |
| Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) | Not required as the use pattern of DEET will not results in any contact with food or feeding stuffs |

### Risk assessment for Physico-chemical properties

MECDEET Solution is not considered to be potentially explosive or contain an oxidising agent. The preparation is not intended to use in combination with other products. The product is not expected to be flammable.

### Efficacy against target organisms

#### **Function and field of use**

Main Group 03: Pest Control

Product Type 19: Repellents and attractants

MECDEET Solution is presented as a ready-for-use lotion to be applied on human skin and dog fur. For humans, the product is sprayed on the areas of skin to be protected and then evenly spread by hand. When applying to facial areas, spray the product onto the palm of your hand and spread sparingly over the face. For dogs, the product is spread onto the fur on the areas to be protected from neck to the top of the tail, the lateral flanks and legs.

The product is intended to be used by the general public (non-professional).

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

According to the uses claimed by the applicant, the product MECDEET Solution is intended to be used to repel arthropods.The products, organisms or objects to be protected are humans and dogs.

The target organisms to be controlled are:

For humans:

- Mosquitoes (adult stage): *Culex quinquefasciatus*, *Aedes aegypti*, *Aedes albopictus*

- Ticks (nymph stage): *Ixodes ricinus*.

For dogs:

- Ticks (adult stage): *Ixodes ricinus*.

The application rates recommended by the applicant are the following:

Humans: 1.67 µL/cm2 of skin. The product is to be applied once to twice a day depending on the age of the user.

Dogs: 5 µL/cm², once a day.

This product is not intended to be used in tropical areas.

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

The applicant submitted following studies:

* For the use against mosquitoes:
* An arm-in-cage study conducted with 5 human volunteers with the product MECDEET Solution (19 % w/w DEET) on two mosquito species(*Aedes aegypti* and *Culex quinquefasciatus*)*.*

The product was sprayed at the dose of 1.67 µL/cm², on the forearm. Beginning one hour after treatment a sleeve with an opening of 3.1 x 8.0 cm (approx. 25 cm²) is fastened around the arm in such a way that the opening is positioned completely over the treated area. The edges of the opening of the sleeve have been also treated with the test material (200 µl) in a width of approx. 1 cm to prevent bites from the edge. The areas above the sleeves are protected by cloth a proboscis cannot penetrate; hands are protected by latex gloves. The control forearm was inserted into the cage, and after validation of this control, the treated forearm was inserted into the cage for 5 minutes every hour until inefficacy considered as the first bite followed by a second one within one hour.

This study has not been accepted since it presented several flaws in the methodology. Indeed, it has been considered that the use of a sleeve, moreover treated with nearly 5 fold the claimed application rate (8 µl/cm² against 1.67 µl/cm²), may bias the results and sur-estimates the efficacy. Furthermore, this efficacy test has only been done on 5 volunteers (without replication). The test should be done with 10 volunteers (indeed the number of volunteers should be sufficient to allow for statistical analysis according to both WHO and EPA methods and the number of 10 has been confirmed by efficacy e-consultation on 2013).

Considering the control, it is to be noted that an additional volunteer has been used for the negative control instead of the second forearm of the same volunteer as required by the TNsG on product evaluation for PT18/19 (2012). Differences between controls and treated conditions may thus be related to innate differences among test subjects.

During the evaluation, the applicant has provided two new arm-in-cage studies:

* An arm-in-cage study conducted with 10 human volunteers with the product MECDEET Solution (19% w/w DEET) on one mosquito species(*Aedes albopictus*)*.*

The product was sprayed at the dose of 1.67µL/cm², on the forearm. Beginning one hour after treatment a sleeve with an opening of 5 x 10 cm (approx. 50 cm²) is fastened around the arm in such a way that the opening is positioned completely over the treated area. The edges of the opening of the sleeve have been also treated with the test material (57 µl) in a width of approx. 1 cm (approx. 34 cm²) to prevent bites from the edge (corresponding to the claimed application rate of 1.67 µl/cm²). The areas above the sleeves are protected by cloth a proboscis cannot penetrate; hands are protected by latex gloves. The control forearm was inserted into the cage, and after validation of this control, the treated forearm of the same volunteer was inserted into the cage for 5 minutes every hour until inefficacy considered as the first bite followed by a second one within one hour.

* An arm-in-cage study conducted with 5 human volunteers with the product MECDEET Solution (19% w/w DEET) on one mosquito species (*Culex quinquefasciatus*).

The product was sprayed at the dose of 1.67 µL/cm², on the forearm: 104 cm² (8 x 13cm) of each test forearm is treated evenly with 174 μl of the test product using a microliter pipette (corresponding to the claimed application rate of 1.67 µl/cm²). Beginning one hour after treatment a sleeve with an opening of 5 x 10 cm (approx. 50 cm²) is fastened around the arm in such a way that the opening is positioned completely over the treated area. The edges of the opening of the sleeve have been also treated with the test material (57 µl) in a width of approx. 1 cm (approx. 34 cm²) to prevent bites from the edge (corresponding to the claimed application rate of 1.67 µl/cm²). The areas above the sleeves are protected by cloth a proboscis cannot penetrate; hands are protected by latex gloves. The control forearm was inserted into the cage, and after validation of this control, the treated forearm of the same volunteer was inserted into the cage for 5 minutes every hour until inefficacy considered as the first bite followed by a second one within one hour. It has to be noted that this test has been done only on 5 volunteers instead of 10 (e-consultation of WG Efficacy in May 2014).

In a first intention, FR CA decided to not accept these new studies since the use of a treated sleeve could bias the results and sur-estimates the efficacy. Indeed, the aim of such a test is to determine a protection time on human skin taking into account factors like for example volatility, skin absorption or interaction with sweat. In this test, the surface of the edges treated corresponds to about 70 % of the surface of the skin exposed (and so 70 % of the quantity of product applied on the skin) and could lead to an increase of the protection time since there will be no effect linked with the interaction with the skin and volatility of the product may thus be modified. Moreover, as confirmed by the applicant, the control is made with a non-treated sleeve. Hence controls are not identical to treated conditions regarding treatment of the sleeve. Thus, use of these controls doesn’t permit to demonstrate that the treatment of the sleeve has no impact on the test results.

FR CA received different views from MS concerned by the mutual recognition:

- 1 MS was in favour to accept the data package for efficacy against mosquitoes*,* because details of the required test methodology are not included in the current guidance and proposes to consider data on *Aedes* as a worst case. Moreover one CA did not consider the use of a treated sleeve as critical flaws and recommends a more balanced approach, weighing both the strengths and potential weaknesses of the studies, but does not conclude about authorising the use against mosquitoes.

- 3 MSs agree with the evaluation of the eCA that efficacy against mosquitoes is not proven with the data package submitted.

- For 1 MS, the opinion was unclear.

After assessment of all the opinions expressed by cM, it was concluded that a majority of MSs consider that the efficacy package for mosquitoes is insufficient, and then the claim against mosquitoes is not accepted.

* For the use against ticks:
* A laboratory study conducted with 10 human volunteers with the product MECDEET Solution (19% w/w DEET) on the nymph stage of *Ixodes ricinus.*

The repellent efficacy of the product MECDEET Solution was tested against nymphs of *Ixodes ricinus* ticksby 10 volunteers. The product was applied with a pipette and spread on one forearm of each volunteer, except on the lowest 5 cm near the wrist. The arm was held vertically (with the fingertips or palm placed on a horizontal surface. Ticks were placed on this untreated area, 3 cm below the treated area, and observed for a maximum of 3 minutes. The test lasted for 7 hours post application, with 10 ticks tested per hour and per volunteer (5 ticks every 30 minutes). But, the last interval of measure is “390 to 420 min” so the last measure is at 390 minutes post application (i.e. 6.5 h), no measure has been done 420 minutes after application.

According to the applicant, ticks were considered "not repelled" when they crawled at least 3 cm upwards onto the treated area. All other ticks were considered as "repelled".

Criteria of the TNsG on product evaluation for PT18 and 19 (2012) are not very precise concerning whether or not a tick is repelled. Indeed, according to the TNsG, a tick is considered as non-repelled if it crosses the line 3 cm above the wrist or a tick is considered repelled when it drops down from the arm. The laboratory followed the criteria mentioned in the EPA guideline[[1]](#footnote-1). But this guideline says that:

- a tick is considered as repelled if:

- it does not cross into the treated area

- it crawls into the treated area but immediately turns back or falls off

- a tick is considered as not repelled if it crosses the boundary line at least 3 cm into the treated area within 3 minutes, and remains in the treated area for at least one minute.

This guideline doesn’t mention for example how to consider a tick that crosses the boundary line but not at least 3 cm into the treated area within 3 minutes, and remains in the treated area for at least one minute. The laboratory proposes to include this case in the “repelled ticks”, but we could consider that if a tick stays for at least one minute in a treated area, this tick could be considered as not repelled.

FR CA decided to follow the recommendation of the EPA guideline and so considers that a tick is repelled only if it not crosses into the treated area or it crawls into the treated area but immediately turns back or falls off.

The submitted study shows that the product MECDEET Solution(19% w/w DEET) when used at a dose of 1.67 µL/cm2 of skin provides a mean protection time of 5.2 hours against nymphs *Ixodes ricinus*. So the product provides up to 5 hours protection instead of 7 hours claimed by the applicant.

* A laboratory study conducted with 6 dogs with the product MECDEET Solution (19% w/w DEET) on adults *Ixodes ricinus.*

This study was performed to determine the repellency effect of MECDEET Solution against artificial infestations of ticks (*Ixodes ricinus*) on dogs.

Based on the results of a parasite selection test, six dogs (3 males and 3 females) were allocated to the study group. The allocated animals were divided into two cohorts. MECDEET Solution was administered as a spray-on product, which is the intended method of application of the product. The product was applied to an area of the right leg of each animal, between the carpal joint and elbow joint.

At the following time points after administration of MECDEET to each animal, (30 minutes, 1 hour, 2 hours, 3 hours, 4 hours and 5 hours), five ticks were individually placed on the dorsal surface of the animals right paw. The ticks were observed for a maximum period of 3 minutes to determine their movements from the paw towards the shoulder.

This study has not been accepted since it presented several flaws in the methodology. Indeed,

- Application rates are highly differing between the dogs (from 0.46 to 5.44 µL/cm²), and results are highly variable (0 to 5 hours protection time). Furthermore, the highest dose of 5.44 µL/cm² (that is the nearest to the claimed application rate) is ineffective.

- The questing behaviour of the tested ticks is not tested before their exposure to the treated surface, so there is no negative control. Indeed the control described in the test has only permit to eliminate dogs that were not sufficiently attractive for ticks and has not permit to evaluate the questing behaviour of ticks.

It is to be noted that the protocol described in the TNsG on product evaluation for PT18/19 (2012) for human tests is not enough relevant for demonstrating effectiveness of the products on dogs. It is specified in the TNsG on product evaluation for PT18/19 (2012), section 1.3, p.6, that “The use of existing guidelines, with revisions to make the guideline more suitable for the specific product or company conditions, is also possible”. Indeed, according to EMA guidelines relative to the evaluation of the efficacy of antiparasitic substances[[2]](#footnote-2)[[3]](#footnote-3), that can be adapted to biocidal products, effects, like for example hair length, dirtiness of animal coat or self-grooming can have an impact on the protection time. These factors have not been taken into consideration in the submitted study. Furthermore, contrary to the human application, the dog application implies to treat the whole animal (except some facial areas) so the treatment of the forearm is not enough representative of the use since length and density of hair varies between the different body parts.

So FR CA considers that the submitted efficacy test doesn’t permit to conclude on the effectiveness of the product MECDEET Solution when used to protect dogs against ticks.

Furthermore, according to the the TNsG on product evaluation for PT18/19 (2012), when a product is intended to be used on dogs, efficacy test on *Rhipicephalus sanguineus* should also be submitted.

Conclusion on efficacy:

Based on the provided efficacy data, only the protection against *Ixodes ricinus* for human skin application can be validated[[4]](#footnote-4). The time of protection for this use at a dose of 1.67 µL/cm2 of skin is up to 5 hours.

Due to several flaws in the methodologies used, efficacy data are not sufficient to validate the protection against mosquitoes for human application and against ticks for dog application.

#### **Mode of action, including time delay**

The DEET molecule has been used for more than 60 years. It has been developed by scientists at the U.S. Department of Agriculture and patented by the U.S. Army in 1946. However, DEET mode of action is still not clearly understood.

Two main hypotheses are presented in available bibliography.

The oldest hypothesis suggested that DEET would mask or blind emanations released by human skin which are attractant for mosquitoes (*e.g*. 1-octen-3-ol). Applying DEET on skin would either reduce the released amounts of these compounds or mask their release. Both cases would lead to a reduction of attractiveness to human skin due to a reduction of attractants quantity perceived by ORNs (Olfactory Receptor Neurons) of mosquito antennae.

Some scientists led studies on DEET action mode and concluded to another hypothesis. Syed and Leal identified specific DEET-sensitive ORNs (Olfactory Receptor Neurons) placed on mosquitoes antennae. DEET could be detected as such and there would be no need of interaction with skin released compounds for DEET-induced repellency (see Document IV Maibach *et al*., 1974, Syed and Leal, 2008 and Stanczyk *et al*., 2010).

By using toxicological, biochemical and electrophysiological techniques, Corbel *et al*.[[5]](#footnote-5) show that DEET is not simply a behaviour-modifying chemical but that it also inhibits cholinesterase activity, in both insect and mammalian neuronal preparations. DEET is commonly used in combination with insecticides and Corbel *et al*. show that DEET has the capacity to strengthen the toxicity of carbamates, a class of insecticides known to block acetylcholinesterase.

In 2011, Lavialle-Defaix *et al*.[[6]](#footnote-6) developed a new biological model based on mosquito neurons isolated from adults *Anopheles gambiae* heads. and revealed that AgNav channel and AChE enzymes which are targeted by insecticide and/or repellent were sensitive to the pyrethroid permethrin and to the repellent DEET, respectively.

In 2013, DeGennaro *et al*.[[7]](#footnote-7) studied the impact of targeted mutations in the Ae. Aegypti orco gene in order to examine the contribution of Orco (an obligate co-receptor of the odorant receptors (ORs)) and the OR pathway to mosquito host selection and sensitivity to the insect repellent DEET. orco mutant olfactory sensory neurons have greatly reduced spontaneous activity and lack odour-evoked responses. Behaviourally, orco mutant mosquitoes have severely reduced attraction to honey, an odour cue related to floral nectar, and do not respond to human scent in the absence of CO2. However, in the presence of CO2, female orco mutant mosquitoes retain strong attraction to both human and animal hosts, but no longer strongly prefer humans. orco mutant females are attracted to human hosts even in the presence of DEET, but are repelled upon contact, indicating that olfactory- and contact-mediated effects of DEET are mechanistically distinct. The authors concluded that the OR pathway is crucial for an anthropophilic vector mosquito to discriminate human from non-human hosts and to be effectively repelled by volatile DEET.

Some studies reported also an insecticidal effect of the DEET, for example:

In 2003, Xue *et al.*[[8]](#footnote-8)wrote an article on a laboratory evaluation of toxicity of sixteen commercial insect repellents (6 botanical and l0 synthetic organic products) in aerosol sprays to adult mosquitoes. These repellents (including 8 insect repellent products containing 6.65 to 38% of DEET) were evaluated in the laboratory for adult knockdown (KD) and mortality of laboratory-reared female *Aedes aegypti*, *Aedes albopictus*, and *Anopheles quadrimaculatus*. All tested formulations except 2 botanical repellent products caused 100% 24-h mortality of *Ae. aegypti* and all but 1 caused 100% 24-h mortality of *Ae. albopictus* and *An. quadrimaculatus*.

In 2006, Licciardi *et al.[[9]](#footnote-9)* evaluated the knock-down, mortality and ‘irritancy’ effects of three synthetic repellents (DEET, IR3535 and KBR 3023) on *Aedes aegypti* (L) (Diptera: Culicidae) in the laboratory in the absence of animal bait. Filter paper tests were carried out to assess the knock-down effect (KDt50 and KDt95) and mortality (LC50 and LC95) induced by each repellent. Irritancy tests were carried out to compare the flight response (time to first take-off, or FT) to increasing concentrations of repellents (2 – 7%) and at five distances from the treated surface (0 – 40 mm). DEET had an insecticidal effect at 7% (KDt50 = 9.7 min; CL50 = 1165 mg/m2). Relative to an untreated control, DEET was an irritant at 2% (RI = 12.3).

#### **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** |
| Repellent | Skin – Human application | MecDEET Solution  (DEET, 19 % w/w) | *Ixodes ricinus* (sheep tick)  Nymph stage | Laboratory test according to OPPTS 810.3700 Insect Repellents for Human Skin and Outdoor Premises.  Product applied on one forearm of each volunteer, leaving the lowest 5 cm near the wrist untreated. The arm was held vertically (with the fingertips or palm placed on a horizontal surface) and a tick was placed on the untreated skin 1 cm below the repellent border and observed fora maximum of 3 min. | 10 volunteers (5 men and 5 women).  The test lasted for 7 hours post application, with 10 ticks tested per hour and per volunteer (5 ticks every 30 minutes).  Between the 30-min test periods, ticks to be tested were screened for activity on the untreated control arm of the same volunteer. Only ticks that walked up and crossed the second mark (limit of the treated area on the treated arm) within the given time period of 3 minutes were further used on the treated arm.  Temperature : 21.2 ± 0.8°C  Relative humidity 36.1 ± 3.4%  Dose of product 1.67 µL/cm². | The effect investigated was the repellency of the product. A tick is considered as repelled if it not crosses into the treated area, or if it crawls into the treated area but immediately turns back or falls off.  Efficacy period: the period after application during which ≥90% of the ticks were repelled.  The product MecDEET Solution showed an efficacy period of 5 hours.  R.I = 1 | Büchel K. (2014) |
| Repellent | Skin – Human application | MecDEET Solution  (DEET, 19 % w/w) | *Culex quinquefasciatus*, *Aedes aegypti*,  Adult stage | Laboratory test.  Arm-in-cage study.  The product was sprayed on the forearm. Beginning one hour after treatment a sleeve with an opening of 3.1 x 8.0 cm (approx. 25 cm²) is fastened around the arm in such a way that the opening is positioned completely over the treated area. The edges of the opening of the sleeve have been also treated with the test material (200 µl so 8µl/cm²) in a width of approx. 1 cm to prevent bites from the edge. The areas above the sleeves are protected by cloth a proboscis cannot penetrate; hands are protected by latex gloves.  The biting activity of an untreated volunteer's forearm was tested in the same method. The time in seconds to achieve 10 bites on the untreated forearm was monitored.  The treated forearm was inserted into the cage for 5 minutes every hour until inefficacy considered as the first bite followed by a second one within one test interval or within one hour. | 1000 insects in each cage (mixed sex, approx. 500 females), 5 volunteers for each test organism.  Ambient conditions in testing chamber were maintained during the period of testing at a temperature of 25°C, a relative humidity of 40-55%.  Dose of the product: 1.67µL/cm², | Study not acceptable  Results are biased by the use of the treated sleeve.  R.I = 3  Mean CPT:  *C. quinquefasciatus*: 8 h  *Ae. aegypti*: 7.4 h | Lüpkes K.-H. (2014) |
| Repellent | Skin – Human application | MecDEET Solution  (DEET, 19 % w/w) | *Aedes albopictus*  Adult stage | Same protocol as above  Opening of the sleeve: 5 x 10 cm  Amount per treated sleeve (approx. 1 cm width = 34 cm²): 57 µl so 1.67 µL/cm².  The biting activity was tested on the second forearm of the same volunteer. The time in seconds to achieve 10 bites on the untreated forearm was monitored. | Same test system but with 10 volunteers instead of 5. | Study not acceptable  Results are biased by the use of the treated sleeve.  R.I = 3  Mean CPT: 7.9 h | Lüpkes K.-H. (2016) |
| Repellent | Skin – Human application | MecDEET Solution  (DEET, 19 % w/w) | *Culex quinquefasciatus*  Adult stage | Same protocol as above  Opening of the sleeve: 5 x 10 cm  Amount per treated sleeve (approx. 1 cm width = 34 cm²): 57 µl so 1.67 µL/cm².  The biting activity was tested on the second forearm of the same volunteer. The time in seconds to achieve 10 bites on the untreated forearm was monitored. | Same test system with 5 volunteers. | Study not acceptable  Results are biased by the use of the treated sleeve.  R.I = 3  Mean CPT: 6.4 h | Lüpkes K.-H. (2016) |
| Repellent | Fur - Dog application | MecDEET Solution  (DEET, 19 % w/w) | *Ixodes ricinus* (sheep tick)  Adult stage | Internal protocol  Small scissor marks, on the lateral aspects of the right carpal joint of each test animal, indicated of the boundary between the treated and untreated areas, and the maximum distance each tick would be expected to move from the paw towards the elbow.  Prior to the study a selection test was performed on study day -3 at which 10 ticks (male and female ticks) were applied to the dorsal surface of the paw on the right fore-limb. The parasites were observed to determine if they moved from the paw, along the leg, toward the elbow. Where at least 5 ticks placed on the paw, passed the upper scissor mark within three minutes of infestation, the animal passed the selection test.  As the selection test showed that ticks will move from the paw, up the leg to the upper 3cm mark, repellency of the control, by definition, was zero. | 5 ticks per animal. 6 dogs.  Two sprays of product were made, the first slightly above the carpal joint and the second slightly above the first. Following administration of the product, each animal was temporarily housed in an individual cage to prevent contamination of other animals and to allow constant observation of the animal to ensure the bandage applied to the paw to prevent contamination, remained in place.  5 ticks were placed on the animals paw. Data was analysed as follows: all ticks crawling onto the treated area and crossing the upper 3cm mark were considered “not repelled”. All other ticks were considered “repelled”.  Application rates vary from 0.46 to 5.44 mg/cm². | Study not acceptable  -Application rates are highly differing between the dogs,  -Negative control is not treated as the treated control.  Results are highly variable (0 to 5 hours protection time). Furthermore, the highest dose of 5.44 mg/cm² (that is the nearest to the claimed application rate) is ineffective.  R.I = 3 | Mc Kenna J. (2014) |

#### **Occurrence of resistance and resistance management**

Resistance to DEET is still uncertain as only one study on this subject has been identified yet.

