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)



**INSECT ECRAN ZONES INFESTEES**

Product type 19

DEET as included in the Union list of approved active substances

NA-APP Case Number in R4BP: PB-12-00194

NA-MIC Case Number in R4BP: BC-TU040220-27

NA-MIC Case Number in R4BP : BC-BW054532-24

NA-MIC Case Number in R4BP : BC-XF071586-22

Evaluating Competent Authority: FR

Date: December 2013

Amended : November 2018

Amended : January 2020

Amended : January 2023

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**Note to the reader**

This consolidated PAR for the **minor** change application of the product authorisation is based on the PAR of the first authorisation, in which all necessary addenda have been included.

In part 3 of this consolidated PAR, each section contains the initial assessment and the subsequent successive assessments (minor change, major change, post authorisation data...) the assessments related to the major / minor change of the product are at the end of each section and are highlighted in grey.

In part 2 of the consolidated PAR: the summary of product characteristics is pointed out and corresponds to the decision for the major/minor change application.

* **Minor change application (2018)**

Following the INSECT ECRAN ZONES INFESTEES last minor change authorisation, change claimed in the frame of a minor change application is the change in the pack size range (addition of a 50 ml packing).

* **Minor change application for INSECT ECRAN ZONES INFESTEES – 2019:**

Following the INSECT ECRAN ZONES INFESTEES last minor change authorisation, change claimed in the frame of a minor change application is the change in the pack size range (addition of a 200 ml packing).

* **Minor change application for INSECT ECRAN ZONES INFESTEES – 2022:**

Minor change claimed in the frame of this application is the extent from 36 months to 60 months of the shelf-life for all registered pack sizes (50ml, 100ml and 200ml).

1. **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* | *PB-12-00194* | 21.11.2014 | Initial assessment : INSECT ECRAN ZONES INFESTEES |
| NA-MIC | *FR* | *BC-CC019852-58* | 26.05.2016 | Minor change application (increase of shelf life : 3 years) |
| NA-ADC | *FR* | *BC-EY038004-26* | 18.04.2018 | Administrative change |
| NA-MIC | *FR* | *BC-TU040220-27* | 10/12/2018 | Minor change application |
| NA-ADC | *FR* | *BC-HC054085-57* | 17/10/2019 | Administrative change |
| NA-MIC | *FR* | *BC-BW054532-24* | 24/02/2020 | Minor change application |
| NA-MIC | *FR* | *BC-XF071586-22* | XX/06/2022 | Minor change application : extent of the shelf-life from 36 months to 60 months |

# CONCLUSION

* **Minor change application (2018)**

The new packaging claimed (50 mL bottle) is acceptable.

* **Minor change application for INSECT ECRAN ZONES INFESTEES – 2019 :**

The new packaging claimed (polypropylene flask of 250 mL with spray pump in polyethylene/polypropylene/polyoxymethylene (PPE/PP/POM). The product is filled with 200 mL of product.) is acceptable.

* **Minor change application for INSECT ECRAN ZONES INFESTEES – 2022:**

Change claimed in the frame of this minor change is the extent from 36 months to 60 months of the shelf-life for all registered pack sizes (50ml, 100ml and 200ml).

# Summary of the product assessment

## Administrative information

### Identifier of the product

| **Identifier** | **Country (if relevant)** |
| --- | --- |
| INSECT ECRAN ZONES INFESTEES  INSECT ECRAN ANTI-TIQUES | France |

### Authorisation holder

|  |  |  |
| --- | --- | --- |
| **Name and address of the authorisation holder** | **Name** | COOPERATION PHARMACEUTIQUE FRANCAISE |
| **Address** | Place Lucien Auvert  77020 Melun cedex  France |
| **Authorisation number** | **FR-2014-0182** | |
| **Date of the authorisation** | **17/05/2023** | |
| **Expiry date of the authorisation** | **21/11/2024** | |

### Manufacturer(s) of the product

|  |  |
| --- | --- |
| **Name of manufacturer** | COOPERATION PHARMACEUTIQUE FRANCAISE |
| **Address of manufacturer** | Place Lucien Auvert  77020 Melun cedex  France |
| **Location of manufacturing sites** | COOPERATION PHARMACEUTIQUE FRANCAISE  Place Lucien Auvert  77020 Melun cedex  France |

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

|  |  |
| --- | --- |
| **Active substance** | N, N'-diethyl-m-toluamide (DEET) |
| **Name of manufacturer** | Vertellus Performance Materials |
| **Address of manufacturer** | 2110 High Point Road  NC 27403 Greensboro  United States |
| **Location of manufacturing sites** | 2110 High Point Road  NC 27403 Greensboro  United States |
|  |

|  |  |
| --- | --- |
| **Active substance** | N, N'-diethyl-m-toluamide (DEET) |
| **Name of manufacturer** | CLARIANT US |
| **Address of manufacturer** | 625 Catawba Avenue  NC 28120 Mount Holly  United States |
| **Location of manufacturing sites** | 625 Catawba Avenue  NC 28120 Mount Holly  United States |
|  |

## 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 (technical)  Purity 97% | N, N'-diethyl-m-toluamide | Substance active | 134-62-3 | 205-149-7 | 50.0 |

### Information on technical equivalence

*Not relevant*

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

*Not relevant*

### Type of formulation

|  |
| --- |
| Any other liquid (AL) |

## Hazard and precautionary statements[[1]](#footnote-1)

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

| **Classification** | |
| --- | --- |
| Hazard category | Flam. Liq. Cat 3  Eye Irrit. Cat 2 A |
| Hazard statement | H226: Flammable liquid and vapour  H319 : Causes serious eye irritation. |
|  | |
| **Labelling** | |
|  |  |
| Signal words | Attention |
| Hazard statements | H226 : Flammable liquid and vapour  H319 : Causes serious eye irritation. |
| Precautionary statements | P101: If medical advice is needed, have product container or label at hand.  P102: Keep out of reach of children.  P210: Keep away from heat/sparks/open flames/hot surfaces. — No smoking.  P233: Keep container tightly closed.  P242: Use only non-sparking tools.  P243: Take precautionary measures against static discharge.  P264: Wash ... thoroughly after handling.  P305+P351+P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.  P337+P313: If eye irritation persists: Get medical advice.  P370+P378: In case of fire: Use carbon dioxide for extinction.  P403+P235: Store in a well-ventilated place. Keep cool  P501: Dispose of contents to CONTAINERS. |
|  | |
| Note | - |

### Authorised use(s)

#### Use description

|  |  |
| --- | --- |
| **Product Type** | 19 –Repellent and Attractant |
| **Where relevant, an exact description of the authorised use** | - |
| **Target organism (including development stage)** | *Ixodidae* (*Ixodes genus ;* adults and nymphs).  *Culicidae* (*Aedes genus, Anopheles genus and Culex genus* ; adults)  *Psychodidae* (*Phlebotomus genus* ; adults) |
| **Field of use** | Use on skin for health protection. |
| **Application method(s)** | The product is sprayed in the hand and then spread on the exposed area of the skin (*i.e.* face, neck, three quarter arms, hands and half-legs) to protect people.  Since the product is formulated as a ready-for-use product, no dilution or other preparation is necessary. |
| **Application rate(s) and frequency** | **Repellent against mosquitoes\* and sand flies:** 0.40 mg/cm2 of skin, protection up to 8 hours.  **Repellent against ticks:** 0.41 mg/cm2 of skin, protection up to 7 hours.  Do not exceed 2 applications of the product per day. |
| **Category(ies) of users** | Non-professional users |
| **Pack sizes and packaging material** | The product INSECT ECRAN ZONES INFESTÉES is packaged in a polypropylene flask of 50 mL with spray pump in polyethylene/polypropylene/polyoxymethylene (PPE/PP/POM). The product is filled with 50 mL of product.  The product INSECT ECRAN ZONES INFESTÉES is packaged in a polypropylene flask of 125 mL with spray pump in polyethylene/polypropylene/polyoxymethylene (PPE/PP/POM). The product is filled with 100 mL of product.  The product INSECT ECRAN ZONES INFESTÉES is packaged in a polypropylene flask of 250 mL with spray pump in polyethylene/polypropylene/polyoxymethylene (PPE/PP/POM). The product is filled with 200 mL of product. |

##### Use-specific instructions for use

|  |
| --- |
| Apply on the different body areas the following number of sprays :  -Children from 2 to <6 years old : 3 sprays for head and neck, 1 for both hands, 1 per feet. Do not apply more than twice a day.  -Children from 6 to <12 years old : 3 sprays for head and neck, 1 per hand, 1 per foot. Do not apply more than twice a day.  -Adults and children (>12 years old) : 5 sprays for head and neck, 3 per arm, 1 sper hand, 7 per leg, 2 per feet. Do not apply more than twice a day. |

##### 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

|  |
| --- |
| * The product must be shaken before use. * Respect the recommended application doses. * Retreat after water exposure without exceeding the maximal recommended application number. * The users should report straightforward to the registration holder any alarming signals which could be assumed to be resistance development. * The label has to respect the recommended conditions of use and the biocidal products labelling guide[[2]](#footnote-2). * The use of the product with other biocidal products or sunscreen products is not recommended. * Protection time can be lowered by sweating, water wash off, rubbing, high temperature (>30°C), wind velocity, etc. * Consider the use of personal protection in combination with a biocidal repellent. |

#### Risk mitigation measures

|  |
| --- |
| * Do not use on children less than two years old * Use should be restricted for children between two and twelve years old, except where motivated by the risk for human health through e.g. outbreaks of insect-borne diseases. * Do not exceed two applications per day * Only apply on uncovered skin * Do not put hands in mouth after application * Keep out of the reach of children * Do not spray directly in the face * Do not apply on young children’s hands. For other users, wash the palm of hands after application. * Do not use the spray near food and surfaces that may come into contact with food or drink intended for human consumption. * Do not use the product before bathing or showering. * Do not exceed 2 applications of the product per day. |

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

|  |
| --- |
| Inhalation: Assure fresh air breathing. In case of symptoms, call a physician.  Skin contact: remove contaminated clothes. Wash amply with water and soap.  Eye contact: rinse amply with clean water holding eye open for at least 10 minutes.  Ingestion: immediately call the emergency services or a physician. Do not induce vomiting. Rinse mouth with water. |

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

|  |
| --- |
| * Do not discharge the product on the ground, into watercourses, into pipes (sink, toilets…) nor down the drains. * 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

|  |
| --- |
| * Shelf life: 5 years. * The product must not be stored more than 6 months at 40°C. |

### Other information

|  |
| --- |
| A monitoring of the resistance phenomenon must be put in place. The collected information must be sent every 5 years to Anses within the framework of a post-authorisation monitoring. |

# GENERAL INFORMATION ABOUT THE PRODUCT APPLICATION

## Applicant

|  |  |
| --- | --- |
| Company Name: | COOPERATION PHARMACEUTIQUE FRANCAISE |
| Address: | Place Lucien Auvert |
| City: | Melun cedex |
| Postal Code: | 77020 |
| Country: | France |
| Telephone: | +33 (0) 1 64 87 7135 |
| Fax: | +33 (0) 1 64 87 7143 |
| E-mail address: | [Sabrina.henaud@cooper.fr](mailto:Sabrina.henaud@cooper.fr) |

### Person authorised for communication on behalf of the applicant

|  |  |
| --- | --- |
| Name: | Ambrosi Scientific Consulting |
| Function: | Consultant |
| Address: | 208 Chemin du Casson |
| City: | Chaintré |
| Postal Code: | 71570 |
| Country: | France |
| Telephone: | +33 3.8535.6714 |
| Fax: | +33 6.1205.8860 |
| E-mail address: | [dambrosi@ambrosiconsulting.com](mailto:dambrosi@ambrosiconsulting.com) |

## Current authorisation holder[[3]](#footnote-3)

|  |  |
| --- | --- |
| Company Name: | COOPERATION PHARMACEUTIQUE FRANCAISE |
| Address: | Place Lucien Auvert |
| City: | Melun cedex |
| Postal Code: | 77020 |
| Country: | France |
| Telephone: | +33 (0) 1 64 87 7135 |
| Fax: | +33 (0) 1 64 87 7143 |
| E-mail address: | [Sabrina.henaud@cooper.fr](mailto:Sabrina.henaud@cooper.fr) |
| Letter of appointment for the applicant to represent the authorisation holder provided (yes/no): | - |

## Proposed authorisation holder

|  |  |
| --- | --- |
| Company Name: | COOPERATION PHARMACEUTIQUE FRANCAISE |
| Address: | Place Lucien Auvert |
| City: | Melun cedex |
| Postal Code: | 77020 |
| Country: | France |
| Telephone: | +33 (0) 1 6487 7135 |
| Fax: | +33 (0) 1 6487 7143 |
| E-mail address: | [Sabrina.henaud@cooper.fr](mailto:Sabrina.henaud@cooper.fr) |
| Letter of appointment for the applicant to represent the authorisation holder provided (yes/no): | - |

## Information about the product application

|  |  |
| --- | --- |
| Application received: | 28/07/2012 |
| Application reported complete: | 09/08/2012 |
| Type of application: | Product authorisation |
| Further information: | New product |

## Information about the biocidal product

### General information

|  |  |
| --- | --- |
| Trade name: | Insect Ecran Zones Infestées |
| Manufacturer’s development code number(s), if appropriate: | IE-DEET-A50 |
| Product type: | PT19 |
| Composition of the product (identity and content of active substance(s) and substances of concern; full composition see confidential annex): | See Confidential annex. |
| Formulation type: | AL |
| Ready to use product (yes/no): | Yes |
| Is the product the very same (identity and content) to another product already authorised under the regime of directive 98/8/EC (yes/no);  If yes: authorisation/registration no. and product name:  or  Has the product the same identity and composition like the product evaluated in connection with the approval for listing of active substance(s) on to Annex I to directive 98/8/EC (yes/no): | No |

### Information on the intended use(s)

|  |  |
| --- | --- |
| Overall use pattern (manner and area of use): | The product IE-DEET-A50is presented as a ready-for-use product to be applied on uncovered human skin to repel mosquitoes, sand flies and ticks for consumer use. |
| Target organisms: | *Aedes aegypti*  *Anopheles gambiae*  *Aedes albopictus*  *Culex pipiens*  *Phlebotomus duboscqi*  *Ixodes ricinus* |
| Category of users: | Public |
| Directions for use including minimum and maximum application rates, application rates per time unit (e.g. number of treatments per day), typical size of application area: | The recommended dose of application of IE-DEET-A50 is 0.4 mg/cm² of skin. The product can be used on children from 1-year old and adults. The number of sprayings recommended to cover face, neck, ¾ arms, hands and ½ legs is from 8 to 28 sprayings depending on the age range. |
| Potential for release into the environment (yes/no): | No |
| Potential for contamination of food/feedingstuff (yes/no) | No |
| Proposed Label: | See Document III-B9, Annex 2, label |
| Use Restrictions: | The proposed label contains detailed instructions for use.  The product must not be used for children under 1-year.  The product can be used for pregnant women in case of risk of disease transmission.  The product must not be applied on eyes, mucous membranes and injured skin.  Number of applications must not exceed two per day.  Resistance of the product to water has not been demonstrated. |