In 2010, Stanczyk *et al.[[10]](#footnote-10)* wrote an article on some mosquitoes' insensitivity to DEET behaviour. Studies were performed in order to show insensitive characters. Over a group of *Aedes aegypti* females, 13% were identified as insensitive to DEET by using the “arm-in-cage test”. The breeding of these insensitive females with males which sensitivity is unknown led to an increase of insensitive individuals along generations. Second generation was composed of more than 50% of insensitive individuals.

This test shows that there might be a resistance effect against DEET and that the insensitivity to DEET would be a heritable trait. The way how resistance works is not clearly identified.

Two hypotheses are presented. There could be a mutation of DEET-sensitive ORNs (Olfactory Receptor Neurons) so that receptors could no longer recognize DEET. Another hypothesis is a mutation in the gene encoding for an odorant-binding protein in charge of transporting DEET to receptors. This mutation would lead to a smaller amount of DEET transported to ORNs and thus a lower sensitive response to this substance.

To ensure a satisfactory level of efficacy and avoid the development of resistance in susceptible insect populations, the following recommendations have to be implemented:

* Always read the label or leaflet before use and follow all the instructions provided.
* Respect the recommended application doses.
* The users should inform the registration holder if the treatment is ineffective.
* The authorization holder should report any observed resistance incidents to the Competent Authorities (CA) or other appointed bodies involved in resistance management.

Considering the importance of this active substance in vector control, the authorisation holder has to monitor the resistance phenomenon toward the active substance DEET. Results of the resistance monitoring must be submitted to the Competent Authorities (CA) or other appointed bodies involved in resistance management every 5 years.

#### **Evaluation of the label claims**

French competent authorities (FR CA) conclude that data presented in the dossier demonstrate that the product MECDEET Solution (DEET 19 % w/w) provides a protection time up to 5 hours when used on skin at the application rate of 1.67 µL/cm² against the tick *Ixodes ricinus[[11]](#footnote-11).*

Provided data are not sufficient to validate the efficacy on mosquitoes for human application and on ticks for dog application.

It is to be noted that no claim has been made concerning efficacy on tropical tick species, so the use of this product against ticks in tropical areas is not demonstrated.

It should also be precised on the label that protection time can be modified by sweating, water wash off, rubbing, high temperature (>30°C), wind velocity, etc.

The application rate validated is the following:

Ticks (Ixodes ricinus): 1.67 µL/cm2 of skin

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

The product MECDEET Solution has shown a sufficient efficacy for the uses proposed in the SPC (§2.1.4).

***Conditions of use linked to efficacy assessment***

* Always read the label or leaflet before use and follow all the instructions provided.
* Respect the recommended application doses.
* The user should inform the registration holder if the treatment is ineffective.
* In case of a concomitant use of the product with sunscreen), first apply the sunscreen and wait 20 minutes before the application of the product.
* The protection time is only indicative. Environmental factors (e.g. high temperature, wind velocity) can modify it.
* The product is not intended to be used in tropical areas.

### Risk assessment for human health

#### **Assessment of effects on Human Health**

***Skin corrosion and irritation***

| **Summary table of animal studies on skin corrosion /irritation** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Method, Guideline,**  **GLP status, Reliability** | **Species, Strain, Sex, No/group** | **Test substance, Dose levels,  Duration of exposure** | **Results** | **Remarks** | **Reference** |
| OECD 404  GLP | Albino rabbits (NZW)  Male  3/group | 0.5 ml of test substance (MecDEET)  Single dose  4 hours (semi-occlusive) | Neither oedema nor erythema was observed  Average score *(24, 48, 72h)*: 0 | No deviations | Beaphar, 2012a |

|  |  |
| --- | --- |
| **Conclusion used in Risk Assessment – Skin corrosion and irritation** | |
| Value/conclusion | Not irritant to the skin |
| Justification for the value/conclusion | The results of a study performed with MecDEET Solution do not trigger classification for skin irritation according to CLP |
| Classification of the product according to CLP | Not classified |

***Eye irritation***

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Summary table of animal studies on serious eye damage and eye irritation** | | | | | |
| **Method, Guideline**  **GLP status, Reliability** | **Species, Strain, Sex, No/group** | **Test substance, Dose levels, Duration of exposure** | **Results**  Average score for each rabbit *(24, 48, 72h)* | **Remarks** | **Reference** |
| OECD 405  GLP | Albino rabbits (NZW)  Male  3/group | 0.1 ml of test substance (MecDEET)  Single dose | Cornea : 0  Iritis : 0  Conjunctivae congestion : 1.67  Conjunctivae chemosis : 1.33 | No deviations | Beaphar, 2012b |

|  |  |
| --- | --- |
| **Conclusion used in Risk Assessment – Eye irritation** | |
| Value/conclusion | Not irritant to the eye |
| Justification for the value/conclusion | The results of a study performed with MecDEET Solution do not trigger classification for eye irritation according to CLP |
| Classification of the product according to CLP | Not classified |

***Respiratory tract irritation***

No studies of respiratory tract irritation are available and none are required. Inhalation exposure to sprays is likely to be negligible.. )

|  |  |
| --- | --- |
| **Conclusion used in the Risk Assessment – Respiratory tract irritation** | |
| Justification for the conclusion | Not a respiratory irritant |
| Classification of the product according to CLP | Not classified |

***Skin sensitization***

| **Summary table of animal studies on skin sensitisation** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Method, Guideline, GLP status, Reliability** | **Species, Strain, Sex, No/group** | **Test substance,**  **Dose levels,  Duration of exposure,**  **Route of exposure** | **Results** | **Remarks** | **Reference** |
| OECD 406  (GPMT)  GLP | Albino guinea pigs  Hartley  Female  10 (treated group)  5 (control group)  3 (preliminary test) | 0.1 ml of test substance (MecDEET)  Intradermal injections | No abnormalities were observed  % sensitising guinea pigs treated: 0% | No deviations | Beaphar, 2012c |

|  |  |
| --- | --- |
| **Conclusion used in Risk Assessment – Skin sensitisation** | |
| Value/conclusion | Not sensitizing |
| Justification for the value/conclusion | No evidence of skin sensitisation was seen in the guinea pig maximization test |
| Classification of the product according to CLP | Not classified |

***Respiratory sensitization (ADS)***

No studies of respiratory tract sensitisation are available and none are required. Inhalation exposure to sprays is likely to be negligible.

|  |  |
| --- | --- |
| **Conclusion** **used in Risk Assessment – Respiratory sensitisation** | |
| Value/conclusion | Not sensitizing |
| Justification for the value/conclusion |  |
| Classification of the product according to CLP | Not classified |

***Acute toxicity***

*Acute toxicity by oral route*

| **Summary table of animal studies on acute oral toxicity** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Method Guideline**  **GLP status, Reliability** | **Species, Strain, Sex, No/group** | **Test substance**  **Dose levels,**  **Type of administration** | **Signs of toxicity***)* | **Value LD50** | **Remarks** | **Reference** |
| OECD 425  GLP | Rats  Sprague-Dawley  Female  5/group | 20 ml/kg of test substance (MecDEET)  Oral gavage | Neither mortality nor mortalities observed | > 2000 mg/kg | No deviations | Beaphar, 2012d |

|  |  |
| --- | --- |
| **Value used in the Risk Assessment – Acute oral toxicity** | |
| Value | LD50 > 2000 mg/kg |
| Justification for the selected value | No evidence of acute toxicity by gavage was seen |
| Classification of the product according to CLP | Not classified |

*Acute toxicity by inhalation*

No acute toxicological study was performed with MECDEET Solution via the inhalation route. According to TNsG – human exposure to Biocidal products – Guidance on Exposure Estimation (European commission, 2002) the inhalation route can be excluded for the use outdoors, and use indoors only when it takes place in the summer, in situations where there is a high ventilation rate. On these grounds, the inhalation exposure to sprays is likely to be negligible.

Droplets are sprayed on skin or fur and exposure to inhalable vapours from the water-based formulation is considered negligible.

|  |  |
| --- | --- |
| **Value used in the Risk Assessment – Acute inhalation toxicity** | |
| Value | - |
| Justification for the selected value |  |
| Classification of the product according to CLP | Not classified |

*Acute toxicity by dermal route*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Summary table of animal studies on acute dermal toxicity** | | | | | | |
| **Method, Guideline,**  **GLP status,**  **Reliability** | **Species, strain, Sex, No/group** | **Test substance, Dose levels, Surface area** | **Signs of toxicity** | **Value LD50** | **Remarks** | **Reference** |
| OECD 402  GLP | Rats  Sprague-Dawley  5 males  5 females | 2000 mg/kg of test substance (MecDeet) | Neither mortality nor mortalities observed | > 2000 mg/kg | No deviations | Beaphar, 2012e |

|  |  |
| --- | --- |
| **Value used in the Risk Assessment – Acute dermal toxicity** | |
| Value | LD50 > 2000 mg/kg |
| Justification for the selected value | No evidence of acute toxicity by dermal application was seen |
| Classification of the product according to CLP | Not classified |

***Information on dermal absorption***

|  |  |
| --- | --- |
| **Value(s) used in the Risk Assessment – Dermal absorption** | |
| Substance | DEET |
| Value(s)\* | 20% |
| Justification for the selected value(s) | No new study was provided. However, dermal absorption value of 20% based on the study of dermally applied dose of DEET, either as a 15% (w/w) solution in ethanol is found in CAR of DEET (AR, 2010). This value is taken as a worst-case compared to the composition of MecDeet.  According to the CAR: “DEET is absorbed slowly, metabolized completely, and excreted rapidly when applied to human skin. Less than 9% (20% when corrected for total recovery) of a dermally applied dose of DEET, either as a 15% (w/w) solution in ethanol or as the undiluted technical grade material, is absorbed through the skin during an 8-hour exposure period as demonstrated by urine samples collected over 5 days following application.”  Moreover, ethanol is a solvent known to enhance dermal absorption, compared to water solution (OECD Guidance, 2010). Therefore, since the tested concentration (15% (w/w) DEET) is lower than the concentration of MecDeet (19% (w/w) DEET) and that the tested formulation contains ethanol (enhancer of the dermal absorption), the read across is considered as a worst-case. |

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

MECDEET Solution does not contain any substance of concern.

#### **Exposure assessment**

MECDEET Solution is intended to be applied on human skin as a mosquito and tick repellant (adults and children). Since the product is formulated as a ready-for-use product, no dilution or other preparation is necessary.

MECDEET Solution is also intended to be applied on dog fur as a tick repellant. The user (Non-professional adult) is exposed when applying MECDEET Solution on the dog and spreading it on the animal body. Both pet-owner(s) and children may be exposed by stroking the fur of the dog after application.

***Human exposure***

**Inhalation exposure:**

MECDEET Solution will be applied by spraying. In this context an exposure by inhalation could be considered. According to consumer spraying model 2 for trigger spray, the user will be exposed to 35.9 mg of product /m3 during few minutes when he will be exposed to 10.5 g of product on skin with a dermal absorption of 20 %. Furthermore, MECDEET Solution is not expected to generate particles which are deposited in tracheobronchial and alveolar regions; therefore the respirable fraction could be considered negligible.

**Oral exposure:**

Oral exposure to MECDEET Solution, especially by hand-to-mouth transfer, is not expected to be a significant and regular route of exposure. Moreover, the product MECDEET Solution contains the active substance DEET and also a co-formulant (denatonium benzoate), which are both known to act as strong deterrents for ingestion.

In this context, a reverse scenario calculation was included to determine the surface of the hands which could be mouthed without risk for human health. This scenario was assessed as an acute exposure.

**Dermal exposure:**

This route is the main route of exposure as the product is directly applied on the skin.The exposures of a person applying MECDEET Solution on him or herself and of a person who applies the product on another person are considered.

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

**Scenario 1 & 2:**

| **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** |
| Inhalation | n.a. | n.a. | Negligible | n.a. | n.a. | Negligible |
| Dermal | n.a. | n.a. | Yes | n.a. | n.a. | No |
| Oral | n.a. | n.a. | No | n.a. | n.a. | Yes |

**Scenario 3 & 4:**

| **Summary table: relevant paths of human exposure** | | |
| --- | --- | --- |
| **Exposure path** | **Primary (direct) exposure** | **Secondary (indirect) exposure** |
| Inhalation | Negligible | Negligible |
| Dermal | Yes | Yes |
| Oral | Yes | Yes |

***List of scenarios***

| **Summary table: scenarios** | | | |
| --- | --- | --- | --- |
| **Scenario number** | **Scenario** | **Primary or secondary exposure**  **Description of scenario** | **Exposed group** |
| 1. | Application by spraying on skin | **Primary exposure, dermal**  The product is spread on the exposed area of human skin. In order to mimic a systemic exposure for consumer, an internal dose of DEET (in mg/kg b.w./day) is calculated from a dose of product first applied on skin and then absorbed. | Non-professional (adults and children) |
| 2. | Hand-to-mouth behaviour | **Secondary exposure, oral**  The product is accidentally ingested following hand-to-mouth behaviour. A reverse scenario is performed to calculate the surface of hands to mouth to reach the acute AEL. | Non professional  (adults and children) |
| 3. | Application by spraying on dog skin by the user | **Primary exposure, oral and dermal**  The product is spread on the exposed area of dog skin. It is considered that the product is administrated by an adult only. Accidental dermal and oral exposure is considered when the product comes into contact with the user’s skin and transferred to the mouth. | Non-professional  Adult |
| 4. | Post-application on dog skin - Hand-to-mouth behaviour | **Secondary exposure, oral and dermal**  The product is accidentally ingested following hand-to-mouth behaviour or comes into contact with children. | Non-professional  Children |

***Industrial exposure***

No industrial exposure is foreseen. MECDEET Solution is an insect repellent containing 19% DEET as active substance and is intended to be used by adult and child. Therefore the assessment of industrial exposure is not relevant.

***Professional exposure***

No professional exposure is foreseen. MECDEET Solution is an insect repellent containing 19% DEET as active substance and is intended to be used by adult and child. Therefore the assessment of professional exposure is not relevant.

***Non-professional exposure***

*Scenario [1] Application by spraying on skin*

| **Description of Scenario [1]** | | | |
| --- | --- | --- | --- |
| It is considered that the exposure of the person spraying the product is covered by the exposure to the product he applies on his skin.  The exposure by dermal route to MecDEET Solution can be calculated according to the following equation:  where:  ID Internal dose (mg/kg b.w./day)  ARp Average dose of product applied on skin (mg/cm²)  CDEET Average concentration of substance in product (%)  BS Body surface exposed to the product (cm²)  DA Dermal absorption (%)  N Number of product application per day (/day)  BW Body weight (kg)  This equation can be applied to adults and to children.  ARp, CDEET, Dermal absorption and N remain the same, body parameters (such as body surface exposed to the product and body weight) vary according to age range.  The body parameters are issued from HEEG opinion 17 and US EPA exposure factor Handbook.  The product is not intended to be applied on the total body surface, according to CG-16 **,** the treated surface area considering light clothing is of 64% of the body.  No protection factor is taken into account. | | | |
|  | Parameters | Value | Reference |
| Tier 1 | Average dose of product applied on skin (mg/cm²) | 1.67 | Applicant data |
| Average concentration of substance in product (% w/w) | 19.59% w/w | Applicant data |
| Body surface exposed to the product (cm²) | See Table below | Heeg opinion 17 and US EPA exposure factor Handbook |
| Dermal absorption (%) | 20% | CAR DEET (AR, 2010) |
| Number of product applications per day (/day) | 2 (adult and children > 12 years old)  1 (children < 12 years old) | Applicant data |
| Body weight (kg) | See Table below | Heeg opinion 17 and US EPA exposure factor Handbook |

***Exposure estimates for 1 or 2 application(s)***

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Population group**  **(application)** | **Body surface area cm2** | **Body weight (kg)** | **Mass of applied product (mg)** | **Mass of applied active substance (g)** | **Mass of absorbed active substance (g)** | **Estimated dermal uptake  (mg a.s./kg bw)** |
| **Treated surface area: 64% of body** | | | | | | |
| Adult  (2) | 10624 | 60 | 17795 | 6.972 | 1.394 | 23.24 |
| Adult  (1) | 10624 | 60 | 17795 | 3.486 | 0.697 | 11.62 |
| Children  (6-11 years-old)  (1) | 5888 | 23.9 | 9862 | 1.932 | 0.386 | 16.17 |
| Children  (3-6 years-old)  (1) | 4352 | 15.8 | 7290 | 1.428 | 0.286 | 18.08 |
| Children  (2-3 years-old)  (1) | 3584 | 12.4 | 6003 | 1.176 | 0.235 | 18.97 |
| Children  (1-2 years-old)  (1) | 3072 | 10 | 5146 | 1.008 | 0.202 | 20.16 |
| Toddler  (6-12 mouth)  (1) | 2624 | 8 | 4395 | 0.861 | 0.172 | 21.53 |

**Further information and considerations on scenario [1]**

None.

**Combined scenarios**

Not relevant as it was stated in the CAR that systemic effect from dermal route and oral route will lead to separated effects.

**Monitoring data**

None.

***Exposure of the general public***

*Scenario [2] Hand-to-mouth behaviour*

| **Description of Scenario [2]** | | | |
| --- | --- | --- | --- |
| Consumers may be incidentally exposed orally to MecDEET Solution *via* hand-to-mouth behaviour. Even if the product contains a bittering agent, so a reverse scenario calculation was included. | | | |
|  | Parameters | Value | Reference |
| Tier 1 | Short-term AEL (mg/kg bw/day) | 0.75 | CAR DEET (AR, 2010) |
| Average dose of product applied on skin (mg/cm²) | 1.67 | Applicant data |
| Average concentration of substance in product (% w/w) | 19.59% w/w | Applicant data |
| Hands surface exposed to the product (cm²) | See Table below | Heeg opinion 17 and US EPA exposure factor Handbook |
| Transfer from hand to mouth (%) | 100% | Default |
| Oral absorption (%) | 100% | Default |
| Body weight | See Table below | Heeg opinion 17 and US EPA exposure factor Handbook |

**Calculations for Scenario [2]**

| **Summary table: systemic exposure from non-professional uses** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Population group**  **(application)** | **Surface of one hand (cm2)** | **Body weight**  **(kg)** | **Dose of product to eat to reach the AEL short-term (mg)** | **Skin surface area to put in the mouth to reach the AEL short-term (cm2)** | **% hand surface area to put in the mouth to reach the AEL short-term** |
| Adult  1 application on skin | 410 | 60 | 45.0 | 137.1 | 33.4% |
| Adult  2 applications on skin | 410 | 60 | 45.0 | 68.6 | 16.7% |
| Child (6-11 years-old) 1 application on skin | 213.9 | 23.9 | 17.9 | 54.6 | 25.5% |
| Child (3-6 years-old) 1 application on skin | 207.4 | 15.8 | 11.9 | 36.1 | 17.4% |
| Child (1-2 years-old) 1 application on skin | 148.4 | 12.4 | 9.3 | 28.3 | 19.1% |
| Toddler (1-2 years-old)  1 application on skin | 115.2 | 10 | 7.5 | 22.9 | 19.8% |
| Toddler (6-12 mouth)  1 application on skin | 98.4 | 8 | 6.0 | 18.3 | 18.6% |

**Further information and considerations on scenario [2]**

None.

**Combined scenarios**

Not relevant as it was stated in the CAR that systemic effect from dermal route and oral route will lead to separated effects.

**Monitoring data**

None.

***Pet-owner(s) exposure***

*Scenario [3] Application by spraying on dog skin by the user*

| **Description of Scenario [3]** | | | |
| --- | --- | --- | --- |
| The exposure by dermal route to MECDEET Solution can be calculated according to the following equations:  Dermal:  Oral (Hand-to-mouth):  where:  PDE Potential Dermal exposure (mg/kg bw/day)  POE Potential Oral exposure (mg/kg bw/day)  AR Application rate (mg)  FA Fraction of the AR available as transferable residue  DA Dermal absorption (%)  OA Oral absoprtion (%)  BW Body weight (60 kg)  Default values come from the Guideline on user safety of topically administered veterinary medicinal products (EMA/CVMP/SWP/721059/2014). Calculation of AR is taken for large dogs as a worst-case (see in Dog exposure: AR = ). | | | |
|  | Parameters | Value | Reference |
| Tier 1 | Application rate on large dog (mg) | 9660 | Efficacy data |
| Fraction of the AR available as transferable residue (dermal) | 0.1 | Default |
| Fraction of the AR available as transferable residue (oral) | 0.01 | Default |
| Body weight (adult) (kg) | 60 | Default |

**Calculations for Scenario [3]**

|  |  |  |  |
| --- | --- | --- | --- |
| **Dermal exposure scenario** | **Application rate (mg)** | **Dermal exposure  (mg/kg bw/day)** | **Potential dermal exposure  (mg/kg bw/day)** |
| Adult | 9 660 | 16.10 | 3.22 |

|  |  |  |  |
| --- | --- | --- | --- |
| **Oral exposure scenario** | **Application rate (mg)** | **Oral exposure  (mg/kg bw/day)** | **Potential oral exposure  (mg/kg bw/day)** |
| Adult | 9 660 | 1.61 | 1.61 |

**Further information and considerations on scenario [3]**

None.

**Combined scenarios**

Not relevant as it was stated in the CAR that systemic effect from dermal route and oral route will lead to separated effects.

**Monitoring data**

None.

*Scenario [4] Post-application on dog skin - Hand-to-mouth behaviour*

| **Description of Scenario [4]** | | | |
| --- | --- | --- | --- |
| Consumers may be incidentally exposed orally to MecDEET Solution *via* hand-to-mouth behaviour. Even if the product contains a bittering agent, calculation was included according to the following equations:  Dermal:  where:  TR Transferable Residue (mg/cm²)  AR Application Rate (mg)  FAR Fraction of the Application Rate available as transferable residue  SAanimal Surface Area of the animal (cm²)  PDE Potential Dermal exposure (mg)  SAcontact Surface area of a child in contact with the animal per day (cm²)  DA Dermal absorption (%)  BW Body weight (kg)  Oral (Hand-to-mouth):  where:  HR Hand Residue loading (mg/cm²)  DE Dermal exposure (mg)  Fh Fraction of total dermal exposure expected to be on the hands  SAh Surface Area of both hands of a child  POE Potential Oral exposure due to hand-to-mouth contact (mg/kg bw/day)  SAm Surface Area mouthed (cm²)  HTM Hand-to-Mouth contacts per day (/day)  HIM Hand-into-Mouth contact  OA Oral absoprtion (%)  BW Body weight (kg)  Default values come from the Guideline on user safety of topically administered veterinary medicinal products (EMA/CVMP/SWP/721059/2014). Calculation of AR is taken for large dogs as a worst-case (see in Dog exposure: AR = ). | | | |
|  | Parameters | Value | Reference |
| Tier 1 | Application rate on large dog (mg) | 9660 | Efficacy data |
| Fraction of the Application Rate (FAR) (acute exposure) | 0.15 | Default |
| Surface Area of the animal (SAanimal) (large dog) (cm²) | 9862 | Merck Veterinary Manual – BSA equation |
| Surface area of a child in contact with dog (SAcontact) (cm²) | 1790 | Default |
| Dermal absorption (%) | 20% | CAR DEET (AR, 2010) |
| Fraction of total DE on hands (Fh)  (270/1790 cm²) | 0.15 | Default |
| Surface Area of both hands (SAh) (cm²) | 270 | Default |
| Surface Area mouthed (SAm)  (2 fingers) (cm²) | 7 | Default |
| Hand-to-Mouth contacts (HTM) (/day) | 20 | Default |
| Hand-into-Mouth contact (HIM) | 0.4 | Default |
| Oral absorption (%) | 100% | Default |
| Body weight (child 2-3 year old) (kg) | 12.5 | Default |

**Calculations for Scenario [4]**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Dermal exposure scenario** | **Application rate (mg)** | **Transferable Residue (mg/cm²)** | **Dermal exposure  (mg/kg bw/day)** | **Potential dermal exposure (mg/kg bw/day)** |
| Child  (2-3 year old) | 9660 | 0.15 | 21.04 | 4.21 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Oral exposure scenario** | **Dermal exposure (mg/day)** | **Hand Residue loading (mg/cm²)** | **Oral exposure hand-to-mouth (mg/kg bw/day)** | **Potential oral exposure (mg/kg bw/day)** |
| Child  (2-3 year old) | 263 | 0.15 | 0.655 | 0.65 |

**Further information and considerations on scenario [4]**

None.

**Combined scenarios**

Not relevant as it was stated in the CAR that systemic effect from dermal route and oral route will lead to separated effects.

**Monitoring data**

None.

***Dietary exposure***

As regards the intended use of the product MECDEET SOLUTION on dog by spraying, no contamination of food is expected.

Nevertheless, regarding the intended use on human skin a contamination of food cannot be excluded. As a consequence, a dietary risk assessment is proposed in framework of this dossier.

Residue definitions

DEET (N,N-diEthyl-m-Toluamide) is the only active substance considers for the biocidal product MECDEET SOLUTION. The parent compound, DEET (N,N-diEthyl-m-Toluamide) was the only compound considered relevant regarding the dietary exposure.

*List of scenarios*

| **Summary table of main representative dietary exposure scenarios** | | | |
| --- | --- | --- | --- |
| **Scenario number** | **Type of use1** | **Description of scenario** | **Subject of exposure2** |
| 1. | General public | Contamination of food with contact of palm of treated hands | All kind of food |

1 e.g. animal husbandry, food industry, professional use, residential use.

2 e.g. chicken, milk, beer

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

DEET (N,N-diEthyl-m-Toluamide) is not known to be used in other areas.

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

Regarding the intended use of the product MECDEET SOLUTION, no livestock exposure to DEET (N,N-diEthyl-m-Toluamide) is expected.

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

The product MECDEET SOLUTION is only intended as non-professional use.

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

**Scenario 1**

Scenario 1 was performed for toddler, children and adult considering reference values mentioned in HEEG opinion 17[[12]](#footnote-12).

The scenario is not considered relevant for infant (<1 year), as the diet of infant consists mainly of milk and puree food, the contamination from hand to food is very limited.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | toddler  1 - 2 years | Child  2-3 years | Child  3-6 years | Child  6-11 years | Adult |
| body weight (kg) | 10 | 12 | 16 | 23,9 | 60 |
| hands (palms and back of both hands) (cm2) | 230,4 | 297 | 415 | 427,8 | 820 |

This biocidal product is intended only for children > 2 years and adults, for a use until 2 applications per day for adult. So, the exposure of children, adults and also for toddlers is estimated in framework of this dossier.

To estimate dietary exposure, the following assumption and reference values were used:

|  |  |
| --- | --- |
| Ratio surface factor of the palm compared to whole hand | 0.5 |
| transfer factor (hand to food) in % | 100% |
| transfer factor (food to mouth) in % | 100% |
| handwash after use (i.e rinsing factor)[[13]](#footnote-13) | 3 (considering that this recommendation could not be applicable and regarding the practical use, this factor is considered not relevant for children) |

Considering the intended use of MECDEET SOLUTION, its concentration of DEET, and the reference values mentioned above, the exposure was estimated as:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Product application rate (mg product/cm²) (effective) | 1.67 | | | | |
| Concentration (a.s in % w/w in the product) | 19 | | | | |
| Applicated active substance (mg a.s/cm²) (effective) | 0,317 | | | | |
| age | Toddler  1-2 years | Child  2-3 years | Child  3-6 years | Child  6-11 years | adult |
| hands (palms and back of both hands) (cm2) | 230 | 297 | 415 | 428 | 820 |
| Intended number of application  (evaluated) | 0 (1 and 2) | 1 (2) | 1 (2) | 1 (2) | 2 |
| Ratio surface factor of the palm compared to whole hand | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| exposure per application (transfered a.s in mg) | 37 | 47 | 66 | 66 | 130 |
| transfer factor (hand to food) in % | 100 | 100 | 100 | 100 | 100 |
| transfer factor (food to mouth) in % | 100 | 100 | 100 | 100 | 100 |
| ingested a.s in mg and per application | 0 | **47** | **66** | **66** | 130 |
| **total ingested a.s in mg** | (37 or 73) | (94) | (132) | (136) | **260** |
| Body weight in kg | 10 | 12 | 16 | 23.9 | 60 |
| Exposure per application in mg a.s/kg b.w./day | 0 | **3.9** | **4.1** | **2.8** | 2.2 |
| **Total exposure in mg a.s/kg b.w./day** | (3.7 or 7.3) | (7.9) | (8.2) | (5.7) | **4.3** |
| handwash after use (i.e rinsing factor) | nr | nr | nr | nr | 3 |
| **Total exposure in mg a.s/kg b.w./day including hand washing** | **-** | **-** | **-** | **-** | **1.43** |

nr: Not relevant

The hand washing factor is not considered appropriated for children especially regarding the practical use: it appears most relevant to recommend to *not treat the hands of children* than to recommend *children hands application* followed *with hands washing.*

**Conclusion**

As regards the intended use of the product MECDEET SOLUTION on dog by spraying, no contamination of food is expected.

Considering the intended use on human skin of MECDEET SOLUTION, and based on the assumptions and the reference values used, an estimation of dietary exposure for toddler, children and adults was performed. These estimations are considered as a worst case using the assumption that all the active substance from the palm hands will be ingested. A rinsing factor of 3 is considered relevant regarding the label recommendation “Wash hands before handling food” (this factor is not considered appropriated for children regarding recommendation applicability and practical use).

#### **Risk characterisation for human health**

Reference values to be used in Risk Characterisation

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Reference** | **Study** | **NOAEL (LOAEL)** | **AF1** | **Correction for (oral/dermal) absorption** | **Value** |
| AEL short-term | 8-week study (dogs, oral, capsule) | 75 mg/kg bw/day | 100 | 100% | 0.75 mg/kg bw/day |
| AEL medium-term | 90 day study (rat, dermal) | 1000 mg/kg bw/day | 100 | 82% | 8.2 mg/kg bw/day |
| ARfD | Not applicable | | | | |
| ADI | Not applicable | | | | |

1 AF 10x10 for inter- and intraspecies.

**Maximum residue limits or equivalent**

Residue definitions

Residue definition is established as DEET (N,N-diEthyl-m-Toluamide).

|  |  |  |  |
| --- | --- | --- | --- |
| **MRLs or other relevant reference values** | **Reference** | **Relevant commodities** | **Value** |
| ARfD | AELacute (8-week oral study in dogs: NOAEL of 75 mg/kg/day divided by a standard assessment factor of 100) (AR, 2010) | DEET | 0.75 mg/kg/day |
| ADI | Not considered necessary regarding the intended uses |  |  |

As DEET is not use in plant protection area, no MRLs are set on crop commodities. However a default MRL of 0.01\* mg/kg related to analytical method available could be used for monitoring purpose.

***Risk for industrial users***

No exposure is foreseen.

***Risk for professional users***

No exposure is foreseen.

***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] application on human skin - treated surface area : 64% of body\*** | | | | | | |
| Adult  2 applications | 1 | 1000 | 8.2 | 23.24 | **283%** | **No** |
| Adult  1 application | 1 | 1000 | 8.2 | 11.62 | **142%** | **No** |
| Child (6-11 years-old) 1 application | 1 | 1000 | 8.2 | 16.17 | **197%** | **No** |
| Child (3-6 years-old) 1 application | 1 | 1000 | 8.2 | 18.08 | **220%** | **No** |
| Child (1-2 years-old) 1 application | 1 | 1000 | 8.2 | 18.97 | **231%** | **No** |
| Toddler (1-2 years-old)  1 application | 1 | 1000 | 8.2 | 20.16 | **246%** | **No** |
| Toddler (6-12 mouth)  1 application | 1 | 1000 | 8.2 | 21.53 | **263%** | **No** |

*\*In the last update (WG V 2017) of HeadHoc recommendation 11, the treated surface area was refined from 64% to 55%. Even considering this value the risk is still not acceptable.*

| **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 [3] application on dog fur** | | | | | | |
| Adult  1 application  **Dermal exposure** | 1 | 1000 | 8.2 | 3.22 | 39 % | Yes |
| Adult  1 application  **Oral exposure** | 1 | 75 | 0.75 | 1.61 | **215 %** | **No** |

**Combined scenarios**

No combined exposure is foreseen.

**Local effects**

No need to consider local effects separately.

**Conclusion**

Considering that 64 %[[14]](#footnote-14) of the body is exposed (Head-hoc recommendation n°11), no use for human is acceptable. Based on standard agreed scenarios, conditions of article 19.1.b) iii) are not met for this product.

The risk for pet owner during application is acceptable only for dermal exposure.

**Authorisation based on article 19 (5) in France:**

In France, it is considered that restricting the uses of PT19 to some parts of the body is applicable. Hence additional RMM can be added, in case the product shall be authorized according to article 19(5).

The assessment below take into consideration a restriction on the surface to be treated (head + ¾ arms + hands + ½ legs).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Population group**  **(application)** | **Body surface area cm2** | **Body weight (kg)** | **Mass of applied product (mg)** | **Mass of applied active substance (g)** | **Mass of absorbed active substance (g)** | **Estimated dermal uptake  (mg a.s./kg bw)** |
| **Treated surface area:** **head + ¾ arms + hands + ½ legs** | | | | | | |
| Adult  (2) | 6297.5 | 60 | 10548.38 | 4.133 | 0.827 | 13.78 |
| Adult  (1) | 6297.5 | 60 | 10548.38 | 2.066 | 0.413 | 6.89 |
| Children  (6-11 years-old)  (1) | 3279.8 | 23.9 | 5493.70 | 1.076 | 0.215 | 9.01 |
| Children  (3-6 years-old)  (1) | 2985.2 | 15.8 | 5000.32 | 0.980 | 0.196 | 12.40 |
| Children  (2-3 years-old)  (1) | 2237.2 | 12.4 | 3747.42 | 0.734 | 0.147 | 11.84 |
| Children  (1-2 years-old)  (1) | 1707.2 | 10 | 2859.49 | 0.560 | 0.112 | 11.20 |
| Toddler  (6-12 mouth)  (1) | 1498.6 | 8 | 2510.09 | 0.492 | 0.098 | 12.29 |

| **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] application on human skin - treated surface area : head + ¾ arm + hands + ½ legs** | | | | | | |
| Adult  2 applications | 1 | 1000 | 8.2 | 13.78 | **168 %** | **No** |
| Adult  1 application | 1 | 1000 | 8.2 | 6.89 | 84 % | Yes |
| Child (6-11 years-old) 1 application | 1 | 1000 | 8.2 | 9.01 | **110 %** | **No\*** |
| Child (3-6 years-old) 1 application | 1 | 1000 | 8.2 | 12.40 | **151 %** | **No** |
| Child (1-2 years-old) 1 application | 1 | 1000 | 8.2 | 11.84 | **144 %** | **No** |
| Toddler (1-2 years-old)  1 application | 1 | 1000 | 8.2 | 11.20 | **137 %** | **No** |
| Toddler (6-12 mouth)  1 application | 1 | 1000 | 8.2 | 12.29 | **150 %** | **No** |

*\*Since the applicant recommends to not applying the product on child’s hand and that the product has to be applied by an adult, a refinement of the exposure was performed excluding the application on the hands of the child. The hands represent 13% of the treated body surface. This refinement was performed when a mitigation measure (reduction of number of application) or an unacceptable risk are observed.*

*Hence, the assessment has been reviewed considering the restriction “do not apply on children hands”.*

*The risk is therefore acceptable for one application per day for children (6 and 11 years old only):*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **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] application on human skin – treated surface area head + ¾ arm + hands + ½ legs** | | | | | | |
| Child (6-11 years-old) 1 application | 2 | 1000 | 8.2 | 7.83 | 96 % | Yes |
| Child (3-6 years-old) 1 application | 2 | 1000 | 8.2 | 10.68 | **130%** | **No** |

* *For* Adult (> 12 y.o) the use is acceptable if the product is applied to face, neck, hands, ¾ arms, ½ legs and feet , once per day only
* *For* children (>6 to 11 years old) the use is acceptable if the product is applied to face, neck, ¾ arms, ½ legs and feet once per day only

For the 125 mL and 200 mL bottles equipped with a nozzle delivering 0.185 g product /stroke, the corresponding application rates expressed as number of strokes is given in the following table:

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | head | | | per 3/4 arm | | | per hand | | | per 1/2 leg | | |
|  | surface (cm²) | product quantity (g) | stroke number (125 and 200 ml) | surface (cm²) | product quantity (g) | stroke number (125 and 200 ml) | surface (cm²) | product quantity (g) | stroke number (125 and 200 ml) | surface (cm²) | product quantity (g) | stroke number (125 and 200 ml) |
| Adult | 1110 | 1,9 | 10 | 851 | 1,4 | 8 | 410 | 0,7 | 4 | 1333 | 2,2 | 12 |
| Children (6-11 years-old) | 529 | 0,9 | 5 | 476 | 0,8 | 4 | 213,9 | 0,4 | 2 | 685 | 1,1 | 6 |

***Risk for the general public***

**Systemic effects**

| **Task/**  **Scenario** | **Skin surface area to put in the mouth to reach the AEL (cm²)** | **% hand surface area to put in the mouth to reach the AEL** | **Acceptable**  **(yes/no)** |
| --- | --- | --- | --- |
| **Scenario [2] Hand-to-mouth behaviour** | | | |
| Adult  1 application on skin | 137.1 | 33.4% | Yes |
| Adult  2 applications on skin | 68.6 | 16.7% | Yes |
| Child (6-11 years-old) 1 application on skin | 54.6 | 25.5% | Yes |
| Child (3-6 years-old) 1 application on skin | 36.1 | 17.4% | Yes |
| Child (1-2 years-old) 1 application on skin | 28.3 | 19.1% | Yes |
| Toddler (1-2 years-old)  1 application on skin | 22.9 | 19.8% | Yes |
| Toddler (6-12 mouth)  1 application on skin | 18.3 | 18.6% | Yes |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Task/**  **Scenario** | **Tier** | **Systemic NOAEL**  **mg/kg bw/d** | **AEL**  **mg/kg bw/d** | **Estimated uptake**  **mg/kg bw/d** | **Estimated uptake/ AEL**  **(%)** | **Acceptable**  **(yes/no)** |
| **Scenario [4] Post-application Hand-to-mouth behaviour after contact with dog fur** | | | | | | |
| Children  **Dermal exposure** | 1 | 1000 | 8.2 | 4.21 | 51 % | Yes |
| Children  **Oral exposure** | 1 | 75 | 0.75 | 0.65 | 87 % | Yes |

**Combined scenarios**

No combined exposure if foreseen.