### Information on active substance(s)[[4]](#footnote-4)

|  |  |
| --- | --- |
| Active substance chemical name: | N,N-Diethyl-m-toluamide (N,N-DIETHYL-M-TOLUAMIDE (DEET)) |
| CAS No: | 134-62-3 |
| EC No: | 205-149-7 |
| Purity (minimum, g/kg or g/l): | 970 g/kg |
| Inclusion directive: | DIRECTIVE 2010/51/EU |
| Date of inclusion: | 1 August 2012 |
| Is the active substance equivalent to the active substance listed in Annex I to 98/8/EC (yes/no): | Yes |
| Manufacturer of active substance(s) used in the biocidal product: | See confidential annex |

### Information on the substance(s) of concern[[5]](#footnote-5)

No substance of concern

## Documentation

### Data submitted in relation to product application

**Identity, physicochemical and analytical method data**

Physico-chemical properties studies and analytical methods on the former and the current composition of biocidal product INSECT ECRAN ZONES INFESTÉES were provided by the applicant

* **Minor change application (2016)**

In the frame of minor technical modification, applicant has sumbitted a Long term stability study in order to support a shelf life of 3 years.

**Efficacy data**

* An arm-in-cage study conducted with ten human volunteers with the product INSECT ECRAN ZONES INFESTEES (50% w/w DEET) on four mosquito species *(Aedes aegypti, Anopheles gambiae, Aedes albopictus and Culex pipiens)* and one sand fly specie *(Phlebotomus duboscqi).*
* An arm-in-cage study conducted with ten human volunteers with the product INSECT ECRAN ZONES INFESTEES (50% w/w DEET) diluted at 25% w/w on two mosquito species *(Aedes aegypti* and *Anopheles gambiae).*
* An arm-in-cage study conducted with ten human volunteers with the product INSECT ECRAN ZONES INFESTEES (50% w/w DEET) diluted at 15% w/w on two mosquito species *(Aedes aegypti* and *Anopheles gambiae).*
* A laboratory study conducted with ten human volunteers with the product INSECT ECRAN ZONES INFESTEES (50% w/w DEET) on one tick specie *(Ixodes ricinus).*

**Residues data**

No specific residue data were submitted in the context of this dossier. The product INSECT ECRAN ZONES INFESTEES will be used as an insect repellent directly applied to the skin and will not result in any direct contact with food in normal condition of use.

**Toxicology data**

Most toxicity studies submitted were performed with an older formulation of INSECT ECRAN ZONES INFESTEES. Since it is not expected that the differences of composition between the old and the current formulation impact the acute toxicity, the extrapolation of study results from the old formulation of INSECT ECRAN ZONES INFESTEES was accepted.

**Ecotoxicology data**

Two new studies have been submitted for the product authorisation level:

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **DOC-III A reference** | **Type of data** | | **Date** | **Guideline** | **GPL** | **Reference** |
| 7.4.1.3. | Acute aquatic toxicity | Algae | 2012 | OECD 201  (23/03/2006) | Yes | [1] Tobor-kaplon, M.A., 2012. GROWTH INHIBITION TEST ON *PSEUDOKIRCHNERIELLA SUBCAPITATA* WITH IE-DEET-A50. Study reference 499243. |
| 7.4.1.4. | Micro-organisms | 2013 | OECD 209  (04/04/1984) | Yes | [2] Desmares-Koopmans, M.J.E., 2013. ACTIVATED SLUDGE RESPIRATION INHIBITION TEST (CARBON AND AMMONIUM OXIDATION) WITH IE-DEET-A50 Study reference 499244. |

### Access to documentation

The access to all active substance data was granted by both Clariant and Vertellus.

# Summary of the product assessment

## Identity related issues

The sources of the active substance used in the biocidal product INSECT ECRAN ZONES INFESTÉES are one of the sources used for annex I inclusion.

There is no substance of concern in the biocidal product.

The formulation of the biocidal product INSECT ECRAN ZONES INFESTÉES is not the same as the formulation of the representative biocidal product assessed for the inclusion of the active substance in annex I of directive 98/8/EC.

## Classification, labelling and packaging

### Classification of the active substance

The current harmonised classification for active substance DEET is presented in the table below.

The classification of DEET does not take into account the new validated data which lead to a consensus during the Technical Meeting I 2009 that DEET can be considered as ready biodegradable. Therefore the current classification needs to be adapted accordingly (i.e. in an Annex XV dossier to be submitted to the ECHA).

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| **Classification - Directive 67/548/EEC** |  |
| Class of danger | Xn – Harmful  Xi – Irritant |
| R phrases | R22: Harmful if swallowed  R36/38: Irritating to eyes and skin.  R52/53- Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment. |

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| **Classification - Regulation (EC) 1272/2008** |  |
| Hazard statement | Acute Tox. 4 - H302: Harmful if swallowed  Eye Irrit. 2 - H319: Causes serious eye irritation  Skin Irrit. 2 - H315: Causes skin irritation.  Aquatic chronic 3 - H412 : Harmful to aquatic life with long lasting effects. |

### Classification of the biocidal product

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| **Classification - Directive 99/45/EEC** |  |
| Class of danger | None |
| R phrases | R10: Flammable |
| S phrases (proposed by the RMS) | S2: Keep out of the reach of children.  S46: If swallowed, seek medical advice immediately and show this container or label |

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| **Classification - Regulation (EC) 1272/2008** |  |
| Hazard statement | Flam. Liq. 3 - H226 : Flammable liquid and vapour  Eye Irrit Cat 2 - H319: Cause serious eye irritation |
| Precautionary statements (proposed by the RMS) | - |

### Labelling of the biocidal product

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| **Labelling - Directive 67/548/EEC** | |
| Symbols: |  |
| Indications of danger: |  |
| Risk phrases: | R10: Flammable. |
| Safety phrases: | S2: Keep out of the reach of children.  S46: If swallowed, seek medical advice immediately and show this container or label |

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| **Labelling - Regulation (EC) 1272/2008** | |
| Pictograms: | http://upload.wikimedia.org/wikipedia/commons/thumb/6/6d/GHS-pictogram-flamme.svg/120px-GHS-pictogram-flamme.svg.png |
| Signal words: | Flam. Liq. 3 ; Warning |
| Hazard statements: | Flam. Liq. 3 H226 : Flammable liquid and vapour  Eye Irrit Cat 2 H319: Cause serious eye irritation |

### Packaging of the biocidal product

The product IE-DEET-A50 is packaged in a polypropylene flask with spray pump (PP/PE/POM[[6]](#footnote-6)). The volume of the flask is 125 mL, and it is filled with 100 mL of product.

## Physico/chemical properties and analytical methods

### Active ingredient

* + - 1. **Identity, origin of active ingredient**

The sources of the active substance used in the biocidal product INSECT ECRAN ZONES INFESTÉES are sources used for annex I inclusion.

* + - 1. **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 ingredient in the technical active ingredient have already been evaluated at EU level and are presented in the CAR of the active substance DEET (2009). The notifier of the product INSECT ECRAN ZONES INFESTÉES is not the applicant that supported the annex I inclusion dossier of the active substance but has a full letter of access to these data.

### Biocidal product

* + - 1. **Identity, composition of the biocidal product, packaging**

The formulation of the biocidal product INSECT ECRAN ZONES INFESTÉES is not the same as the formulation of the representative biocidal product assessed for the inclusion of the active substance in annex I of directive 98/8/EC.

Trade name: Insect Ecran Zones Infestées

Code number: IE-DEET-A50

The composition of the product is confidential and is presented in a confidential annex. There is no substance of concern.