**Local effects**

No need to consider local effects separately.

**Conclusion**

No unacceptable risk is identified for secondary exposure of general public.

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

Not relevant.

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

As regards the intended use of the product MECDEET SOLUTION on dogs by spraying, no contamination of food is expected.

Considering the exposure estimated for the intended use on skin of MECDEET SOLUTION, and the ARfD proposed for DEET, the following dietary risk assessments were performed:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| age | Toddler  1-2 years | Child  2-3 years | Child  3-6 years | Child  6-11 years | adult |
| Exposure for **1** application in mg a.s/kg b.w./day | 0 | **3.9** | **4.1** | **2.8** | (2.2) |
| Exposure for **2** applications in mg a.s/kg b.w./day | (3.7 or 7.3) | (7.9) | (8.2) | (5.7) | **4.3** |
| ARfD (mg a.s/kg b.w./day ) | 0.75 | 0.75 | 0.75 | 0.75 | 0.75 |
| % of ARfD for **1** application |  | **524** | **549** | **379** | (289) |
| % of ARfD for **2** applications | (487 or 975) | (1047) | (1097) | (757) | 578 |
| % of ARfD for **1** application including hand washing | nr | nr | nr | nr | **96** |
| % of ARfD for **2** applications including hand washing | **-** | **-** | **-** | **-** | 193 |

nr: not relevant

The hand washing factor is not considered appropriated for children specially regarding the practical use: it appears most relevant to recommend to *not treat the hands of children* than to recommend *children hands application* followed *with hands washing.*

**Conclusion**

As regards the intended use of the product MECDEET SOLUTION on dog by spraying, no contamination of food is expected.

Considering the intended use on human skin of MECDEET SOLUTION and based on the assumption and the reference values used, a dietary risk was identified for toddler and for children with a single application per day (nevertheless a primary risk was already identified), and for adult with 2 applications per day. However, no dietary risk for adults with **1 application per day** (instead 2 applications) considering hand washing factor.

As a consequence the following label recommendations are proposed:

* “Do not apply more than once a day”
* “Wash hands before handling food”
* “Do not apply directly on or near food, feed or drinks, or on surfaces or utensils likely to be in direct contact with food, feed and drinks”.
* “To prevent contamination of food, avoid contact of treated skin with food”.

Moreover a co-formulant (denatonium benzoate) is a strong deterrent contained in MECDEET SOLUTION to limit any ingestion of this biocide product.

### Risk assessment for animal health

#### **Exposure assessment**

***Dog exposure***

MECDEET Solution is intended to be applied on dog fur as a tick repellant. Since the product is formulated as a ready-for-use product, no dilution or other preparation is necessary.

**Identification of main paths of dog exposure towards active substance from its use in biocidal product**

| **Summary table: relevant paths of dog exposure** | | |
| --- | --- | --- |
| **Exposure path** | **Primary (direct) exposure** | **Secondary (indirect) exposure** |
| Inhalation | Negligible | Negligible |
| Dermal | Yes | No |
| Oral | No | Yes |

***List of scenarios***

| **Summary table: scenarios** | | | |
| --- | --- | --- | --- |
| **Scenario number** | **Scenario** | **Primary or secondary exposure**  **Description of scenario** | **Exposed group** |
| 1. | Application by spraying on dog fur | Primary exposure, dermal  The product is spread on the exposed area of dog skin. In order to mimic a systemic exposure for dogs, an internal dose of DEET (in mg/kg b.w./day) is calculated from a dose of product first applied on skin and then absorbed. | Dogs |
| 2. | Licking and chewing behaviour | Secondary exposure, oral  The product is accidentally ingested by licking the fur. | Dogs |

*Scenario [1] Application by spraying on dog fur*

| **Description of Scenario [1]** | | | |
| --- | --- | --- | --- |
| The exposure by dermal route to MecDEET Solution can be calculated according to the following equations:  where Km dogs = 10.1  where:  ID Internal dose (mg/kg b.w./day)  ARp Average dose of product applied on skin (mg/cm²)  CDEET Average concentration of substance in product (%)  BSA Body surface area exposed to the product (m²)  DA Dermal absorption (%)  N Number of product application per day (/day)  BW Body weight (kg)  ARp, CDEET, Dermal absorption and N remain the same, body parameters (such as body surface area and body weight) vary according to the dog profile.  No protection factor is taken into account. | | | |
|  | Parameters | Value | Reference |
| Tier 1 | Average dose of product applied on skin (mg/cm²) | 5 | Efficacy/applicant data |
| Average concentration of substance in product | 19% w/w | Applicant data |
| Body surface area (m²) | See Table below | Merck Veterinary Manual- BSA equation |
| Dermal absorption (%) | 20 | Applicant data |
| Number of product applications per day (/day) | 1 | Applicant data |
| Body weight (kg) | See Table below | Applicant data |

***Exposure estimitate for 1 application***

|  |  |  |  |
| --- | --- | --- | --- |
| **Dog profile** | **Weight (kg)** | **BSA (m²)** | **Estimated dermal uptake (ID)**  **(mg/kg b.w./day)** |
| Small dog | 7.5 | 0.390 | 98.70 |
| Medium dog | 15 | 0.620 | 78.52 |
| Large dog / Large dog + | 30 | 0.986 | 62.46 |

**Calculations for Scenario [1]**

| **Summary table: systemic exposure from dog uses** | | | | |
| --- | --- | --- | --- | --- |
| **Dog profile** | **Estimated inhalation uptake** | **Estimated dermal uptake** | **Estimated oral uptake** | **Estimated total uptake** |
| Small dog | n.a. | 98.70 | n.a. | 101.76 |
| Medium dog | n.a. | 78.52 | n.a. | 80.96 |
| Large dog / Large dog + | n.a. | 62.46 | n.a. | 64.40 |

**Further information and considerations on scenario**

None.

*Scenario [2] Licking and chewing behaviour*

| **Description of Scenario [2]** | | | |
| --- | --- | --- | --- |
| Dogs may be incidentally exposed orally to MecDEET Solution bylicking or chewing its fur. A worst-case scenario oral exposure not taking into account the efficacy of a bittering agent is performed according to the following equations:  where Km dogs = 10.1  where:  ID Internal dose (mg/kg b.w./day)  ARp Average dose of product applied on skin (mg/cm²)  CDEET Average concentration of substance in product (%)  BSA Body surface area exposed to the product (m²)  DO Oral absorption (%)  Ig Ingested fraction (%)  N Number of product application per day (/day)  BW Body weight (kg)  ARp, CDEET, oral absorption, ingested fraction and N remain the same, body parameters (such as body surface area and body weight) vary according to the dog profile. | | | |
|  | Parameters | Value | Reference |
| Tier 1 | Average dose of product applied on skin (mg/cm²) | 5 | Efficacy/Applicant data |
| Average concentration of substance in product | 19.59% w/w | Applicant data |
| Body surface area (m²) | See Table below | Merck Veterinary Manual |
| Ingested fraction | 9% | Applicant data |
| Oral absorption | 100% | Default |
| Number of product applications per day (/day) | 1 | Applicant data |
| Body weight | See Table below | Applicant data |

**Calculations for Scenario [2]**

|  |  |  |  |
| --- | --- | --- | --- |
| **Dog profile** | **Weight (kg)** | **BSA (m²)** | **Estimated oral uptake (ID)**  **(mg/kg b.w./day)** |
| Small dog | 7.5 | 0.390 | 45.79 |
| Medium dog | 15 | 0.620 | 36.43 |
| Large dog / Large dog + | 30 | 0.986 | 28.98 |

**Further information and considerations on scenario [2]**

When applying the product on the dog, the dog can lick its fur. However the normal licking behavior of a dog is limited to specific area of the fur. Ingested fraction was determined by the applicant considering that the most common areas are the lower part of the front legs and the 4 paws. In order to determine the surface area of the dog legs, it is considered that the dog body surface area is distributed proportionally to the body surface area of a human. According to the HEEG, 2013 values, the hands, the lower arms and the feet surface areas of a human represents 16-18% of the total body surface area.  
The dog is mainly licking the side of the legs and paws easily accessible (top side of the paws and front side of the legs), so only 50% of the total surface of the lower part of the front legs and the 4 paws.

As a default value, applicant proposed that the dog is licking 9% (18%x50%) of the product applied on the fur.

RMS disagree with this factor because it is calculated from human value and do not consider the frequency of licking and chewing behaviour (which must be depending of different causes, such as irritation or parasites for example) and the other parts of the body that a dog could reach (such as chest, hips or tail). This value was considered as a first tier and kept in the dossier as with this underestimated value risk are unacceptable.

**Combined scenarios**

Not relevant as it was stated in the CAR that systemic effect from dermal route and oral route will lead to separated effects.

**Monitoring data**

None.

#### **Risk characterisation for dog**

Reference values to be used in Risk Characterisation

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Reference** | **Study** | **NOAEL (LOAEL)** | **AF1** | **Correction for (oral/dermal) absorption** | **Value** |
| AEL oral | 8-week study (dogs, oral, capsule) | 75 mg/kg bw/day | 10 | 100% | 7.5 mg/kg bw/day |
| AEL dermal | 90 day study (rat, dermal) | 100 mg/kg bw/day | 100 | 82% | 8.2 mg/kg bw/day |
| ARfD | Not applicable | | | | |
| ADI | Not applicable | | | | |

1 AF 10 for intraspecies for AEL oral. AF 10x10 for inter- and intraspecies for AEL dermal.

**Systemic effects: dermal exposure**

|  |  |  |  |
| --- | --- | --- | --- |
| **Task/**  **Scenario** | **Estimated dermal uptake**  **(mg/kg b.w./day)** | **Estimated uptake/ AEL**  **(%)\*** | **Acceptable**  **(yes/no)** |
| Small dog | 101.76 | **1241** | **No** |
| Medium dog | 80.96 | **987** | **No** |
| Large dog / Large dog + | 64.40 | **785** | **No** |

*\*AEL of 7.5 mg/kg b.w./day is used (based on NOAEL of 75 mg/kg bw/day in a 8-week study on dog, 1 dose/day, based on clinical signs of neurotoxicity, body weight reduction. The 8-week study was terminated after 5 days.*

**Systemic effects: oral exposure**

|  |  |  |  |
| --- | --- | --- | --- |
| **Task/**  **Scenario** | **Estimated dermal uptake**  **(mg/kg b.w./day)** | **Estimated uptake/ AEL**  **(%)\*** | **Acceptable**  **(yes/no)** |
| Small dog | 45.79 | **611** | **No** |
| Medium dog | 36.43 | **486** | **No** |
| Large dog / Large dog + | 28.98 | **386** | **No** |

*\*AEL of 7.5 mg/kg b.w./day is used (based on NOAEL of 75 mg/kg bw/day in a 8-week study on dog, 1 dose/day, based on clinical signs of neurotoxicity, body weight reduction. The 8-week study was terminated after 5 days.*

**Combined scenarios**

No combined exposure if foreseen.

**Local effects**

No need to consider local effects separately.

**Conclusion**

Unacceptable risk is identified for dog exposure.

### Risk assessment for the environment

No new data on the ecotoxicity, fate and behaviour or environmental exposure has been submitted for the product or for the active substance(s) compared to the Annex-I-CAR.

As the product contains no substance of concern exceptN,N-diethyl-*m*-toluamide (DEET)*,* it is considered that risks posed to environment following the use of MECDEET SOLUTION can adequately be assessed based on the evaluation conducted for the active substance. Therefore the exposure assessment is carried out with the data obtained from the active substance N,N-diethyl-m-toluamide (DEET) only*.*

#### **Fate and distribution in the environment of the active substance N,N-diethyl-m-toluamide (DEET)**

##### Degradation

###### Abiotic degradation

Hydrolysis in function of ph

According to the test OECD 111, DEET is considered stable to hydrolysis. It was concluded that the hydrolytic half-life (DT50) was above one year at environmentally relevant temperature at pH 4, 7 and 9. The hydrolytic degradation is deemed negligible.

Photolysis in water

Abiotic degradation of DEET through phototransformation in water is not expected to occur based on the UV-Vis absorption spectra of the substance.

Photolysis in soil

Not relevant for DEET according to the active substance CAR.

Photodegradation in air

The photo-oxidative degradation of DEET in air was estimated by a structural activity relationship (QSAR) method using the Atmospheric Oxidation Program v1.91 (AOPWIN) at 24h period and a hydroxyl radical concentration of 0.5 E06 mol/cm3. The estimated half-live for the hydroxyl reactions in air is 0.63 days or 15.2 hours. DEET has a low volatility (Henry’s law constant = 3.93 \* 10-3 Pa.m3.mol-1) and emissions to the air compartment are expected be low. Thus, an extensive accumulation of DEET in air and long range transport is unlikely.

###### Biotic degradation

Aquatic compartment

* Ready biodegradation / inherent biodegradation

According to the test OECD 301B submitted in the CAR of DEET, the substance is considered ready biodegradable (within 10-days window) since 83.8% is degraded in 28 days.

* Degradation in water/sediment system

No study on degradation in water/sediment system of DEET is submitted. It is accepted as DEET is ready biodegradable.

Degradation in STP

As DEET is ready biodegradable, no study on degradation in STP is required in the CAR.

Terrestrial compartment

No tests on degradation of DEET in soil have been submitted in the CAR as the substance is ready biodegradable and not directly emitted to soil.

##### Distribution

A study on adsorption/desorption using HPLC determination indicates that DEET has a Koc of 43.3 mL/g, suggesting that it is very mobile in soil and therefore could leach to the groundwater.

##### Accumulation

DEET has a log Pow of 2.4 and is not highly adsorptive. This indicates that DEET is not likely to bioaccumulate in aquatic or terrestrial species.

The aquatic and terrestrial BCF have been estimated using a linear Quantitative Structure Activity Relationship (QSAR) model and the log Pow for DEET.

**BCFfish = 22 L/kg**(according to TGDII Equation 74)

**BCFearthworm = 63.1 L/kg**(according to TGDIII 4.6)

These BCF values confirm the very low bioaccumulation potential of DEET in aquatic and terrestrial organisms.

##### Behaviour in air

The vapour pressure of DEET has been determined to be 0.23 Pa at 25°C. Furthermore, Henry’s law constant for DEET has been calculated to 3.93 \* 10-3 Pa.m3.mol-1 based on a water solubility of 11.2 g/L. In addition, DEET is expected to be quickly degraded by photo-oxidation, the atmospheric photochemical half-life was 15.2 hours (2.2.9.1.1.1.4). Based on these data, DEET is not expected to volatilise or persist in air.

#### **Effects on environmental organisms for active substance DEET**

The summary of information about the active substance DEET is carried out with the data from the Competent Authority Report (CAR) of DEET owned by the applicant McKenna, Long & Aldridge (Competent Authority Report According to Directive 98/8/EC, Active substance in Biocidal Products, N,N-diethyl-*m*-toluamide (DEET) CAS 134-62-3, Product Type 19 (Repellents), RMS Sweden, march 2010). No new ecotoxicological information on the active substance DEET has been submitted in the product dossier.

##### Aquatic compartment (including water, sediment and STP)

###### Aquatic organisms

Based on the results of acute toxicity studies, DEET is not very toxic to aquatic organisms. The EC/LC50 values for the tested organisms (*Oncorhynchus mykiss, Daphnia magna, and Pseudokirchneriella subcapitata)* are all in the same range (10-100 mg/L), although algae represented the most sensitive (ErC50 = 43 mg/L) of the three aquatic trophic levels tested. No long-term tests have been performed.

Table 1: Existing endpoints for the aquatic organisms- DEET

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Test item** | **Species** | **Guideline** | **Endpoints** | **Toxicity (mg as/L)** | **Reference** |
| ***Fish*** | | | | | |
| **DEET** | *Onchorhynchus mykiss* | OECD 203  Static conditions | LC50 – 96h | 971 | CAR DEET III‑A 7.4.1.(1) |
| ***Invertebrates*** | | | | | |
| **DEET** | *Daphnia magna* | U.S. EPA Ecol;Res; Series 660/375009; Standard methods for the Examination of Water and Wastewater (1980)  Static conditions | EC50 – 51h | 751 | CAR DEET III‑A 7.4.1.2(1) |
| ***Algae*** | | | | | |
| **DEET** | *Pseudokirchneriella subcapitata* | OECD 201  Static conditions | ErC50 – 96h  EbC50 – 72h | 431  17 | CAR DEET III‑A 7.4.1.3(1) |

1 Measured concentration

Additional endpoints: Not relevant

Justification of PNECwater

According to the TGD for Risk Assessment (2003), if only short-term toxicity data are available, an assessment factor of 1000 will be applied on the lowest L(E)C50 of the relevant available toxicity data. The PNECwater is derived from the ErC50 values (43 mg a.s./L) for *Pseudokirchneriella subcapitata* exposed to the active substance divided by an assessment factor of 1000. Therefore,

**PNECwater = 0.043 mg a.s./L**

###### Sediment dwelling organisms

According to the TGD, as the log Kow value of DEET is < 3 and the Koc values are < 500 L/kg, sediment effects assessment is not considered as relevant for this active substance. Nevertheless, the PNEC and the PEC values for sediment have been calculated using the equilibrium partitioning method, and the risk to the sediment will be the same as described for surface water. These calculations should be performed according to equation 72 in the TGD (2003):

**PNECsedEP = 0.0741 mg/kg wet weight sediment**

###### STP micro-organisms

DEET had only an inhibitory effect on aquatic microbial activity at concentration above 1000 mg/L (26.8% inhibition at the highest tested concentration, 1000 mg/l).