The product INSECT ECRAN ZONES INFESTÉES is packaged in a polypropylene flask with spray pump (PP/PE/POM). The volume of the flask is 125 mL, and it is filled with 100 mL of product.

* **Minor change application for INSECT ECRAN ZONES INFESTEES – 2018 :**

Additionnal packagings : 50 mL

* **Minor change application for INSECT ECRAN ZONES INFESTEES – 2019 :**

Additionnal packagings : 250 mL

* **Minor change application for INSECT ECRAN ZONES INFESTEES – 2022:**

No change

* + - 1. **Physico-chemical properties**

Studies have been performed on former or current compositions of biocidal product INSECT ECRAN ZONES INFESTÉES.

Former and actual compositions are considered to be similar (0.15% w/w difference) for physicochemical properties.

| **Subsection (Annex Point IIB. 3/TNsG)** | **Method** | **Purity/ Specification** | **Results** | **Reference** |
| --- | --- | --- | --- | --- |
| **3.1 Appearance (IIB3.1/Pt. I-B3.1)** | Visual | Former composition | limpid liquid | Grevin P. 2012 |
| **3.1.1 Physical state and nature**  **3.1.2 Colour**  **3.1.3 Odour** | Visual | Former composition | Colourless | Grevin P. 2012 |
| **3.2 Explosive properties (IIB3.2/Pt. I-B3.2)** | DSC | Former composition | During both heating phases, neither endothermic nor exothermic peak was observed up to 500°C under the experimental conditions used.  The test item shall not be classified as explosive.  Not explosive | FERRON N.2012 |
| **3.3 Oxidising properties (IIB3.3/Pt. I-B3.3)** | Statement | - | Based on structural considerations, INSECT ECRAN ZONES INFESTÉES is not expected to have oxidising properties.  Not oxidizing | ASC report 11/36-2 |
| **3.4 Flash-point and other indications of flammability or spontaneous ignition (IIB3.4/Pt. I-B3.4)** | | | | |
| Flammability | EC A.9 | Former composition | Flash point: 34°C  Classified as R10 | FERRON N.2012 |
| Self ignition temperature of solids | Statement | - | Based on composition, INSECT ECRAN ZONES INFESTÉES is expected to have auto-flammability point higher than 360 °C. | ASC report 11/36-2 |
| **3.5 Acidity/Alkalinity (IIB3.5/Pt. I-B3.5)** |  | Current formulation | Alkalinity of biocidal product is equivalent to 0.6 mL of NaOH 0.01M | Laurent E. 2013 |
| **3.5 pH pure material** | CIPAC MT 75.3 | Former composition | pH of pure test item at 21°C: 8.39 | Grevin P. 2012 |
| **3.6 Relative density (IIB3.6/Pt. I-B3.6)** | EC A.3  OECD 109 | Former composition | Relative density at 20 °C: 0.959 | FERRON N.2012 |
| **3.7 Storage stability - (IIB3.7/Pt. I-B3.7)** | 2 weeks at 54 °C | Former composition | After 14 days at 54°C in white opaque PP bottle with spray with translucent plastic stopper:   |  |  |  | | --- | --- | --- | |  | T0 | 14 d 54 °C | | Appearance | As initial | | | Packaging | As initial | | | Content of DEET | 50.4% | 49.8%  (-1.2%) | | pH value (CIPAC MT) | 8.39 | 8.98 |   Biocidal product is stable 14 days at 54 °C in commercial packaging | Grevin P. 2012 |
|  | high temperature (40°C)  Test performed until 6 months | Former composition | After 6 months at 40°C in commercial packaging:   |  |  |  | | --- | --- | --- | |  | T0 | 6 M 40°C | | Appearance | As initial | | | Packaging | As initial | | | Content of DEET | 50.6% | 50.4% | | pH value | 9.0 | 9.0 | | Density | 0.959 | 0.960 |   As this study was conducted on former composition, a new shelf life study was started on actual composition. | Laurent E. 2012 |
|  | high temperature (40°C)  Test performed until 6 months | IE-DEET-A50 (50% DEET), Batch 006815  (current composition) | After 6 months at 40°C in commercial packaging:   |  |  |  | | --- | --- | --- | |  | T0 | 6 M 40°C | | Appearance | As initial | | | Packaging | As initial | | | Content of DEET | 50.8% | 50.8% | | Alkalinity / NaOH 0.01M | 0.6 mL | 0.7 mL | | Density | 0.958 | 0.959 |   Biocidal product is stable 6 months at 40 °C in commercial packaging | Laurent E. 2013 |
|  | 3 years at ambient temperature (stopped study) | Former composition | After 1 year at 25°C in commercial packaging:   |  |  |  | | --- | --- | --- | |  | T0 | 1Y 25°C | | Appearance | As initial | | | Packaging | As initial | | | Volume delivered by pump | 0.13 mL | 0.13 mL | | Content of DEET | 50.6% | 50.7% | | pH value (pHmeter) | 9.0 | 8.6 | | density | 0.959 | 0.959 | | Microbial contamination | | | | DGAT | <100 UFC /mL | <100 UFC /mL | | DMLT | <10 UFC /mL | <10 UFC /mL | | Pseudomonas aeruginosa | Not detected | Not detected | | Staphylococcus aureus | Not detected | Not detected |   Content of Microbial contamination are submitted are reported here but are not evaluated in biocidal product dossier.  As this study was conducted on former composition, a new shelf life study was started on actual composition. | Laurent E. 2012 |
|  | 3 years at ambient temperature (ongoing study) | IE-DEET-A50 (50% DEET), Batch 006815  (current composition) | After 6 months years at 25°C in commercial packaging:   |  |  |  | | --- | --- | --- | |  | T0 | 6M 25°C | | Appearance | As initial | | | Packaging | As initial | | | Volume delivered by pump | Not available | Not available | | Content of DEET | 50.8% | 50.7% | | Alkalinity / NaOH 0.01M | 0.6 mL | 0.6 mL | | density | 0.958 | 0.959 | | Microbial contamination | | | | DGAT | <100 UFC /mL | <100 UFC /mL | | DMLT | <10 UFC /mL | <10 UFC /mL | | Pseudomonas aeruginosa | Not detected | Not detected | | Staphylococcus aureus | Not detected | Not detected |   Content of Microbial contamination are submitted are reported here but are not evaluated in biocidal product dossier.  Biocidal product is stable 6 months at 25°C in its commercial packaging  Final study including data on volume delivered by pump is required in post registration. | Laurent E. 2013 |
| **Effect of low temperature** | CIPAC MT 39.3 | IE-DEET-A50 (50% DEET), Batch 006815  (current composition) | After 7 days at 0 ± 2°C:  Colourless limpid liquid with a big bubble (aqueous phase) at the surface and some little bubbles in suspension.  Biocidal product is not considered stable after 7 days at 0°C.  The test item has to be manually shaken before use.  The label on the packaging of the test item should mention “Shaken before use”. | Ferron N., Demangel B., 2013 |
| **Effects of light** |  |  | Not relevant as the product is not in contact with light |  |
| **3.8 Technical characteristics (IIB3.8/Pt. I-B3.8)** | | | | |
| Wettability |  |  | Data not required as the product is a ready to use spray |  |
| Persistent foaming |  |  | Data not required as the product is a ready to use spray |  |
| Suspensibility |  |  | Data not required as the product is a ready to use spray |  |
| Spontaneity of dispersion |  |  | Data not required as the product is a ready to use spray |  |
| Dilution stability |  |  | Data not required as the product is a ready to use spray |  |
| Dry sieve test |  |  | Data not required as the product is a ready to use spray |  |
| Wet sieve test |  |  | Data not required as the product is a ready to use spray |  |
| Dustiness |  |  | Data not required as the product is a ready to use spray |  |
| Attrition/friability of granules; integrity of tablets |  |  | Data not required as the product is a ready to use spray |  |
| Emulsifiability / Emulsion stability / Re-emulsifiability |  |  | Data not required as the product is a ready to use spray |  |
| Stability of dilute emulsions |  |  | Data not required as the product is a ready to use spray |  |
| Flowability |  |  | Data not required as the product is a ready to use spray |  |
| Pourability (including rinsed residue) |  |  | Data not required as the product is a ready to use spray |  |
| **3.9 Compatibility with other products (IIB3.9/Pt. I-B3.9)** |  |  | Data not required as the product is a ready to use spray |  |
| **3.10 Surface tension (Pt. I-B3.10)** | OECD 115 | Former composition | Surface tension of pure test item at 20°C: 32.8 mN/m  Test item is surface active | FERRON N.2012 |
| **3.11 Viscosity (Pt. I-B3.10)** | OECD 114 | Former composition | Dynamic viscosity of pure test item:  5.99 mPa\*s at 20°C  3.01 mPa\*s at 40°C  the test item was considered to have newtonian properties in the experimental conditions used | FERRON N.2012 |
| **3.12 Particle size distribution (Pt. I-B3.11)** | CIPAC MT 187 | Former composition | Particle size distribution of droplets when sprayed:  Dv (1%) ≤ 16 µm  Dv (10%) = 33 µm  Dv (50%) = 59 µm  Dv (90%) = 99 µm | Rodrigez N. 2012 |
| **Other** |  | Former composition | Volume delivered by pump = 0.13mL | Laurent E. 2012 |

A shelf life of 3 years is requested by the applicant. Due to available data (stable 14 days at 54°C), a shelf life of 2 years is granted.

As biocidal product is suseptible to be used in tropical countries, the following recommandation is added : Do not store more than 6 month at 40°.

* **Minor change (2016)**

A shelf life of 3 years is requested by the applicant during the previous assessment. Due to available data (stable 14 days at 54°C), a shelf life of 2 years is granted.

In the frame of minor technical modification, applicant has sumbitted a Long term stability study in order to support a shelf life of 3 years. The conclusion of this study is summarized below:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Subsection (Annex Point IIB. 3/TNsG)** | **Method** | **Purity/ Specification** | **Results** | **Reference** |
| **3.7 Long term stability study** | 3 years at ambient temperature  Analytical method validated in original PAR | actual composition | After 3 years at 25°C in PP bottle with spray:   |  |  |  | | --- | --- | --- | |  | T0 | 3Y 25°C | | Appearance | As initial | | | Packaging | As initial | | | Volume delivered by pump | 0.13 mL | 0.13 mL | | Content of DEET | 50.8% | 50.7% | | acidity | 0.6 mL NaOH 0.01M | 0.2 mL NaOH 0.01M | | density | 0.959 | 0.958 | | Microbial contamination | | | | DGAT | <100 UFC /mL | <100 UFC /mL | | DMLT | <10 UFC /mL | <10 UFC /mL | | Pseudomonas aeruginosa | Not detected in 1mL | Not detected in 1mL | | Staphylococcus aureus | Not detected in 1mL | Not detected in 1mL |   Content of Microbial contamination are submitted are reported here but are not evaluated in biocidal product dossier. | Laurent E. 2014 |
| **Conclusion on the physical, chemical and technical properties of the product** | | | | |
| Provided study is acceptable  The requested shelf life of 3 years is acceptable. As biocidal product is suseptible to be used in tropical countries, the following recommandation is added : Do not store more than 6 month at 40°C. | | | | |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| * **Minor change application (2018)**   In the frame of the minor technical modification, applicant has submitted a long term stability study and an accelerated stability study in order to support a new commercial packaging (50 mL bottle). The conclusion of this study is summarized below:   | **Subsection (Annex Point IIB. 3/TNsG)** | **Method** | **Purity/ Specification** | **Results** | **Reference** | | --- | --- | --- | --- | --- | | **3.7 Long term stability study** | 3 years at ambient temperature  Analytical method validated in original PAR | Composition with bitrex | After 3 years at 25°C and 6 months at 40°C in commercial packaging (there is no more precision of the packaging):   |  |  |  |  | | --- | --- | --- | --- | |  | T0 | 3Y 25°C | 6M 40°C | | Appearance | As initial | | | | Content of DEET | 50.8% | 50.7% | 50.8% | | acidity | 0.6 mL NaOH 0.01M | 0.2 mL NaOH 0.01M | 0.7 mL NaOH 0.01M | | density | 0.958 | 0.958 | 0.0959 | | Microbial contamination | | |  | | DGAT | <100 UFC /mL | <100 UFC /mL | Not performed | | DMLT | <10 UFC /mL | <10 UFC /mL | | Pseudomonas aeruginosa | Not detected in 1mL | Not detected in 1mL | | Staphylococcus aureus | Not detected in 1mL | Not detected in 1mL |   Content of Microbial contamination are submitted and are reported here but are not evaluated in biocidal product dossier.  eCA: this study could not be to taken into account because the packaging is not reported in the study. | Laurent E. 2015 report No 1548-5 | | **3.7 Storage stability - (IIB3.7/Pt. I-B3.7)** | 2 weeks at 54 °C | Former composition  IE-DEET-A50 | After 14 days at 54°C in a 50 mL polypropylene white bottle with a crimped pump and a polypropylene cap   |  |  |  | | --- | --- | --- | |  | T0 | 14 d 54 °C | | Appearance | As initial | | | Packaging | As initial | | | pH at 20°C | 8.6 | 8.5 | | Volume delivered by pump | 0.13 mL | 0.12 mL | | Content of DEET | 50.8% | 50.7% | | acidity | 0.3 mL NaOH 0.01M | 0.2 mL NaOH 0.01M | | density | 0.959 | 0.958 |   Biocidal product is stable 14 days at 54 °C in 50mL commercial packaging  eCA: Product’s composition has not changed since the minor change in 2016. The product is stable 3 years in PP bottle (125 mL). The accelerate storage study in PP bottle (50 mL) is acceptable and the product is stable.  Considering these elements, eCA considers that the product in PP bottle (50 mL) is stable 3 years. | Laurent E. 2018 report No 2779 | | **Conclusion on the physical, chemical and technical properties of the product** | | | | | | Provided accelerated storage stability study is acceptable.  The long term storage stability study provided is not acceptable as no information on the packaging was indicated. However, as the long term storage stability study provided for the Minor change application in 2016 was considered acceptable, results have been taken into account for the minor change 2018 evaluation.  The requested change in the pack size range (addition of a 50 mL packing) is acceptable. As biocidal product is suseptible to be used in tropical countries, the following recommandation is added : Do not store more than 6 month at 40°C. | | | | | |