Table 2: Existing endpoints for the STP micro-organisms- DEET

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Test item** | **Guideline/Test method** | **Species/inoculums** | **Endpoint / type of test** | **Exposure design duration** | **Result [mg a.s./L]** | | | **reference** |
| EC20 | EC50 | EC80 |
| **DEET** | OECD 209; EEC Method C11 | Activated sludge | Inhibition of oxygen consumption | 3h | N.D.1 | >10002 | N.D. | CAR DEET A7.4.1.4 |

1 at 300 mg/l there was 13.8 % stimulation

2 at 1000 mg/l there was 26.8% inhibition

Additional endpoints: not relevant

Justification of PNECmicroorganisms

According to TGD for Risk Assessment (2003), considering the EC50 toxicity data, an assessment factor of 100 will be applied to derive the PNEC from the EC50 value for the activated sludge exposed to the product. Therefore,

**PNECSTP microorganisms = 10 mg/L**

##### Atmosphere

No data are available on the biotic effects in the atmosphere. The active substance DEET is not expected to be subject to long range air transport (half-life is less than 2d)**,** or contribute to global warming (although the substance has a vapour pressure higher than 0.01 Pa, the Henry´s law constant is low (3.93.10-3 Pa.m3/mol). DEET do not contribute to ozone depletion in the stratosphere (atmospheric lifetime is <<1year, and it does not contain Cl, Br or F substituents) or acidification (low AP (Acidification Potential) of 0.17).

##### Terrestrial compartment

No terrestrial toxicitytests were performed. DEET is not expected to reach the terrestrial environment in significant amounts, and because of a low log Kow, a low Koc and the substance being ready biodegradable, DEET is not likely to become accumulated in soil in large amounts. Nevertheless, PNECsoil has been calculated based on equilibrium partitioning method (EPM) and PNECwater. These calculations should be performed according to equation 72 in the TGD (2003):

**PNECsoil EPM = 0.0379 mg/kg wet weight soil**

##### Summary of PNECs of the active substance DEET

Table 3: Summary of PNECs of the active substance DEET

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Compartment** | **Species** | **Endpoint (mg DEET/L)** | **Safety factor** | **PNEC** |
| **(*Fresh*) Water** | *Pseudokirchneriella subcapitata* | ErC50=43 | 1000 | 0.043 mg /L |
| **Sediment** | EPM | - | - | 0.0741 mg /kg ww |
| **Microorganisms (STP)** | Activated sludge | EC50>1000 | 100 | 10 mg /L |
| **Soil** | EPM\* | - | - | 0.0379 mg /kg ww |

\* Equilibrium partitioning method

##### Non compartment specific effect relevant to the food chain

The low BCF values suggest that DEET has a low bioaccumulation potential. Therefore, no risk of secondary poisoning *via* ingestion of potentially contaminated food (*e g* earthworms or fish) by birds or mammals was identified. For the terrestrial compartment, the expected negligible exposure adds to this conclusion. No avian dietary tests were required. However, acute oral avian toxicity was investigated and LD50 was determined to 1375 mg/kg bw.

##### PBT and ED Assessment

DEET does not meet any of the criteria for Persistent, Bioaccumulative and Toxic (PBT) substances or the very Persistent, very Bioaccumulative (vPvB) category.

DEET is not known to cause endocrine disruption.

#### **Effects on environmental organisms for biocidal product**

The biocidal product MECDEET SOLUTION is different from the representative product evaluated in the framework of the Annex I inclusion of the active substance DEET ((Competent Authority Report According to Directive 98/8/EC, Active substance in Biocidal Products, N,N-diethyl-*m*-toluamide (DEET) CAS 134-62-3, Product Type 19 (Repellents), RMS Sweden, march 2010)).

The applicant did not provide ecotoxicological data about the biocidal product MECDEET SOLUTION. The risk assessment is based on the data obtained from the active substance DEET (McKenna, Long & Aldridge, Competent Authority Report According to Directive 98/8/EC, Active substance in Biocidal Products, N,N-diethyl-*m*-toluamide (DEET) CAS 134-62-3, Product Type 19 (Repellents), RMS Sweden, march 2010).

Denatonium benzoate is used in the biocidal product as bittering agent. This substance has no harmonized classification but is classified as Aquatic chronic 3 according to the MSDS. At the concentration used in MECDEET SOLUTION, the substance does not contribute to the classification of the biocidal product.

Therefore, FR CA considered that the effects of DEET outweigh those of the non-active components of the product and that the effects assessment for the product MECDEET SOLUTION can be extrapolated from the effects assessment of the active substance DEET.

##### Aquatic compartment (including water, sediment and STP)

###### Aquatic organisms

Refer to section 2.2.9.2.1.1

###### Sediment dwelling organisms

Refer to section 2.2.9.2.1.2

###### STP micro-organisms

Refer to section 2.2.9.2.1.3

###### Terrestrial compartment

Refer to section 2.2.9.2.3

###### Non compartment specific effect relevant to the food chain

Refer to section 2.2.9.2.5

#### **Environmental exposure assessment**

|  |
| --- |
| Please notice that the environmental exposure assessment (section 2.2.9.4) is reported as provided by the applicant. The FR CA position is presented in **green evaluation boxes at the end of each part of the environmental exposure section.**  Please note that risk assessment has been conducted with the pure active ingredient content (19 %) and not the technical grade (19.59%). Nevertheless, the conclusions remain unchanged considering the technical grade.  For information, some uses have not been validated for efficacy reasons (refer to section 2.2.6.7). |

##### Assessment of exposure to the environment

Environmental exposure towards N,N-diethyl-m-toluamide after application of MecDEET Solution is estimated in accordance with ECHA Guidance on Biocidal Products Regulation: Volume IV Environment Part B Risk Assessment (Version 1.0, April 2015) (ECHA, 2015b). This exposure assessment is based on recent evaluations of DEET containing biocides by the Board for the Authorisation of Plant Protection Products and Biocides, Ctgb (Ctgb, 2014).

Major emissions from the application of mosquito and tick repellents on human skin result from indoor showering or bathing with emission via the STP to surface water and sediment (waste phase). Emissions from indoor showering or bathing are not considered relevant for the use of MecDEET Solution on dog skin.

Direct emission to surface water and sediment can result from outdoor showering or bathing after application of the product on human or dog skin (waste phase) (Ctgb, 2014). In this assessment it is assumed that dogs swim as often as humans, and that the amount of product applied on dog skin is similar to the amount of product applied on human skin. Therefore the direction emission to the environment from the application on dog skin is included in the emission from the application on human skin.

Emission to fresh water is expected to be worst case. Therefore risk for the marine environment is considered covered by the freshwater risk assessment (Ctgb, 2014).

For the proposed applications emissions during the application phase and the service life of the products are also considered less relevant and these routes are therefore not assessed (Ctgb, 2014).

|  |
| --- |
| FR-CA: unlike the applicant, the exposure assessment is carried out according to the ESD PT19 (May 2015)[[15]](#footnote-15):  - Indirect emission towards the environment, via STP:  - spray on human skin and emission towards the wastewater through showering or bathing  - indoor spray on dog fur and emission towards the wastewater through cleaning of applicator and floor  - Direct emission towards the environment:  - spray on dog fur, outdoor use leading to direct contamination of soil  - emission due to swimmer using the repellent on skin |

##### Uses with indirect emission via STP

The water compartment (both inland and marine) is expected to be indirectly exposed to DEET mainly from STP effluents, and because of the physiochemical character of the substance, the emissions will continue to primarily remain in this compartment (supported by level III fugacity modelling; see Assessment Report of N,N-diethyl-m-toluamide (DEET), Product-type 19 prepared by Sweden (AR, 2010), cited by Ctgb (2014)). The most relevant environmental compartment of concern for DEET is therefore the aquatic (Ctgb, 2014).

A user survey study has been performed in the USA involving human use and exposure to insect repellents containing DEET (Boomsma and Parthasarathy, 1990, cited by Ctgb (2014)). This study is part of the data package for DEET and is presented in Doc III of the final CAR of DEET (AR, 2010). According to this user survey study, on average 1.2 g of active ingredient of a repellent containing 20% DEET is consumed per application, of which 0.9 g (75%) is applied to the skin and 0.3 g (25%) to the clothes. One can also assume some of the product to be “spilled” during application (a direct release to the air compartment) and absorbed by the skin during the “leave on phase”.

In Industrial Category (IC) 5 (Personal/domestic), Use Category (UC) 36 (odour agents), 5% of the applied amount (for substances having vapour pressure below 100 Pa) is assumed to be emitted to the air (Appendix 7 of BPR Guidance Volume IV, Part B, page 243 (ECHA, 2015b)).

This figure was therefore adopted by Ctgb, 2014. All absorbed DEET (6.4%) is assumed to be metabolized (and excreted primarily as urine metabolites). Therefore, the rest of the initially applied dose (88.7%) is assumed to be released to the STP (see Figure 1, extracted from Ctgb, 2014).

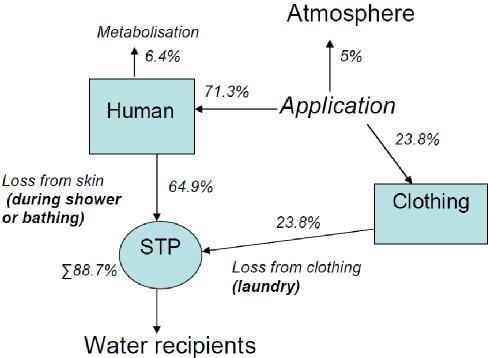


Figure 1:Assumed flows of DEET into the STP and environment. All percentages are referring to the initially applied dose (Ctgb, 2014).

Final environmental exposure will to a large extent depend on whether households are connected to STPs equipped with at least secondary (biological) treatment. Other efficient treatment processes include ozonation and PAC (Powdered Activated Carbon) addition, although these are more common in drinking water treatment3.

In the following sections, PECs (Predicted Environmental Concentration) are derived by using the draft Emission Scenario Document (ESD) for PT19 (repellents and attractants). These calculations are based on data on amount consumed by individuals. The TNsG on human exposure, part II, 2002 (European Commission, 2002) sets a default value for the amount of dermally applied repellent product to 6 g. Estimated PEC values are compared to monitoring data found in some recent publications in scientific peer reviewed journals (Ctgb, 2014).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FR-CA:  For the PEC calculation, the input data below are used, according to the Simple Treat (3.1) software to calculate the emission fraction after the STP:  Table 4: Parameters for the exposure assessment and Simple Treat outputs   |  |  |  |  | | --- | --- | --- | --- | | **Symbol** | **Parameter** | **Value** | **Unit** | | **INPUTS** | | | | |  | Characterisation of biodegradability | Readily biodegradable | [-] | | VP | Vapour pressure | 0.23 (at 25°C) | [Pa] | | Sol | Solubility in water | 11.2 | [g.L-1] | | Koc | Partition coefficient organic carbon-water | 43.3 | [L.kg-1] | | HENRY | Henry’s law constant | 3.93E-03 (at 25°C) | [Pa.m3.mol-1] | | **OUTPUTS** | | | | | FSTP air | Fraction of emission to air by STP | 8.15E-04 | [%] | | FSTP water | Fraction of emission to effluent by STP | 12.6 | [%] | | FSTP sludge | Fraction of emission to sludge by STP | 0.407 | [%] | | FSTP degrad | Fraction of emission degraded in the STP | 87 | [%] | | Ftotal | Total fractions | 100 | [%] | |

###### Spray on human skin

PECSTP and local concentrations in surface water (Clocalwater, or PECsurface water) were calculated using the draft ESD for PT19 and SimpleTreat 3.1 (a computer model developed by the Dutch National Institute of Public Health and Environment (RIVM) and used to simulate the fate of chemicals in wastewater treatment in the EU). The input parameters used in SimpleTreat 3.1 are listed in the table below.

Table 5: input parameters used in SimpleTreat 3.1

|  |  |  |
| --- | --- | --- |
| **Parameter** | **DEET**  **(N,N-diethyl-m-toluamide)** | **remarks** |
| Molecular weight (g/mole) | 191.27 | LoEP |
| Vapour pressure at test temperature (Pa) | 0.23 | LoEP |
| Test temperature vapour pressure (°C) | 25 | LoEP |
| Solubility at test temperature (mg/L) | 11200 | LoEP |
| Test temperature solubility (°C) | 25 | LoEP |
| Octanol-water partition coefficient (L/kg) as log Kow | 2.4 | LoEP |
| Organic carbon-water partition coefficient (L/kg) as Koc | 43.3 | LoEP |
| Henry constant (Pa x m3 x mol- 1) | 3.93x10-3 | LoEP |
| Rate constant for degradation in a STP (d-1) | 24 | Default value for readily  biodegradable substances |
| Half-life for biodegradation in fresh water at 12°C (days) | 15 | LoEP |

According to the calculation formula for emission rate to STP (cf. table 3-7 in draft ESD for PT19), Elocalwater (Emission rate to wastewater (standard STP), kg/d), i.e. the inflow of DEET to an STP during an emission episode, can be calculated.

If using the input values in the table below, Elocalwater is 1.05 kg/d for MecDEET Solution. This value is used as input for the PT19 scenario in SimpleTreat 3.1. The output of SimpleTreat 3.1 calculations is listed in the table below.

Table 6: output of SimpleTreat 3.1

|  |  |  |  |
| --- | --- | --- | --- |
| FSTP air | Fraction of emission to air by STP | 8,15E-04 | [%] |
| FSTP water | Fraction of emission to effluent by STP | 12,6 | [%] |
| FSTP sludge | Fraction of emission to sludge by STP | 0,407 | [%] |

Table 7: Input values used to estimate Elocalwater (Emission rate to wastewater) in accordance with the draft ESD for PT19.

|  |  |  |  |
| --- | --- | --- | --- |
| **Input**  **parameters** | **Explanation** | **Input value** | **Remark** |
| Nlocal | Number of inhabitants feeding one STP | 10000 | Default according to draft ESD PT19 and TGD Part II |
| Nappl | Number of applications per day | 1 | According to the list of intended uses, the product is applied once per day. |
| Finh | Fraction of inhabitants  using product | 0.37 | According to the final CAR for DEET 37% (Finh = 0.37) of the population is using any insect repellent (AR, 2010). |
| Fwater | Fraction released to  wastewater | 0.887 | See figure 1 |
| Qformappl | Consumption of product per application | 6 g | The TNsG on human exposure  (European Commission, 2002) sets a  default value for the amount of dermally applied repellent product  to 6 g |
| Cformweight | Amount of active  substance in product | 190 g/kg | i.e. 19% w/w |
| Fpenetr | Market share of  products applied for this purpose | 0.28 | According to the final CAR for DEET (AR,  2010) and cited by the Ctgb (2014).  (Default value in draft ESD for PT19 is 0.5.) |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FR-CA:  As claimed by the applicant and based on the efficacy data, the following application rates are used for the exposure assessment:   |  |  |  | | --- | --- | --- | | Human protection | 1.67 µL BP\*/cm2 | Twice a day | | Animal protection | 5 μl BP/cm2 | Once a day |   The use on human skin by spray leads to emission of DEET towards the environment via wastewater after bathing and showering. According to the CAR, a fraction of released to wastewater of 0.887 can be used for the calculation of the DEET emission via the STP. The efficient dose rate has been used in the risk assessment, following the harmonized exposure parameters of the ESD PT19, instead of the theoretical product use of 6 g/person proposed by the applicant. A treated area of human skin of 10 660 cm2 has been considered as a generic value according to the ESD, covering the head, arms, hands, legs and feet.  \* Biocidal product  Table 8: Emission calculation for the spray on human skin- STP   |  |  |  |  |  | | --- | --- | --- | --- | --- | | **Variable/parameter** | **Symbol** | **ESD approach** | **Unit** | **S/D/O/P** | | Number of inhabitants per STP | Nlocal | 10000 | [-] | D | | Number of application per day | Nappl | 2 | [d-1] | S | | Treated area of human skin | AREAskin | 10660 | [cm2/application] | D | | Fraction of inhabitants using product | Finh | 0.2 | [-] | D | | Fraction released to wastewater | Fwater | 0.887[[16]](#footnote-16) | [-] | D/S | | Consumption per application (per inhabitant) | Vformappl | 1.67E-06 | [L BP/cm²] | S | | Consumption per inhabitant per application | Vforminh | 1.78E-02 | [L BP/application] | S | | Amount of active substance in product | Cformvolume | 190 | [g.L-1] | S | | Market share | Fpenetr | 0.5 | [-] | D | | **Emission rate to wastewater** | **Elocalwater** | **6.00E+00** | **[kg.d-1]** | **O** | |

Aquatic compartment (surface water, sediment, STP)

The table below summarizes the concentrations in STP effluent as well as the PECs in surface water and sediment.

Table 9: PECSTP, PECsurface water and PECsediment for indirect emission to surface water and sediment via the STP due to body cleaning and washing of treated clothes.

|  |  |  |
| --- | --- | --- |
| PECSTP  (mg/L) | PECsurface water  (mg/L) | PECsediment  (mg/kg ww) |
| 6.62X10-2 | 6.62X10-3 | 1.14X10-2 |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FR-CA:  The PEC for the aquatic compartment following indirect release via the STP after human skin application, calculated according to the Biocidal Guidance Vol. IV, part B are presented below:  Table 10: PEC calculation for the aquatic compartment - Spray on human skin - STP emission   |  |  |  |  |  | | --- | --- | --- | --- | --- | | **Variable/parameter** | **Symbol** | **ESD approach** | **Unit** | **S/D/O/P** | | Emission rate to wastewater | Elocalwater | 6.00E+00 | [kg.d-1] | O | | Concentration in the untreated wastewater | Clocalinf | 3.00E+00 | [mg.L -1] | O | | **Concentration in the treated wastewater** | **PECSTP** | **3.78E-01** | **[mg.L-1]** | O | | **Local concentration in surface water** | **PEClocal water** | **3.78E-02** | **[mg.L-1]** | O |   As the PNEC sediment is derived by Equilibrium partitioning method (EPM) from the PNEC water, the risk ratios for surface water and sediment will be identical. Therefore no PEC values for sediment are derived. |

Atmospheric compartment

The active substance DEET is moderately volatile. The vapour pressure is 0.11 Pa at 20°C. A Henry’s law constant of 3.93x10-3 Pa m3 mol-1 is reported, confirming its relatively low volatility.