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| * **Minor change application for INSECT ECRAN ZONES INFESTEES - 2019 :**   In the frame of the minor technical modification, applicant has submitted an accelerate stability study in order to support a new commercial packaging (250 mL bottle). The conclusion of this study is summarized below:   |  |  |  |  |  | | --- | --- | --- | --- | --- | | **Subsection (Annex Point IIB. 3/TNsG)** | **Method** | **Purity/ Specification** | **Results** | **Reference** | |  | 4 weeks at 54 °C  Guideline ICH Q1A (R2): Stability Testing of New Drug Substances and Products | Actual composition | After 28 days at 54°C in a 250 ml polypropylene white bottle with a crimped pump and a polypropylene cap, and filled with 200 ml of product   |  |  |  |  | | --- | --- | --- | --- | |  | T0 | 14 d 54 °C | 28 d 54°C | | Appearance of packaging | As initial | | | | Content of DEET | 51.2 % | 51.4 % | 51.8% | | pH value (CIPAC MT) | 9.4 | 9.4 | 9.2 | | acidity | 0.2 mL | 0.5 mL |  | | Pump delivery content | 0.12 mL | 0.12 mL | 0.12 mL |   Biocidal product with 2019 composition is stable 28 days at 54 °C in commercial packaging | Laurent E. 2019 |   **Conclusion on the physical, chemical and technical properties of the product :**  Provided accelerated storage stability study is acceptable. The requested change in the pack size range (addition of a 250 mL packing) is acceptable. |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| * **Minor change application for INSECT ECRAN ZONES INFESTEES – 2022:**  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | **3.7 Long term stability study** | 5 years at ambient temperature  Analytical method validated in original PAR  (Chauvet 2011 ; Nb1332) | Composition with bitrex | After 5 years at 25°C in 125 mL PP bottle:   |  |  |  | | --- | --- | --- | |  | T0 | 63 months 25°C | | Appearance | As initial | | | Content of DEET | 50.8% | 50.7% | | alkalinity | 0.8 mL NaOH 0.01M | 0.5 mL NaOH 0.01M | | density | 0.958 | 0.958 | | Content delivered by spray | Not tested | 0.13 mL | | Microbial contamination | | | | TAMC | <1 CFU /mL | <100 CFU /mL | | TYMC | <1 CFU /mL | <10 CFU /mL | | Pseudomonas aeruginosa | Not detected in 1mL | Not detected in 1mL | | Staphylococcus aureus | Not detected in 1mL | Not detected in 1mL | |  |  |  |   Content of Microbial contamination are submitted and are reported here but are not evaluated in biocidal product dossier.  Content of product delivered by pump is not available at initial point but was provided by applicant afterward  However, in other studies for all pack sizes (250 ml, 100 ml and 200 ml), the volume varied between 0.11 ml and 0.13 ml from initial time to end of storage. The results obtained after 60 months storage is consistent with other studies and expected results. | Laurent E. 2021 report No 3468  Laurent E. 2021 report  Report no. 3468/2 |   **eCA Conclusion:**  A storage stability study after 63 months was provided. The results of the study show that the product is stable after 63 months. The content of product delivered by pump is not available in the study but was provided by applicant afterward. No further data required  Biocidal product is stable after 63 months. The requested shelf life of 5 years is acceptable. |

* + - 1. **Analytical method for determining the active substance and relevant component in the biocidal product**

Reference: C. Chauvet 2011; DEET determination in “insecte ecran peau Zones Infestées” ; report Nb1332.

The method to determine the content of DEET in former composition of DEET biocidal product INSECT ECRAN ZONES INFESTÉES by HPLC-UV (230 nm) using external standard is validated according to document SANCO 3030/99.

Validation data

|  |  |  |  |
| --- | --- | --- | --- |
| Linearity | Repeatability | Recovery rate (%) | Specificity |
| Range : 80-120% of nominal concentration  n=5x3  r> 0.999 | 6 samples injected one time by 2 operators  RSD= 0.26% and 0.31% | 5 fortification levels tested 3 times in the range 80-120% of nominal value.  Mean recovery (%) = 100.0%  RSD= 0.13% | Chromatograms data (Dilution solvent and placebo) demonstrate that method is specific |

The provided method is acceptable for the former composition of product INSECT ECRAN ZONES INFESTÉES.

Reference: Laurent E. 2013 ; Insect ecran famille insect ecran zone infestées. Report Nbr 1545

In this report, it is demonstrated that additional formulants added in the current composition compared to the former composition do not affect the specificity of the method described in study Nb 1332.

Conclusion: method described in study Nb 1332 is applicable to determine DEET in INSECT ECRAN ZONES INFESTÉES

* + - 1. **Analytical methods for determining relevant components and/or residues in different matrices**

Analytical methods for DEET residues in soil and water are available in Assessment Report N,N-diethyl-meta-toluamide (DEET) Product-type 19 (repellents and attractants), 2010/03/11. This is acceptable.

Analytical method for DEET residues in body fluids (plasma) is available in Assessment Report N,N-diethyl-meta-toluamide (DEET) Product-type 19 (repellents and attractants), 2010/03/11. However, no data required as DEET is not classified as toxic or highly toxic.

Considering the use pattern of the biocidal product PREBUTIX and the properties of DEET, the contamination of air compartment during application is not significant and no method of analysis in air is required.

According to Assessment report N,N- diethyl-meta-toluamide (DEET) Product-type 19 (repellents and attractants), 2010/03/11, analytical methods for residues in food/feed of plant and animal origins are not required as the use pattern of DEET will not result in any contact with food or feeding stuffs.

## Risk assessment for Physico-chemical properties

INSECT ECRAN ZONES INFESTEES is a ready-to-use TP 19. It is under the form of limpid liquid, not auto-flammable (up to 360°C), not explosive and does not have oxidizing properties but is classified as flammable R10 according to regulation 99/45/EC and flam. Liq. 3 / H226 according to CLP regulation.

The product is stable 14 days at 54 °C, 6 months at 40°C and 6 months at ambient temperature in commercial packaging. A shelf life of 2 years is granted.

As storage stability study at low temperature demonstrate a phase separation after storage, the following restriction is required on the label : the product must be shaken before use.

Results of the two years storage stability study including data on volume delivered by pump should be provided in post registration. Compatibility of biocidal product with commercial packaging material (PP) was demonstrated.

***Risk mitigation measures linked to assessment of physico-chemical properties***

The product must be shaken before use.

The product must not be stored more than 6 months at 40°C.

* **Minor change (2016)**

The shelf life is 3 years.

* **Minor change application for INSECT ECRAN ZONES INFESTEES – 2022:**

The shelf life is 5 years

## Effectiveness against target organisms

### Function

Main Group 03: Pest Control

Product Type 19: Repellents and attractants

INSECT ECRAN ZONES INFESTEES is presented as a ready-for-use lotion to be applied on human skin. The product is sprayed in the hand and then spread on the exposed area of the skin (*i.e.* face, neck, three-quarter arms, hands and half-legs).

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

According to the uses claimed by the applicant, INSECT ECRAN ZONE INFESTEES is intended to be used to repel arthropods. The target organisms to be controlled are mosquitoes, sand flies and ticks.The organisms to be protected are humans.

The application rate recommended by the applicant is the following: 0.40 mg/cm2 of skin

It has to be noted that most of the tested arthropods are present in France and in the overseas territories:

- *Aedes aegypti (stegomya aegypti)*: this species occurs in the Reunion, Mayotte, Guadeloupe, Martinique islands and in Guyane. This species is a vector of Dengue and Chikungunya notably in the French Antilles.

- *Aedes albopictus*: this species occurs in the Indian Ocean, including Reunion island, and Southern Europe, including France. This species is a vector of Dengue and Chikungunya notably in the French Antilles.

- Anopheles gambiae: this species is a vector of malaria (paludism), in tropical areas.

- *Culex pipiens*: mosquitoes of the Culex genus are the most present in France. It is a vector of diseases, such as Japanese encephalitis, meningitis, and West Nile fever.

- *Phlebotomus duboscqi*: This species is found in Sub-Saharan Africa. It is not present in France or in overseas territories. However, the species *P. papatasi*, very close to P*. duboscqi*, and convey the same cutaneous leishmaniasis is present in France, from the Mediterranean to the Cévennes.

- *Ixodes ricinus*: this tick species is present in Central Europe and in the North-East of France. It is a vector of Lyme disease in France.