AOPWIN model calculation estimates that DEET in the atmosphere reacts with photochemically produced hydroxyl radicals in air, with a half-life of 0.634 days (24 hr day; 0.5x106 OH/cm3). This calculated half-life is below the trigger of < 2 days that is used as cut-off value to identify chemicals that could be of potential concern for with the potential for long-range transport through the atmosphere. As the substance unlikely shows significant long-range transport, it is considered of no concern for ozone depletion (Ctgb, 2014).

Criteria for the examination of environmental risks to air are not specified in the form of a numerical standard. Therefore, effects on air quality only are taken into account when adverse effects are foreseen. The assessment of potential impacts on air quality, yet, is aimed to minimize the risk for stratospheric ozone depletion. There are no indications that this substance contributes to depletion of the ozone layer and the compounds are furthermore not listed as ‘controlled substance’ listed in Annex I of Regulation (EC) No 1005/2009 of the European Parliament, the environmental risk to air is considered acceptable (Ctgb, 2014).

|  |
| --- |
| FR-CA: Not relevant, see 2.2.9.1.4 |

Terrestrial compartment (soil and groundwater)

The estimation of the local PECs for the terrestrial compartment includes soil and groundwater: PECsoil according to equation (55), chapter 2.3.8.5, EU TGD (EU, 2003):



In which:

Dair= aerial deposition flux per kg of soil, according to equation (52) of the TGD.

T= averaging time, according to Table 11 of the TGD

k= first order rate constant for removal from top soil, according to equation (56) of the

TGD.

Csoil(0)= initial concentration (after sludge application), according to equation (63) of the TGD.

PECporewater according to equation (67), chapter 2.3.8.5, EU TGD (EU, 2003) as a first worst-case estimation:



In which:

RHOsoil= bulk density of wet soil, according to equation (18) of the TGD.

Ksoil-water= soil-water partitioning coefficient, according to equation (24) of the TGD.

The estimation of releases to the soil compartment premises calculation of predicted concentrations of the active substance DEET in dry sewage sludge (Csludge) as part of active substance DEET load leaving a STP, which are calculated with SimpleTreat 3.1 (Appendix Ib). The input parameters used in equations (55) and (67) are listed in Appendix Ic.

The table below summarises the concentration in dry sewage sludge Csludge as well as the PECs in soil and porewater.

Table 11: Csludge, PECsoil and PECgroundwater for indirect emission to soil and groundwater due to body cleaning.

|  |  |  |  |
| --- | --- | --- | --- |
|  | Local soil | Local agricultural soil | Local grassland |
| Csludge (mg/kg) | 5.41 | | |
| PECsoil (µg/kg ww) | 5.61 | 1.76 | 0.71 |
| PECporewater soil (μg/L) | **6.36** | **1.99** | **0.79** |

The calculated PEC for porewater was addressed further by as the drinking water limit for groundwater of 0.1 μg/L was exceeded. PECgw for the nine FOCUS groundwater scenarios, as developed for plant protection products, were calculated. Model used, input data and assumptions are shown in Table 28. The overall assumption being that the only exposure route to groundwater is via the application of sludge from STPs.

Table 12: Summary of data used and assumptions made to calculate PECgroundwater for DEET in FOCUS scenarios (Ctgb, 2014).

|  |  |
| --- | --- |
| **Parameter** | **Value** |
| Model used: | FOCUS PEARL 4.4.4 |
| Years of simulation: | 26 (including 6 years “warming-up” period) |
| Application rate: | 0.027 kg/ha5 |
| Application method: | To the soil surface |
| Date of application: | 1 October annually for 20 years6 |
| Molar mass: | 191.3 g/mol |
| Vapour pressure: | 0.23 Pa (25°C) |
| Water solubility: | 11200 mg/L (25°C) |
| Kom: | 25.1 L/kg7 |
| Freundlich exponent 1/n: | 0.9 (FOCUS default) |
| DT50 soil | 30 days (12°C)8 |
| Coefficient for uptake in plants: | 0 (worst-case assumption) |

The resulting PECgw (as FOCUS standard output; 80th percentile annual average PECgw at 1 m depth) are shown in Table 29. These results show that the predicted groundwater concentrations of DEET following the intended use of this substance are <0.1 μg/L for all FOCUS scenarios.

Table 13: 80th percentile annual average PEC of DEET in groundwater (at 1 m depth) calculated for nine FOCUS scenarios, assuming application of sewage sludge from STP to land.

|  |  |
| --- | --- |
| **Scenario** | **PECgw, µg/L** |
| Châteaudun | <0.001 |
| Hamburg | <0.1 |
| Jokioinen | <0.01 |
| Kremsmünster | <0.01 |
| Okehampton | <0.1 |
| Piacenza | <0.1 |
| Porto | <0.1 |
| Sevilla | <0.001 |
| Thiva | <0.001 |

A report by Verhagen *et al* (2008; in Dutch) presents the results from screening the presence of 149 pesticides and some biocides in groundwater at 189 locations in the Netherlands in 2007. The monitoring data were collected by two provinces and two drinking water companies from the Southern part of the Netherlands.

The majority of the samples were taken during July-December. DEET was the substance that was found above the detection limit (0.01 μg/L) at the highest number of occasions (30%). In 189 samples from 189 groundwater monitoring points 57 samples had a concentration >0.01 ug/L, and out of these three samples (1.6%) were above the drinking water limit, i.e. > 0.1 ug/L (range was 0.36-1.48 μg/L). The report also referred to monitoring data from 2003 during which DEET was found above the detection limit in 5% of the samples, and in no sample concentrations >0.1 μg/L were measured (Ctgb, 2014).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FR-CA:  The PEC for the terrestrial compartment following indirect release via the STP after human skin application, calculated according to the Biocidal Guidance Vol. IV, part B are presented below (considering a Sludge rate of 790 kg/d):  Table 14: PEC calculation for the terrestrial compartment - Spray on human skin-STP emission   |  |  |  |  |  | | --- | --- | --- | --- | --- | | **Variable/parameter** | **Symbol** | **ESD approach** | **Unit** | **S/D/O/P** | | Emission rate to wastewater | Elocalwater | 6.00E+00 | [kg.d-1] | O | | Concentration in dry sewage sludge | Csludge | 3.09E+01 | [mg.kg-1] | O | | Concentration in agric. soil in first year at T0 | Csludge soil 1 (0) | 4.55E-02 | [mg.kg-1] | O | | Initial concentration in agric.soil after 10 years | C sludge soil 10 (0) | 4.55E-02 | [mg.kg-1] | O | | **Twa concentration in agric. soil after 10 years over 30 days** | **PEC soil** | **3.20E-02** | **[mg.kg-1]** | O | | Twa concentration in agric. soil after 10 years over 180 days | C sludge soil 10 (180) | 1.00E-02 | [mg.kg-1] | O | | **Concentration in porewater** | **PEC soil porewater** | **1.14E+01** | **[µg.L-1]** | O |   **Refinement of PEC groundwater using modeling with FOCUS Pearl 4.4.4**  As DEET concentrations in groundwater estimated in Tier I are higher than 0.1 µg/L, they are refined using the leaching model FOCUS-PEARL 4.4.4., which integrates transformation and dilution of the active substance in deeper soil layers.  Table 15: Summary of data used and assumptions made to calculate PECgw for DEET in FOCUS scenarios parameters   |  |  |  | | --- | --- | --- | |  | **Values for agricultural land** | **Values for grassland land** | | Model used | FOCUS PEARL 4.4.4. | FOCUS PEARL 4.4.4. | | Years of simulation | 26 (including 6 yrs "warming-up" period) | 26 (including 6 yrs "warming-up" period) | | Application rate | 5000 x Csludge x 10-6  **= 0.155 kg.ha-1** | 5000 x Csludge x 10-6  **= 0.0309 kg.ha-1** | | Application depth | 20 cm | 10 cm | | Date of application | one application per year, 20 days before crop emergence | 1 March 1901 | | Standard crop for arable land | Maize & Winter Cereals | Grass/alfalfa | | Molar mass | 191.3 g/mol | 191.3 g/mol | | Vapour pressure | 0.23 Pa, 25°C | 0.23 Pa, 25°C | | Water solubility | 11200 mg/L, 25°C | 11200 mg/L, 25°C | | Kom | 25.1 L/kg | 25.1 L/kg | | Freundlich exponent | 1 (FOCUS Default) | 1 (FOCUS Default) | | DT50soil | 30d, 12°C | 30d, 12°C | | Coefficient for uptake by plant | 0 | 0 | | Molar activation energy | 54 kJ.mol-1 | 54 kJ.mol-1 |   Table 16: 80th percentile annual average PEC of DEET in groundwater (at 1 m depth) calculated with FOCUS assuming application of sewage sludge from STP to agricultural land and grassland   |  |  |  | | --- | --- | --- | | **Scenario** | **PECGroundwater (µg/L) (µg DEET/L)** | | |  | **Maize** | **Grass/alfalfa** | | **Chateaudun** | 0.211983 | 0.020840 | | **Hamburg** | 0.587631 | 0.052402 | | **Jokioinen** | - | 0.041469 | | **Kremsmuenster** | 0.355553 | 0.027477 | | **Okehampton** | 0.649138 | 0.046074 | | **Piacenza** | 0.221098 | 0.044058 | | **Porto** | 0.054479 | 0.015752 | | **Sevilla** | 0.005677 | 0.003072 | | **Thiva** | 0.079784 | 0.002534 |   As the concentrations levels are still over the trigger value of 0.1 µL/L for the agricultural soil, further refinement is needed. A tonnage based approach as proposed in the CAR of the active substance is then applied.  **Tonnage based approach for PEC groundwater**  For this approach, modeling is based on the annual tonnage of DEET placed on the EU market as proposed in the CAR for the active substance inclusion covering all the products based on DEET at the EU level, given that it was verified that the annual tonnage of DEET placed on the French market (representing 3 EU regions) is covered by the EU tonnage considered in the CAR. This approach covers all the uses presented in the product dossier.  A tonnage approach has been favored for groundwater compared to a consumption approach for different reasons. The consumption approach represents a peak of release with worst case assumptions which can be considered realistic in case of daily emission to environmental compartments (surface water downstream the STP for instance). Nevertheless, sludge applied as a soil enrichment product is collected in the STP over weeks or months. This matter is stored and sometimes mixed with other additives (for instance during composting). However, no dilution or degradation can be taken into account in the exposure calculations without validated data. The actual assessment model probably overestimates the concentration of DEET in sludge at the time of land spreading considering the ready biodegradability property of the substance. It was therefore considered more relevant to follow a tonnage approach that allows taking into consideration a mean emission to the sludge which seems more realistic for exposure of groundwater.  The model used, input data and assumptions presented below are chosen according to DE proposals (Klein, 2011[[17]](#footnote-17)). Two representative crops for arable lands (maize and winter cereals) and one for grassland (grass/alfalfa) are investigated to estimate the potential leaching to groundwater. The overall assumption being that the only exposure route to groundwater is *via* the application of sludge from STPs.  Application rate is calculated from DEET concentration in dry sewage sludge proposed in the CAR (2.63 mg.kg-1dwt), and the maximum sewage sludge application of 5000 kg dry sludge.ha-1.yr-1 on arable land and 1000 kg dry sludge.ha-1.yr-1 on grassland (at a single event as suggested in the Biocidal Guidance Vol. IV, part B), leading to dose rates of 1.31.10-2 kg.ha-1.yr-1 and 2.63.10-3 kg.ha-1.yr-1 respectively. The DT50 soil value used is in accordance with EUSES/Biocidal Guidance Vol. IV, part B, for readily biodegradable substances (30 days at 12°C).  Table 16: Summary of data used and assumptions made to calculate PECgw for DEET in FOCUS scenarios parameters   |  |  |  | | --- | --- | --- | |  | **Values for arable land** | **Values for grassland land** | | Model used | FOCUS PEARL 4.4.4. | FOCUS PEARL 4.4.4. | | Years of simulation | 26 (including 6 yrs "warming-up" period) | 26 (including 6 yrs "warming-up" period) | | Application rate | **0.0131 kg.ha-1** | **0.00263 kg.ha-1** | | Application depth | 20 cm | 10 cm | | Date of application | one application per year, 20 days before crop emergence | 1 March 1901 | | Standard crop for arable land | Maize | Grass/alfalfa | | Molar mass | 191.3 g/mol | 191.3 g/mol | | Vapour pressure | 0.23 Pa, 25°C | 0.23 Pa, 25°C | | Water solubility | 11200 mg/L, 25°C | 11200 mg/L, 25°C | | Kom | 25.1 L/kg | 25.1 L/kg | | Freundlich exponent | 1 (FOCUS Default) | 1 (FOCUS Default) | | DT50soil | 30d, 12°C | 30d, 12°C | | Coefficient for uptake by plant | 0 | 0 | | Molar activation energy | 54 kJ.mol-1 | 54 kJ.mol-1 |   Results in the following table show that the predicted groundwater concentrations of DEET are below the threshold value of 0.1 µg.L-1 for all the tested conditions.  Table 16: 80th percentile annual average PEC of DEET in groundwater (at 1 m depth) calculated with FOCUS assuming application of sewage sludge from STP to agricultural land and grassland   |  |  |  |  | | --- | --- | --- | --- | | **Scenario** | **PECGroundwater (µg/L) (µg DEET/L)** | | | |  | **Maize** |  | **Grass/alfalfa** | | **Chateaudun** | 0.017916 |  | 0.001774 | | **Hamburg** | 0.049664 |  | 0.004460 | | **Jokioinen** | - |  | 0.003530 | | **Kremsmuenster** | 0.030050 |  | 0.002339 | | **Okehampton** | 0.054863 |  | 0.003922 | | **Piacenza** | 0.018686 |  | 0.003750 | | **Porto** | 0.004604 |  | 0.001341 | | **Sevilla** | 0.000480 |  | 0.000261 | | **Thiva** | 0.006743 |  | 0.000216 | |

Non-compartmental-specific exposure relevant to the food chain (secondary poisoning)

As the log Kow is < 3 (2.4), a risk for bioconcentration and biomagnification is not expected (conform the biomagnification trigger value proposed for Kow in the TGD).

As DEET is not bioaccumulative and the concentrations in surface water and soil are low, the risk for the primary and secondary poisoning is considered acceptable (Ctgb, 2014).

The risk characterisation for the environment is the comparison of the toxicity of the substance to the exposure estimates. Both aspects were already discussed in section 1 and 2, respectively, and only the relevant values are summarised below (Ctgb, 2014).

|  |
| --- |
| FR-CA: Not relevant, see 2.2.9.2.5 |

###### Indoor spray on dog fur

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FR-CA:  The emission scenario for spray use on dog fur was not assessed according to ESD PT19 approach by the applicant, despite a request by the FR-CA at the information request period.  According to the ESD PT19, spray repellents on dogs can be applied indoors. During the application, product may reach the indoor air, the applicator, the treated surface and the floor. For PT19, it was stated that only emission to the applicator and the floor will be discharged to STPs; either by washing clothes or by cleaning operations. The parameters for the emission calculations are presented in ESD PT19 p 40, in the tables 3-16 and 3-18.  For the worst case scenario, only the default values from the ESD PT19 are used.  To calculate the emission towards one STP, a fraction of inhabitants using this product on their dogs is used to refine the worst case scenario. Indeed, in the worst case scenario, one dog was considered in each of the 4000 houses linked to the STP and 100% of the dogs are considered to be treated with a repellent. In the realistic worst case, only 20% of dogs are considered treated by a repellent, as the value taken for application on human skin. This refined value is also supported by the percentage of dog owners defined in a French survey for 2016 (<http://www.facco.fr/-population-animale->) which is about 20 %.  **Table 17: Emission calculation for indoor spray on dog fur - STP emission**   |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | | **Variable/parameters** | **Symbol** | **Worst case** | **Realistic case** | **Type of data** | **Unit** | | **Emission due to application** |  |  |  |  |  | | Consumption per application | Vformappl | 5.00E-06 | 5.00E-06 | S | [L BP/cm²] | | Treated area of dog skin | AREAskin | 1.21E+04 | 1.21E+04 | D | cm² | | Amount of active substance in product | Cformvolume | 190 | 190 | S | [g.L-1] | | Number of application per day | Nappl | 1 | 1 | S/D | [-] | | Fraction emitted to applicator | Fapplication, applicator | 0.02 | 0.02 | D | [-] | | Fraction emitted to floor | Fapplication, floor | 0.11 | 0.11 | D | [-] | | Emission to applicator during the application step | Eappli, application | 2.30E-04 | 2.30E-04 | O | [kg.d-1] | | Emission to floor during the application step | Eappli,floor | 1.26E-03 | 1.26E-03 | O | [kg.d-1] | | **Emission due to cleaning** |  |  |  |  |  | | Fraction emitted to wastewater from applicator after after the application | Fapplicator, ww | 1 | 1 | D | [-] | | Fraction emitted to wastewater during the cleaning step | Fww | 1 | 1 | D | [-] | | Cleaning efficacy floor | Fce | 0.50 | 0.50 | D | [-] | | Cleaning efficacy clothes | Fce | 1 | 1 | D | [-] | | Number of houses contributing to the same sewage treatment plant | Nhouses | 4000 | 4000 | D | [-] | | Fraction of houses with a dog and using PT19 product | Finh | 1 | 0.2 | D | [-] | | Market share | Fpenetr | 0.5 | 0.5 | D | [-] | | Emission from applicator to wastewater during cleaning step | Eapplicator, ww | 2.30E-04 | 2.30E-04 | O | [kg.d-1] | | Emission from floor/treated to wastewater during the cleaning step | Etreated, ww | 6.32E-04 | 6.32E-04 | O | [kg.d-1] | | Combined emission from floor and applicator to wastewater during the cleaning step for one house | Eww | 8.62E-04 | 8.62E-04 | O | [kg.d-1] | | **Emission rate to wastewater** | **Elocalwater** | **1.72** | **0.34** | **O** | **[kg.d-1]** | |

Aquatic compartment (surface water, sediment, STP)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
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| FR-CA:  The PEC for the aquatic compartment following indirect release via the STP after indoor application on dogs, calculated according to the Biocidal Guidance Vol. IV, part B, are presented below:  Table 18: PEC calculation for the aquatic compartment- Dog fur- STP Emission   |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | **Variable/parameter** | | **Symbol** | | **Worst case** | | **Realistic case** | | **Unit** | | **S/D/O/P** | | **INPUT** |  | |  | |  | |  | |  | | | Emission rate to wastewater | | Elocalwater | | 1.72 | | 0.34 | | [kg.d-1] | | O | | **OUTPUT** |  | |  | |  | |  | |  | | | Concentration in the untreated wastewater | | Clocalinf | | 8.62E-01 | | 1.72E-01 | | [mg.L -1] | | O | | **Concentration in the treated wastewater** | | **PECSTP** | | 1.09E-01 | | 2.17E-02 | | **[mg.L-1]** | | O | | **Local concentration in surface water** | | **PEClocal water** | | 1.09E-02 | | 2.17E-03 | | **[mg.L-1]** | | O |   As the PNEC sediment is derived by EPM from the PNEC water, the risk ratios for surface water and sediment will be identical. Therefore no PEC values for sediment are derived. |