### Effects on target organisms and efficacy

The applicant submitted following studies:

For the use against mosquitoes and sand flies:

* **An arm-in-cage study conducted with ten human volunteers with the product INSECT ECRAN ZONES INFESTEES (50% w/w DEET) on four mosquito species *(Aedes aegypti, Anopheles gambiae, Aedes albopictus and Culex pipiens)* and one sand fly specie *(Phlebotomus duboscqi).***

The duration of efficacy of the product INSECT ECRAN ZONES INFESTÉES (liquid, DEET 50% w/w) was tested under laboratory conditions against 4 mosquito species: *Culex pipiens, Aedes albopictus, Aedes aegypti and Anopheles gambiae,* and one sand fly specie: *Phlebotomus duboscqi*.

The product was sprayed at the dose of 0.40 mg/cm² i.e. 0.2 mg/cm² of DEET on the forearm. The trial began 30 minutes after the product had been applied. The control forearm was inserted into the cage, and after validation of this control (10 landings), the treated forearm was inserted into the cage for 3 minutes every hour until 8.5 to 9 hours or inefficacy considered as the first bite followed by a second one within 30 minutes.

The time of protection is up to 8.00 hours for the 4 mosquito species and up to 8.05 hours for the sand fly specie.

* **An arm-in-cage study conducted with ten human volunteers with the product INSECT ECRAN ZONES INFESTEES (50 % w/w DEET) diluted at 15 % w/w, on two mosquito species *(Aedes aegypti* and *Anopheles gambiae).***

The duration of efficacy of the product INSECT ECRAN ZONES INFESTÉES diluted at 15% w/w was tested under laboratory conditions against 2 mosquito species: *Aedes aegypti and Anopheles gambiae*.

The product was sprayed at the dose of 0.40 mg/cm² i.e. 0.06 mg/cm² of DEET on the forearm. The trial began 30 minutes after the product had been applied. The control forearm was inserted into the cage, and after validation of this control (10 landings), the treated forearm was inserted into the cage for 3 min every ½ hour until 1.5 hours or inefficacy considered as the first bite followed by a second one within 30 minutes.

As concluded by the applicant, the product containing 15 % w/w DEET hasn’t provided any protection (0.1 hour protection for both species).

* **An arm-in-cage study conducted with ten human volunteers with the product INSECT ECRAN ZONES INFESTEES (50 % w/w DEET) diluted at 25 % w/w, on two mosquito species (Aedes aegypti and Anopheles gambiae).**

The duration of efficacy of the product INSECT ECRAN ZONES INFESTEES diluted at 25% w/w was tested under laboratory conditions against 2 mosquito species: *Aedes aegypti and Anopheles gambiae*.

The product was sprayed at the dose of 0.41 mg/cm² i.e. 0.10 mg/cm² of DEET on the forearm. The trial began 30 minutes after the product had been applied. The control forearm was inserted into the cage, and after validation of this control (10 landings), the treated forearm was inserted into the cage for 3 min every ½ hour until 1.5 hours or inefficacy considered as the first bite followed by a second one within 30 minutes.

As concluded by the applicant, the product containing 25 % w/w DEET has provided 4.7 hours protection against both mosquito species: *Aedes aegypti* and *Anopheles gambiae*.

Based on these laboratory efficacy data, the time of protection of the product INSECT ECRAN ZONES INFESTEES when used at a dose of 0.40 mg/cm2 of skin is up to 8 hours for the 4 mosquito species: *Culex pipiens, Aedes albopictus, Aedes aegypti and Anopheles gambiae,* and the sand fly: *Phlebotomus duboscqi*.

Furthermore, no field studies have been submitted in support of this authorisation. As under field conditions, many factors can influence and even decrease the protection observed in the laboratory: over sweat due to high temperature, aggressiveness of wild mosquitoes compare to laboratory colonies; this kind of tests should have been performed especially to prove the effectiveness of this product in the French overseas regions.

Moreover, the TNsG on product evaluation (PT18 and 19) and the WHO guidelines require field trials to confirm the effectiveness of repellents in real in use-conditions.

To confirm this approach, FR CA has launched a European consultation. Most of the consulted Member States think that field tests are not mandatory. Given the available literature on the active substance DEET and for reasons of standardization of testing and ethics, new field trials would not be justified. Based on the results of this consultation, FR CA agrees to consider the data presented as sufficient to demonstrate the efficacy of the product INSECT ECRAN ZONES INFESTEES (50% w/w DEET).

In addition, the applicant has also provided a scientific review about efficacy of a similar product with 50 % w/w DEET concentration performed at a dose of 0.11 mg of DEET/cm2 in field conditions on Anophelesin Cameroun. This product provided 86% protection against *Anopheles gambiae* during 5 hours.

For the use against ticks:

* **A laboratory study conducted with ten human volunteers with the product INSECT ECRAN ZONES INFESTEES (50% m/m DEET) on one tick specie *(Ixodes ricinus).***

The repellent efficacy of the product INSECT ECRAN ZONES INFESTEES (DEET 50% w/w) 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 8 hours post application, with 10 ticks tested per hour and per volunteer (5 ticks every 30 minutes).

According to the applicant, all ticks crawling onto the treated area, crossing the second mark in direction to the elbow (3 cm above the border), and spending at least 60 seconds onto the treated zone were considered "not repelled". All other ticks were considered "repelled".

Criteria of the TNsG on product evaluation (PT18 and 19) 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. But this guideline says that:

- a tick is considered as repelled if:

- it not crosses 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.

This approach doesn’t modify much the laboratory’s results.

The product INSECT ECRAN ZONES INFESTEES (DEET 50 % w/w) when used at a dose of 0.41 mg/cm2 of skin provides up to 7 hours protection time against *Ixodes ricinus* (instead of 8 hours concluded by the laboratory).

As stated by the applicant, this product will be used in the French overseas regions but in the absence of supporting data on tropical species, the use of this product against ticks in tropical aeras hasn’t be authorized.

All efficacy studies are presented in annex 8.

### 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.

Recently, 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*.[[7]](#footnote-7) 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*.[[8]](#footnote-8) developed a new biological model based on mosquito neurons isolated from adults *Anopheles gambiae* heads. and revealed that AgNav ch annel and AChE enzymes which are targeted by insecticide and/or repellent were sensitive to the pyrethroid permethrin and to the repellent DEET, respectively.

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

In 2003, Xue *et al.*[[9]](#footnote-9)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.[[10]](#footnote-10)* 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).

### Occurrence of resistance – resistance management / Unacceptable Effect

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

In 2010, Stanczyk *et al[[11]](#footnote-11).* 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 (see Document IV Stanczyk *et al*., 2010).

### Evaluation of the Label Claims

French competent authorities (FR CA) assessed data presented in the dossier demonstrate that the product INSECT ECRAN ZONES INFESTÉES (DEET 50 % w/w) provides a protection time up to 8 hours when used on skin at the application rate of 0.40 mg/cm² against four representative species of mosquitoes (*Culex pipiens, Aedes albopictus, Aedes aegypti and Anopheles gambiae*) and one sand fly (*Phlebotomus duboscqi*) and, up to 7 hours when used on skin at an application rate of 0.41 mg/cm², against the tick *Ixodes ricinus*.

Moreover, in the absence of supporting data on tropical tick species, the use of this product against ticks in tropical aeras hasn’t be authorized.

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

The application rates validated are the following:

Mosquitoes (Aedes, Anopheles and Culex genus) and sand flies (Phlebotomus genus): 0.40 mg/cm2 of skin

Ticks (Ixodes genus): 0.41 mg/cm2 of skin

### Conclusion of the efficacy assessment

The product INSECT ECRAN ZONES INFESTÉES has shown a sufficient efficacy for the uses proposed in annex 0b. Nevertheless, a monitoring of the resistance phenomenon must be put in place. The collected information must be sent every 5 years to Anses within the framework of a post-authorisation monitoring.