Atmospheric compartment

|  |
| --- |
| FR-CA: Not relevant, see 2.2.9.1.4 |

Terrestrial compartment (soil and groundwater)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FR-CA: The PEC for the terrestrial compartment following indirect release via the STP after indoor application on dogs, calculated according to the Biocidal Guidance Vol. IV, part B, are presented below. The refinement for groundwater presented in Table 15 and Table 16 also applies for this use.  Table 19: PEC calculation for the terrestrial compartment-Dog fur- STP emission   |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | **Variable/parameter** | | **Symbol** | | | **Worst case** | | **Realistic case** | **Unit** | | **S/D/O/P** | | **INPUT** |  | |  |  | |  | | |  | | | Emission rate to wastewater | | Elocalwater | | | 1.72 | | 0.34 | [kg.d-1] | | O | | **OUTPUT** |  | |  |  | |  | | |  | | | Concentration in dry sewage sludge | | Csludge | | | 8.88E+00 | | 1.78E+00 | [mg.kg-1] | | O | | Concentration in agric. soil in first year at T0 | | Csludge soil 1 (0) | | | 1.31E-02 | | 2.61E-03 | [mg.kg-1] | | O | | Initial concentration in agric.soil after 10 years | | C sludge soil 10 (0) | | | 1.31E-02 | | 2.61E-03 | [mg.kg-1] | | O | | **Twa concentration in agric. soil after 10 years over 30 days** | | **PEC soil** | | | 9.20E-03 | | 1.84E-03 | **[mg.kg-1]** | | O | | Twa concentration in agric. soil after 10 years over 180 days | | C sludge soil 10 (180) | | | 2.88E-03 | | 5.76E-04 | [mg.kg-1] | | O | | **Concentration in porewater** | | **PEC soil porewater** | | | 3.27E+00 | | 6.54E-01 | **[µg.L-1]** | | O | |

Non-compartmental-specific exposure relevant to the food chain (secondary poisoning)

|  |
| --- |
| FR-CA: Not relevant, see 2.2.9.2.5 |

###### Cumulative uses with releases via stp

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FR-CA:  The cumulative exposure for the indirect releases via the STP must be taken into account according to the uses claimed by the applicant. Indeed, there can be at the STP scale releases of DEET due to applications on human skin and also due to applications on dog fur.  If only the realistic cases for application on human skin and on dog fur are taken into account, PEC values for the environmental compartments are:  Table 20: Cumulative PEC for both human and dog uses leading to releases via STP   |  |  |  |  | | --- | --- | --- | --- | | **Variable/parameter** | **Symbol** | **Realistic case** | **Unit** | | Emission rate to wastewater from application on dog fur | Elocalwater dog | 0.34 | [kg.d-1] | | Emission rate to wastewater from application on human skin | Elocalwater hum | 6.00E+00 | [kg.d-1] | | Concentration in the untreated wastewater for human and dog uses (releases via STP) | Clocalinf | 3.17E+00 | [mg.L -1] | | **Concentration in the treated wastewater** | **PECSTP** | 4.00E-01 | **[mg.L-1]** | | **Local concentration in surface water** | **PEClocal water** | 4.00E-02 | **[mg.L-1]** | | **Local concentration in sediment** | **PEC local sed** | 6.89E-02 | **[mg.kg-1]** | | Concentration in dry sewage sludge | Csludge | 3.27E+01 | [mg.kg-1] | | Concentration in agric. soil in first year at T0 | Csludge soil 1 (0) | 4.81E-02 | [mg.kg-1] | | Initial concentration in agric.soil after 10 years | Csludge soil 10 (0) | 4.81E-02 | [mg.kg-1] | | **Twa concentration in agric. soil after 10 years over 30 days** | **PECsoil** | 3.39E-02 | **[mg.kg-1]** | | **Twa concentration in agric. soil after 10 years over 180 days** | **C sludge soil 10 (180)** | 1.06E-02 | **[mg.kg-1]** | | **Concentration in porewater** | **PEC soil porewater** | 1.20E+01 | **[µg.L-1]** | |

##### Uses with direct emission towards the environment

At the Technical Meeting I 2009 (Cited by Ctgb, 2014) several member states had questions about possible direct emissions due to swimming for these type of products. Germany presented a swimming scenario at TM II 2011 (draft CAR for lauric acid) and proposed to include this scenario in the ESD for PT19 which Germany has drafted (Cited by Ctgb, 2014). The draft ESD for PT19 which contains a modified swimming scenario when compared to the one applied in the draft CAR for lauric acid, has been distributed to Member States Competent Authorities at 18th September 2013 for consultation. Germany requested other member states to submit data on natural swimming lakes in order to revise the swimming scenario for inclusion in the draft ESD for PT19. The Netherlands has developed a swimming scenario based on data from the more isolated freshwater swimming lakes to which officially the function ‘swimming water’ is assigned and has submitted these data to Germany for inclusion in the ESD for PT19. The German ESD swimming scenario (Cited by Ctgb, 2014) is applied in the risk assessment for MecDEET Solution.

|  |
| --- |
| FR-CA: the exposure assessment is realized according to the ESD PT19 (May 2015)[[18]](#footnote-18). |

###### Direct emission due to outdoor spray on dog fur

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FR-CA:  Not assessed by the applicant but required according to the ESD PT19, the use of spray on dog outdoor can lead to direct emission on soil. For exposure assessment, the default values from the ESD PT19 are used, tables 3-9, 3-10 and 3-11.  Table 21: Emission calculation for the outdoor spray on dog fur - Direct emission scenario   |  |  |  |  |  | | --- | --- | --- | --- | --- | | **Variable/parameters** | **Symbol** | **ESD approach** | **Type of data** | Unit | | Consumption per application (per dog) | Qformappl | 5.00E-06 | P | [L BP/cm²] | | Number of application per day | Nappl | 1 | S/D | d-1 | | Amount of active substance in product | Cformvolume | 190 | S | [g.L-1] | | Treated area of dog skin | AREAskin | 1.21E+04 | D | cm² | | Fraction entering to soil | Fsoil | 0.1 | D | [-] | | Soil volume | Vsoil | 0.75 | D | m3 | | **Emission rate to soil** | **Elocalsoil** | **1.15E-03** | **O** | **kg/d** | |

Aquatic compartment (surface water, sediment, STP)

|  |
| --- |
| FR-CA:  Not relevant for this scenario according to the ESD PT19 |

Atmospheric compartment

|  |
| --- |
| FR-CA: Not relevant, see 2.2.9.1.4 |

Terrestrial compartment (soil and groundwater)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FR-CA:  The PEC calculations for the terrestrial compartment following direct release after outdoor application on dogs, calculated according to the ESD for PT19, are presented below:  Table 22: PEC calculation for the terrestrial compartment-Dog fur- Direct emission scenario   |  |  |  |  |  | | --- | --- | --- | --- | --- | | **Symbol** | **Parameter** | **ESD approach** |  | **Unit** | | Emission rate to wastewater | Elocalsoil | 1.15E-03 |  | kg/d | | Concentration in soil | PECsoil | 9.01E-01 |  | mg/kgwwt | | Predicted concentration in porewater | PECgw | Not relevant |  | µg/L | |

Non-compartmental-specific exposure relevant to the food chain (secondary poisoning)

|  |
| --- |
| FR-CA: Not relevant, see 2.2.9.2.5 |

###### Swimming scenario

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FR-CA:  When the product is applied on skin, there can be a release of DEET by swimmers in waterbodies. Two scenarios have to be taken into account: high infested area with a fraction of inhabitant using repellent of 0.1 (Finh), called high infested area scenario, and a scenario for low infested area with a Finh value of 0.02 as presented below:  Table 23: Emission calculation for the spray on human skin - Swimming scenario   |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | **Symbol** | **Variable/parameters** | | **High infested area** | **Low infested area** | **Type of data** | **Unit** | | Nlocal | Number of swimmers | | 1500 | 1500 | D | [-] | | AREAskin | Body surface |  | 10660 | 10660 | D | cm² | | Vformappl | Application |  | 1.67E-06 | 1.67E-06 | S | L BP/cm² | | Nappl | Number of application per day | | 1 | 1 | D | [d-1] | | Finh | Fraction of inhabitants using product | | 0.1 | 0.02 | P | [-] | | Fwater | Fraction released to water | | 0.887 | 0.887 | D | [-] | | Cformvolume | Amount of active substance in product | | 1.90E+02 | 1.90E+02 | S | [g.L-1] | | **Elocalwater** | **Emission rate to wastewater** | | **4.50E-01** | **9.00E-02** | **O** | **[kg.d-1]** | |

Aquatic compartment (surface water, sediment, STP)

The estimation of the local PECs for the aquatic compartment only includes surface water and sediment for the “swimming”-pathway because of direct entry of the biocide in the environment.

*ESD swimming scenario*

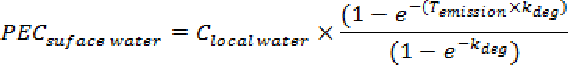
The development of the ‘swimming scenario’ is based on a proposal made by the Competent Authority Germany at TM II/2011, and the comments made thereafter by other Competent Authorities, and industry (Cited by Ctgb, 2014). A detailed description of the derivation of default parameter referring to the volume of the surface water body, the number of swimmers, and the swimming season is given in Appendix 6.4 of the draft ESD for PT19 (cited by the Ctgb, 2014). The average number of swimmers per day is set at 1500 per default in the draft ESD for PT19.

No information is available regarding the fraction of swimmers using an insect repellent. Surface water bodies are often located in forested areas where the occurrence of biting and sucking arthropods is likely. Furthermore, some surface water bodies have camping locations nearby and campers can be assumed to be equipped more often with an insect repellent than daily visitors of the lake. As a best guess it is assumed in the draft ESD for PT 19, that 2% of the swimmers use an insect repellent before entering the surface water body Visits of swimmers at Dutch fresh- and seawater sites lasted 41-79 minutes per occasion in 2007 and 2009 (Ctgb, 2014). It can be expected that during this time period treatment with a repellent will take place only once.

The fraction released to the surface water body is set to 1 per default. The volume of the water body is 1.2 million m3 per default.

The rate constant for biodegradation in surface water for DEET which is readily biodegradable is set to 0.047 d-1 according to Table 7 (TGD[[19]](#footnote-19) EU, 2003). Time-weighted average concentration of the repellent was calculated for an emission period of 91 days.

PECsurface water is calculated as:



In which:

Temission= the time of swimming during the year. This value is limited by the temperature of the   
air and the water, therefore it was estimated that swimming will take place for 1 hour a day on 91 days per year as a maximum limit.

Kdeg= the rate constant for the biodegradability. According to Table 7 of the TGD (EU, 2003) k = 0.047 d-1 for surface water as DEET is readily biodegradable. Formation of metabolites is considered as not relevant.

Clocal water= initial concentration of DEET released by swimmers, calculated as:



In which:

Nappl= 1 (see Table 22)

Qformappl= 6 g (see Table 22)

Cformweight= 190 g/kg (see Table 22)

Nswimmer= average number of swimmers per day, which is set at 1500 per default.

Fswim= fraction of swimmers which is swimming at the same day in one lake or pond while using the biocidal product, which is set at 0.02 per default.

Femitted= fraction released to the surface water body, which is set at 1 per default.

Vwaterbody= volume of the water body, which is set at 1.2 million m3 per default (90th percentile   
Netherlands & Germany).

The PECsediment was calculated with the equilibrium partitioning method according to equation (50) of the TGD (EU, 2003):



In which:

Ksusp-water= 1.9825 (calculated according to equation (24) of the TGD)

RHOsusp= 1150 (wet bulk density calculated according to equation (18) of the TGD)

The PECsurface water and PECsediment for direct emission to the aquatic environment due to swimming based on the DE swimming scenario presented in Ctgb (2014) are included in Table 24. Biodegradation of DEET in the water compartment has been taken into account for the PEC calculations.

**PECsurface water and PECsediment due to swimming based on the DE swimming scenario including biodegradation.**

|  |  |  |
| --- | --- | --- |
| Natural swimming areas | PECsurface water (mg/L)  6.12X10-4 | PECsediment (mg/kg ww)  1.06X10-3 |

**Exposure monitoring – data published in the open literature**

53

Publications in scientific peer reviewed journals regarding DEET concentrations in the environment were used to compare the calculated values with measured data.

Before making comparisons between measured and modelled data one needs to be aware of the uncertainty associated with measured values, due to temporal and spatial variation.

Temporal fluctuations are of special concern when it comes to PEC estimations of DEET; the highest values expected during peak bug season. There may also be geographical variations. These monitoring data should therefore only be regarded as examples of DEET concentrations found in order to evaluate the calculated PEC values, not as substitutes (Ctgb, 2014).

The highest surface freshwater concentration found in a study of 56 American streams was 1.1 μg/L, which is 4.5 times lower than the worst case Clocalwater of 0.005 mg/L, see Table 25.

A few data on DEET in American raw waste water influents (150 and 365 ng/L) have been found in the open literature (Snyder *et al*. 2007). These values are at least 1479 times lower than the lowest concentration in influent calculated (0.53 mg/L).

DEET concentrations in Norwegian and German STP effluents (10-60 ng/L and 130 ng/L respectively (Weigel *et al*, 2004)), are at least 538 times lower than what was estimated through model calculations (0.07 mg/L). The Norwegian data are from an STP without biological treatment whereas the German data are from an STP with biological treatment. The DEET concentrations found in the German influent was 0.21 μg/L, before the biological treatment step, which is more than 2571 times lower than estimated from the calculations (Ctgb, 2014).

|  |  |  |  |
| --- | --- | --- | --- |
| **Area information** | **Analytical information** | **Concentrations found** | **Reference** |
| **Seawater**  North Sea Sampling locations mostly coastal | Polymeric sorbent extraction + GC-MS LOQ: 26 pg/L  Sampling period: June-July 1998 2x10L samples at 5m depth 15 sampling locations | Highest values 1.09 and 1.06 ng/L respectively [found in the German Bight; (53°40.00’N; 06°25.00’E) and (54°15.00’N; 07°48.00’E)] DEET was detected in all but two samples. | Weigel *et al*. 2002. (cited by Ctgb, 2014) |
| **Seawater**  Tromsø Sound (Norway), (into which sewage is discharged) | Glass fibre filtration, sorbent extraction + GC/MS  LOQ: 0.20 ng/L Sampling period: 2002 (most samples taken in April, the rest in October) 2.5L samples.  12 sampling locations | Range: 0.4-13 ng/L (STP data: 10 and 60 ng/L in April and October respectively) | Weigel *et al*. 2004. (cited by Ctgb, 2014) |
| **Surface freshwater** Las Vegas Wash, a waterway receiving tertiary treated municipal effluent from the city of Las Vegas, NV. | Whole water (incl dissolved and particulate phases)  Solid Phase Extraction + LC/MS/MS  1L samples  3 replicates  Reporting level: 1.0 ng/L | Average: 40 ng/L | Vanderford *et al*., 2003. (cited by Ctgb, 2014) |
| **Surface freshwater** 56 streams across the USA, some bias to streams downstreams intense urbanization and livestock | Whole water (incl  dissolved and particulate phases)  Continuous Liquid- Liquid Extraction + GC/MS Sampling period: 2000 Reporting level: 40 ng/L4 Duplicate composite samples (from 4-6 vertical profiles) | Highest value: 1.1 μg/L (measured at urban site) Median concentration: 0.06 μg/L (all sites)  Frequency of detection: 73.2% | Kolpin *et al*., 2002 (cited by Ctgb, 2014) |

4 Reporting level: lowest concentration standard that could be quantitated reliably. Initially set to 0.04 μg/l, and then revised to 0.08 μg/l, but lower concentrations reported if GC/MS criteria (retention time and abundance of three characteristic ions in the same ratio as that of standard) were met. Sandström *et al*, 2005. (cited by Ctgb, 2014). Compared to monitoring data from STP influents/effluents all estimated values are conservative. Similarly, the estimated values were in the range of, or above the peak maximum measured concentration in fresh surface water (Ctgb, 2014).

DEET has been on the Dutch market for > 3 years (authorised since 1986). This period is sufficiently large to consider the market share to be established. DEET is included in the list of substances of concern relevant for surface water at drinking water abstraction points as established by VEWIN/CTGB. This list is based on monitoring data for eight Dutch drinking water abstraction periods and measured during period 2008-2012.

The active substance DEET was detected at several drinking water abstraction points in surface waters in the Netherlands. However exceeding of the drinking water limit occurred only occasionally (Ctgb, 2014). Based on the available data it can be concluded that the 90th percentile of the measurements over the period 2008-2012 is below the drinking water limit of 0.1 μg/L and for five out of eight drinking water abstraction points even below the detection limit of 0.02 μg/L, see Table below.

|  |  |  |  |
| --- | --- | --- | --- |
| **Abstraction point** | **Number of measurements above detection limit/ Number of measurements [n/N]** | **Number of measurements above drinking water limit/ Number of measurements**  **[n/N]** | **Overall 90th percentile [µg/L]** |
| Andijk | 0/52 | 0/52 | < d.l.\* |
| Nieuwegein | 8/65 | 0/65 | < d.l. |
| Amsterdam-Rijn kanaal (Nieuwersluis) | 21/52 | 0/52 | < d.l. |
| Brakel | 30/100 | 1/100 | 0.03 |
| Heel | 17/59 | 1/59 | 0.05 |
| Petrusplaat/ Keizersveer | 42/103 | 1/103 | 0.06 |
| Scheelhoek/ Stellendam | 7/35 | 0/35 | < d.l. |
| Drentse Aa (De Punt) | 0/125 | 0/125 | < d.l. |

\* d.l.: detection limit, in general the detection limit for DEET is 0.02 µg/L

Furthermore, the RIVM did not include this active substance on the recommended list of surface water to be monitored for drinking water from surface water (Bakker, 2010) because all measured concentrations in the Rhine and Meuse were below the drinking water limit of 0.1 μg/L (Ctgb, 2014). From the general scientific knowledge about the products and their active substance, it is concluded that there are no concrete indications for concern about the consequences of these products for surface water from which drinking water is produced when used in compliance with the directions for use. The standards for surface water destined for the production of drinking water are met.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FR-CA: The PEC for the aquatic compartment following direct release during swimming after human skin application, calculated according to the ESD for PT19, are presented below:  Table 24: PEC calculation for the aquatic compartment - Swimming scenario   |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | | **Variable/parameter** | **Symbol** | **High infested area** | **Low infested area** | **Unit** | **S/D/O/P** | | **INPUT** | | | | | | | Emission rate to surface water | Elocalwater | 4.50E-01 | 9.00E-02 | [kg.d-1] | O | | **OUTPUT** | | | | | | | Volume of water body | Vwaterbody | 4.35E+05 | 4.35E+05 | [m3] | O | | Number of emission days | Temission, 1d | 1 | 1 | [d] | O | | Number of emission days | Temission, 91d | 91 | 91 | [d] | O | | Concentration in water after 1d | Clocal water,1d | 1.03E-03 | 2.07E-04 | [mg.L-1] | O | | Concentration in water after 91d | Clocal water,91d | 9.41E-02 | 1.88E-02 | [mg.L-1] | O | | Concentration in water after 91d (refined) | Clocal water,91d deg | 2.26E-02 | 4.51E-03 | [mg.L-1] | O |   As the PNEC sediment is derived by EPM from the PNEC water, the risk ratios for surface water and sediment will be identical. Therefore no PEC values for sediment are derived. |

Atmospheric compartment

|  |
| --- |
| FR-CA: Not relevant, see 2.2.9.1.4 |

Terrestrial compartment (soil and groundwater)

|  |
| --- |
| FR-CA:  Not relevant for this scenario according to the ESD PT19 |

Non-compartmental-specific exposure relevant to the food chain (secondary poisoning)

|  |
| --- |
| FR-CA: Not relevant, see 2.2.9.2.5 |

#### **Risk characterisation for the environment**

|  |
| --- |
| Please notice that the risk characterization for the environment (section 2.2.8.5) is reported as provided by the applicant. The FR CA position is presented in **green evaluation boxes at the end of each part of the environmental section.** |

##### Spray on human skin- Emission through STP

###### Aquatic compartment (including water, sediment and stp)

The PNEC values for the water compartment and STP microorganisms were calculated from toxicity data by using recommended assessment factors, see section 1. The PNEC for STP microorganisms is 10 mg/L which is based on and EC50 > 1000 mg/L and an assessment factor of 100.

Because only three acute aquatic tests were performed, all on freshwater species, the assessment factor for the freshwater compartment was 1000. For the sediment compartment, there are no toxicity data available. The low Koc value indicates that sorption to sediment is not likely. Nevertheless, a PNEC value of 0.0741 mg/kg ww for sediment has been calculated based on the equilibrium partitioning theory and PNECwater of 0.043 mg/L. As both the PEC and PNEC for sediment are based on equilibrium partitioning with the PEC and PNEC for surface water, the risk assessment for the aquatic environment covers the surface water and sediment compartments.

Even when making worst case assumptions for the local environment, none of the PEC/PNEC ratios exceed 1, see Table below.

**PEC/PNEC ratios for indirect emission to the aquatic environment via the STP due to body cleaning indoors.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | PEC(mg/L) | PNEC (mg/L) | PEC/PNEC |
| Microorganisms in STP | 6.62X10-2 | 10 | 6.61X10-3 |
| Aquatic environment | 6.62X10-3 | 0.043 | 1.54X10-1 |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FR-CA: The PEC/PNEC ratios for the aquatic compartment following indirect release via the STP after human skin application are presented below:  Table 25: Risk for the aquatic compartment - Spray on human skin - STP emission   |  |  |  | | --- | --- | --- | | **Compartment** | **PEC** | **PEC/PNEC** | | Surface water  (covering sediment) | *PNEC water = 4.30E-02 mg/L* | | | 3.78E-02 | 0.879 | | STP | *PNEC STP =10 mg/L* | | | 3.78E-01 | 0.038 |   The risks are acceptable for the aquatic compartment (surface water and sediment) in case of human skin application after an indirect release via the STP. |

###### Terrestrial compartment (including soil and groundwater)

For the soil compartment, there are no toxicity data available. The low Koc value indicates that sorption to soil is not likely. Nevertheless, PNEC values have been calculated based on equilibrium partitioning theory and PNECwater. Even when making worst case assumptions for the local environment, the PEC/PNEC ratio does not exceed 1.

**PEC/PNEC ratios for indirect emission to soil due to body cleaning after product use.**

|  |  |  |
| --- | --- | --- |
| PECsoil (µg/kg ww) | PNEC (µg/kg ww) | PEC/PNEC |
| 5.61 | 37.9 | 1.48x10-1 |

The PEC/PNEC ratio for soil is < 1. Therefore the risk to terrestrial compartment is considered acceptable. The environmental risk assessment is performed for 1 application per day. For an application twice per day, the PEC/PNEC ratio will be multiply by a factor 2 and stay below < 1. Therefore the risk to terrestrial compartment is considered acceptable for two applications per day.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FR-CA: The PEC/PNEC ratios for the terrestrial compartment following indirect release *via* the STP after human skin application are presented below:  Table 26: Risk for the terrestrial compartment - Spray on human skin- STP emission   |  |  |  | | --- | --- | --- | | **Compartment** | **PEC** | **PEC/PNEC** | | Soil | *PNEC soil = 3.79E-02 mg/kgwwt* | | | 3.20E-02 | 0.845 | | Groundwater | *Threshold value 0.1 µg/L* | | | Acceptable\* | Acceptable\* |   \* refer to section 0 in the green box of FR-CA for the Tonnage based approach for PEC groundwater  The risks are acceptable for soil and groundwater in case of indirect release via the STP after application on human skin. |

###### Conclusions

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| --- |
| FR-CA: The risks are acceptable for the use on human skin leading to releases in the environment *via* STP after bathing and showering in the conditions of application claimed by the applicant. |

##### Spray on dog fur- Emission through STP

###### Aquatic compartment (including water, sediment and STP)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FR-CA: The PEC/PNEC ratios for the aquatic compartment following indirect release *via* the STP after indoor application on dogs are presented below:  Table 27: Risk for the aquatic compartment - Spray on dog fur - STP emission – Worst case (Finh = 1)   |  |  |  | | --- | --- | --- | | **Compartment** | **PEC** | **PEC/PNEC** | | Surface water  (covering sediment) | *PNEC water = 4.30E-02 mg/L* | | | 1.09E-02 | 0.253 | | STP | *PNEC STP = 10 mg/L* | | | 1.09E-01 | 0.011 |   Table 28: Risk for the aquatic compartment-Spray on dog fur- STP emission – Realistic case (Finh = 0.2)   |  |  |  | | --- | --- | --- | | **Compartment** | **PEC** | **PEC/PNEC** | | Surface water | *PNEC water = 4.30E-02 mg/L* | | | 2.17E-03 | 0.051 | | STP | *PNEC STP =10 mg/L* | | | 2.17E-02 | 0.002 |   The risks are acceptable for the aquatic compartment (surface water and sediment) for indirect releases via the STP after applications on dogs. |

###### Terrestrial compartment (including soil and groundwater)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FR-CA:  Table 29: Risk for the terrestrial compartment-Spray on dog fur- STP emission- Worst case (Finh = 1)   |  |  |  | | --- | --- | --- | | **Compartment** | **PEC** | **PEC/PNEC** | | Soil | *PNEC soil = 3.79E-02 mg/kgwwt* | | | 9.20E-03 | 0.243 | | Groundwater | *Threshold value 0.1 µg/L* | | | Acceptable\* | Acceptable\* |   Table 30: Risk for the terrestrial compartment-Spray on dog fur- STP emission- Worst case (Finh = 0.2)   |  |  |  | | --- | --- | --- | | **Compartment** | **PEC** | **PEC/PNEC** | | Soil | *PNEC soil = 3.79E-02 mg/kgwwt* | | | 1.84E-03 | 0.049 | | Groundwater | *Threshold value 0.1 µg/L* | | | Acceptable\* | Acceptable\* |   \* refer to section 0 in the green box of FR-CA for the Tonnage based approach for PEC groundwater  The risks are acceptable for the terrestrial compartment (soil and groundwater) for indirect releases via the STP after indoor applications on dogs. |

###### Conclusions

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| FR-CA: The risks are acceptable for all the compartments for indirect releases via the STP after indoor applications on dogs. |

###### Cumulative risk assessment for uses with releases via STP

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FR-CA:  The PEC/PNEC ratios for the cumulative assessment following indirect release via the STP after human skin application and indoor treatment of dogs are presented below:  **Table 31: PEC/PNEc ratio for the cumulative scenario**   |  |  |  | | --- | --- | --- | | **Compartment** | **PEC** | **PEC/PNEC** | | Surface water  (covering sediment) | *PNECwater = 0.043mg/L* | | | 4.00E-02 | 0.93 | | STP | *PNEC STP =10 mg/L* | | | 4.00E-01 | 0.04 | | Soil | *PNECsoil = 3.79E-02mg/kgwwt* | | | 3.39E-02 | 0.89 | | Groundwater | *Threshold value 0.1 µg/L* | | | Acceptable\* | Acceptable\* |   \* refer to section 0 in the green box of FR-CA for the Tonnage based approach for PEC groundwater  The risks are acceptable for all the environmental compartments when applications on humans and dogs are aggregated. |

##### Spray on dog fur- Direct emission towards soil

###### Aquatic compartment (including water, sediment and stp)

|  |
| --- |
| FR-CA:  Not relevant. |

###### Terrestrial compartment (including soil and groundwater)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FR-CA: The PEC/PNEC ratios for the terrestrial compartment following direct release to soil after outdoor application on dogs are presented below:  Table 32: Risk for the terrestrial compartment-Spray on dog fur - Direct emission   |  |  |  | | --- | --- | --- | |  | **PEC** | **PEC/PNEC** | | Soil | *PNEC soil = 3.79E-02mg/kgwwt* | | |  | 9.01E-01 | **2.38E+01** | | Groundwater | *Threshold value 0.1 µg/L* | | |  | Not relevant | Not relevant |   The risks are unacceptable for the terrestrial compartment after direct release to soil during outdoor application of the product on dogs. |

###### Conclusions

|  |
| --- |
| FR-CA: The risk to soil is unacceptable for the terrestrial compartment when the product is used outdoor on dog fur by spray, due to direct emission to soil. **Risk mitigation measure is necessary to reduce the release to soil.** Nevertheless, the use on dog is finally not proposed for authorization because of insufficient data to validate the efficacy. |

##### Swimming scenario

###### Aquatic compartment (including water, sediment and STP)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FR-CA: The PEC/PNEC ratios for the aquatic compartment following direct release via swimming after human skin application are presented below:  Table 33: Risk for the aquatic compartment-Swimmer- “Highly infested area”   |  |  |  | | --- | --- | --- | |  | **PEC** | **PEC/PNEC** | | Surface water (91d) considering degradation/dissipation  (covering sediment) | *PNEC water = 4.30E-02 mg/L* | | | 2.26E-02 | 5.25E-01 |   Table 34: Risk for the aquatic compartment-Swimmer- “Low infested area”   |  |  |  | | --- | --- | --- | |  | **PEC** | **PEC/PNEC** | | Surface water (91d) considering degradation/dissipation  (covering sediment) | *PNEC water = 4.30E-02 mg/L* | | | 4.51E-03 | 1.05E-01 |   Risks are acceptable for the aquatic compartment (surface water and sediment) after the direct release during swimming when the product is applied on human skin. |

###### Terrestrial compartment (including soil and groundwater)

|  |
| --- |
| FR-CA:  Not relevant. |

###### Conclusions

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| --- |
| FR-CA: The risk is acceptable for the use on human skin, considering the swimming scenario. |

##### Overall conclusions for the environment

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FR-CA: The overall conclusions are presented in the table below  Table 35: Overall conclusions on the uses of the product   |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | | Phase | Type of application / Uses | STP | Surface water  (covering sediment) | | Soil | | Groundwater | Secondary Poisoning | | Direct Release | *Via* STP | Direct Release | *Via* STP | | Application | Human skin | Acceptable | Acceptable | Acceptable | n.r. | Acceptable | Acceptable | n.r. | | Dogs | Acceptable | n.r. | Acceptable | **Unacceptable** | Acceptable | Acceptable | n.r. | | Aggregate risk | Acceptable | n.r. | Acceptable | n.r. | Acceptable | Acceptable | n.r. |   n.r. Not relevant  For the environment, the only unacceptable use is when the product is applied outdoor on dogs. The following risk mitigation measure shall be applied to limit the emission to the terrestrial compartment: ‘Applications on dogs shall be conducted indoor’. Nevertheless, the use on dog is finally not proposed for authorization because of insufficient data to validate the efficacy. |

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

*Please see the SPC*.

### Assessment of a combination of biocidal products

*Not relevant.*

### Comparative assessment

*Not relevant.*

# Annexes[[20]](#footnote-20)

## List of studies for the biocidal product

##### List of new data submitted in support of the evaluation of the biocidal product

| **Section No** | **Reference No** | **Author** | **Year** | **Title** | **Owner of data** | **Letter of Access** | | **Data protection claimed** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  | **Yes** | **No** | **Yes** | **No** |
| **2.2.2** | 2012-1669 AMi | Meluso A. | 2012 | Analytical method validation for the identification and quantification of active ingredient N, N-diethyl-meta-toludamide (DEET) in the test item 'MECDEET' | BEAPHAR BV |  |  |  |  |
| **2.2.2** | report n°: 347 | Grootkarzijn, A | 2014 | Spray output pattern MecDEET | BEAPHAR |  |  |  |  |
| **2.2.2** | final report S-2015-03393 AM | Meluso A. | 2016 | Viscosity of test item “MecDEET Solution” | BEAPHAR |  |  |  |  |
| **2.2.2** | Report 201504109 | Mazzei A. | 2015 | Surface tension on the sample MecDEET Solution | BEAPHAR |  |  |  |  |
| **2.2.2** | final report No. 2012/1671AMi | Lanata M | 2014 | Shelf life stability study on the test item “MecDeet” | BEAPHAR BV |  |  |  |  |
| **2.2.2** | report 2012/1670 | Meluso A. | 2012 | Accelerated stability study on the test item “MecDeet” | BEAPHAR BV |  |  |  |  |
| **2.2.2** | report 2012/1667AMi Cert-1 | Meluso A. | 2012 | Certificate of analysis: Appearance (at 20 °C and 101.3 kPA), acidity, alkalinity, relative density (liquids) and bulk, tap density (solids) | BEAPHAR BV |  |  |  |  |
| **2.2.2** | Report AQ018-18-2 | Matyssek F. | 2018 | MMAD study - CIPAC MT 187. Particle size distribution. | BEAPHAR BV |  |  |  |  |
| **2.2.6** | report number BIO001a-14 | Lüpkes K.-H. | 2014 | Repellent Efficacy of a Product on Human Arms against Mosquitoes. BioGenius | BEAPHAR BV |  |  |  |  |
| **2.2.6** | report number NWB-0114-BPR. |  | 2014 | Repellency effect of MecDEET against artificial infestations of ticks (*Ixodes ricinus*) in dogs. NorthWest Biopharm Limited | BEAPHAR BV |  |  |  |  |
| **2.2.6** | report number BGN\_IR\_0113. | Büchel K., Dautel H. | 2014 | Evaluation of the efficacy of the spray "MecDEET" against the European Sheep Tick *lxodes ricinus* on human volunteers. IS Insect Services | BEAPHAR BV |  |  |  |  |
| **2.2.6** | report number BIO059a-16 | Lüpkes K.-H. | 2016 | Determination of the repellent efficacy of a product on human arms against Asian tiger mosquito, *Aedes albopictus*. BioGenius. | BEAPHAR BV |  |  |  |  |
| **2.2.7** | 2012/1675 AMi | xxx | 2012 | Acute dermal irritation test on MecDEET | BEAPHAR  BV |  |  |  |  |
| **2.2.7** | 2012/1676 | xxx | 2012 | Acute ocular irritation test on MecDEET | BEAPHAR  BV |  |  |  |  |
| **2.2.7** | 2012/1677 AMi | xxx | 2012 | Skin sensitisation on MecDEET | BEAPHAR  BV |  |  |  |  |
| **2.2.7** | 2012/1673AMi + Amendment | xxx | 2012 | Acute oral toxicity -up and down procedure - ON MECDEET (Limit test) | BEAPHAR BV |  |  |  |  |
| **2.2.7** | 2012/1674 AMi | xxx | 2012 | Acute dermal toxicity on MeeDeet. | BEAPHAR BV |  |  |  |  |

## Output tables from exposure assessment tools

****

1. OPPTS 810.3700 Insect Repellents for Human Skin and Outdoor Premises (2010). [↑](#footnote-ref-1)
2. Guideline for testing and evaluation of the efficacy of antiparasitic substances for the treatment and prevention of tick and flea infestation in dog and cats (EMEA, 2007) [↑](#footnote-ref-2)
3. Demonstration of efficacy of ectoparasiticides (notably requirements of section 3.1 relative to products for topical use) (1994) [↑](#footnote-ref-3)
4. According to the conclusion of CG-28, based on experimental data on nymphs the use “against ticks” (without precision on the developmental) stage is accepted. [↑](#footnote-ref-4)
5. V. Corbel, M. Stankiewicz, C. Pennetier, D. Fournier, J. Stojan, E. Girard, M. Dimitrov, J. Molgó, J-M. Hougard, B. Lapied, *Evidence for inhibition of cholinesterases in insect and mammalian nervous systems by the insect repellent deet*, *BMC Biology* 2009, **7**:47. [↑](#footnote-ref-5)
6. C. Lavialle-Defaix, V. Apaire-Marchais, C. Legros, C. Pennetier, A. Mohamed, P. Licznar, V. Corbel, B. Lapied, *Anopheles gambiae* mosquito isolated neurons: A new biological model for optimizing insecticide/repellent efficacy, Journal of Neuroscience Methods, 200 (2011) 68-73 [↑](#footnote-ref-6)
7. M. DeGennaro, C.S. McBride, L. Seeholzer, T. Nakagawa, E.J. Dennis, C. Goldman, N. Jasinskiene, A.A. James, L. B. Vosshall, *orco* mutant mosquitoes lose strong preference for humans and are not repelled by volatile DEET, Nature, 2013, June 27; 498(7455): 487–491. [↑](#footnote-ref-7)
8. R. D. Xue, A. Ali, D. R. Barnard,*Laboratory evaluation of toxicity of sixteen insect repellents in aerosol sprays to adult mosquitoes*, Journal of the American Mosquito Control Association, 19(3) :271-274, 2003 [↑](#footnote-ref-8)
9. S. Licciardi, J.P. Herve, F. Darriet, J.-M. Hougard, V. Corbel, *Lethal and behavioural effects of three synthetic repellents (DEET, IR3535 and KBR3023) on Aedes aegypti mosquitoes in laboratory assays*, Medical and Veterinary Entomology, 20 :288-293, 2006 [↑](#footnote-ref-9)
10. Stanczyk, N. M., J. F. Y. Brookfield, R. Ignell, J. G. Logan and L. M. Field (2010). "Behavioral insensitivity to DEET in *Aedes aegypti* is a genetically determined trait residing in changes in sensillum function." Proceedings of the National Academy of Sciences of the United States of America **107**(19): 8575-8580. [↑](#footnote-ref-10)
11. According to the conclusion of CG-28, the developmental stage won’t be specified in the SPC. [↑](#footnote-ref-11)
12. HEEG opinion 17: US EPA Exposure Factors Handbook (2011 Issue), which are derived from US EPA Analysis of NHANES 1999-2006 [↑](#footnote-ref-12)
13. Dilution factor from ConsExpo 4.0, Consumer Exposure and Uptake Models. Program Manuel. Bilthoven, The Netherlands: National Institute for Public Health and the Environment (RIVM). Report no. 320104004. & RIVM report 320104001/2006 : Cosmetics Fact Sheet To assess the risks for the consumer (Updated version for ConsExpo 4) H.J. Bremmer, L.C.H. Prud’homme de Lodder, J.G.M. van Engelen [p34 : "Weight fraction dilution Wf / 3" " Estimate dilution factor 3 (wetting hands)] [↑](#footnote-ref-13)
14. The 64% value indicated in the Head-Hoc Recommendation n°11 has been very recently reviewed  and a new value of 55%  is now proposed (Nov. 2017). If the value of body surface 55% is used, the conclusion on the human health risk assessment does not change. No use for human is acceptable. [↑](#footnote-ref-14)
15. <https://echa.europa.eu/documents/10162/16908203/esd_for_pt_19_final_en.pdf> [↑](#footnote-ref-15)
16. Data from the harmonized risk assessment validated in the CAR of DEET covering all the products containing DEET. [↑](#footnote-ref-16)
17. Klein M. (2011). Proposals for standard scenarios and parameter setting of the FOCUS groundwater scenarios when used in biocide exposure assessments. FKZ: 360 04 035, pp 1-40 [↑](#footnote-ref-17)
18. <https://echa.europa.eu/documents/10162/16908203/esd_for_pt_19_final_en.pdf> [↑](#footnote-ref-18)
19. Technical guidance document, EU, 2003 [↑](#footnote-ref-19)
20. 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-20)