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

* Respect the recommended application doses.
* Retreat after water exposure without exceeding the maximal recommended application number.
* The users should report straightforward to the registration holder any alarming signals which could be assumed to be resistance development.
* The label has to respect the recommended conditions of use and the biocidal products labelling guide[[12]](#footnote-12).
* The use of the product with other biocidal products or sunscreen products is not recommended.
* Protection time can be lowered by sweating, water wash off, rubbing, high temperature (>30°C), wind velocity, etc.

***Required information linked to efficacy assessment***

A monitoring of the resistance phenomenon must be put in place. The collected information must be sent every 5 years to Anses within the framework of a post-authorisation monitoring.

## Description of the intended use(s)

The validated application rates and intended uses are the following:

|  |  |  |
| --- | --- | --- |
| MG/PT | Field of uses envisaged | Likely doses at which product will be used |
| Main Group 03; Pest Control  PT19:  Repellents and attractants | Repellent against mosquitoes  *Aedes aegypti, Anopheles gambiae, Aedes albopictus*and *Culex pipiens* | 0.40 mg/cm2 of skin, protection up to 8 hours |
| Repellent against sand flies  *Phlebotomus duboscqi* |
| Repellent against ticks  *Ixodes ricinus* | 0.41 mg/cm2 of skin, protection up to 7 hours |

**Method of application**

The product INSECT ECRAN ZONES INFESTEES is an insect repellent lotion containing 50 % w/w DEET as active substance and intended to be applied on human skin to repel mosquitoes, sand flies and ticks. It is to be used by adults and children.

The product is sprayed in the hand and then spread on the exposed area of the skin (i.e. face, neck, three quarter arms, hands and half-legs) to protect people .

Since the product is formulated as a ready-for-use product, no dilution or other preparation is necessary.

INSECT ECRAN ZONES INFESTEES is packaged in 100 mL bottles for use by consumers.

## Risk assessment for human health

### Hazard potential

#### Toxicology of the active substance

The toxicology of the active substance was examined extensively according to standard requirements. The results of this toxicological assessment can be found in the CAR. The threshold limits and labelling regarding human health risks listed in Annex 4 „Toxicology and metabolism” must be taken into consideration.

The following corresponds to the summary from the final Assessment report of DEET.

*The absorption, distribution, metabolism, and excretion studies (ADME) show that, more than 80% of DEET given orally to rats is absorbed and excreted in the urine. DEET showed no evidence for accumulation. When applied dermally to rats 74-78% is absorbed and excreted in the urine. The dermal absorption of DEET occurred at a slower rate than oral absorption (peak plasma concentration ≥4 hr vs.<1 hr, respectively). Seventy-four to ninety-one percent of the administered radioactivity was excreted via urine and about 3-7% was excreted via the faeces. DEET was metabolised completely in all oral and dermal treatment groups with little or no parent compound excreted in the urine. DEET is extensively metabolized to 2 major metabolites, m-[(N,N-diethylamino)carbonyl] benzoic acid and m-[(ethylamino)carbonyl] benzoic acid. DEET is absorbed slowly (peak plasma concentration ≥8 hr), metabolised completely, and excreted rapidly when applied to human skin. Less than 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. Plasma level studies were performed in rats (oral and dermal exposure) and in dogs (oral exposure) to compare plasma levels and area under the curve (AUC) at NOAEL levels with human plasma levels and AUC (dermal exposure).*

*The acute toxicity studies show that the oral LD50 for DEET warrants a classification as Xn, R22, Harmful if swallowed. The rabbit acute dermal LD50 of DEET is greater than 2000 mg/kg and the rodent acute dermal LD50 is > 5000 mg/kg. The acute inhalation LD50 of DEET is greater than 2.02 mg/L, the highest concentration tested which is lower than the upper EU classification limit, acute toxicity category 4 according to GHS and recommended highest dose according to the OECD guideline. However, in light of animal welfare consideration, testing of animals at higher doses is not considered warranted since inhalation exposure to the product is considered negligible. Even if no mortality was observed at the limit dose tested (2.02 mg/l/4h), it can’t be fully ensured that the LC50 would be > 5mg/l/4h. The classification R20 can therefore not be fully ruled out based on this test.*

*DEET is slightly irritating to the skin. However, repeated dose studies (dermal) in pigs and rats showed that repeated dermal dosing resulted in dermal irritation at all doses tested and remained at study end. A classification as R36, Irritating to eyes is not warranted based on the results in the eye irritation test. However, the mean score for corneal opacity is 1 for three animals at 24, 48 h and 72 h, and warrants a classification as Eye Irrit 2 – H319 according to the GHS.*

*DEET did not result in a skin sensitisation response in the Buehler test.*

*Several repeated dose toxicity studies for the oral and dermal route was submitted for DEET. Male rats were the most sensitive gender to DEET for repeated dose effects. Male rats developed alpha2u-globulin nephropathy that is considered gender and species specific. This effect was not considered relevant for risk assessment. Clinical signs of neurotoxicity also occurred in dogs shortly after oral dosing. In both rats and dogs decreased body weights was observed after oral dosing with DEET. Dermal application of DEET to rats and minipigs resulted mainly in skin irritations but no systemic toxicity or pathological findings.*

*DEET showed no genotoxic potential in a battery of in vitro tests in bacteria and mammalian cells. DEET did not result in an increase in tumours in rats and mice and was not considered oncogenic in the carcinogenicity studies.*

*The teratogenicity of DEET was investigated in two species, rat and rabbit. The studies were performed according to the OECD 414 guideline and both studies were preceded by dose finding studies. However the studies were performed prior to the latest revision of the OECD guideline in 2001 and has therefore some discrepancies compared to the current guideline. The mothers were treated only during the organogenesis and not to scheduled sacrifice. The studies therefore have some limitations in assessing potential effects during later stages of embryonal development. However considered that the 2-generation study in rats gave no further indications of an embryotoxic or teratogenic effects at comparable doses, these studies are considered acceptable for risk assessment purposes. There were no teratogenic effects observed in the studies up to maternally toxic doses, embryotoxicity was only expressed as decreased foetal body weights (rats).*

*There were no effects on reproduction in a 2-generation study in rats. Parental males were the most sensitive gender based on kidney effects that were considered species specific and irrelevant for risk assessment to man. There were no effects on reproduction. The effects observed in mothers and offspring were reduced body weights, in offspring during later parts of the lactation period. The study was performed in 1989 and shows therefore some discrepancies compared to the current OECD 416 guideline. The 2-generation study was considered suitable for risk assessment despite deviations from the current OECD 416 guideline.*

*No studies were submitted by the applicant that specifically investigated neurotoxicity after dermal application. However, neurotoxicity of DEET was investigated in an acute oral delayed neurotoxicity study and in a delayed neurotoxicity study following multigenerational exposure in rats. In the acute neurotoxicity study an increased response time to heat stimulus and decreased rearing activity at one hour post-dose was observed in the high dose group. The multigenerational exposure resulted in a transient increase in locomotor activity in the high dose group. The multigenerational neurotoxicity study has some limitations in assessing the risk on exposure to the developing brain in children since there was no information on exposure to pups during lactation and no functional tests were performed on young animals.*

*Other studies were submitted to support the conclusion that the kidney effects observed in rats were species specific.*

*Medical data were collected from various resources, direct observations from clinical cases and published literature. No studies on manufacturing plant personnel were submitted in the dossier. A report was submitted where detailed information was collected in a registry from individuals who used DEET-containing insect repellents and reported local, neurologic or systemic effects. Information on concentrations of DEET products used was available but information was not obtained for application rate. In a 7 year span 12 reports of cases of major (temporary) severity were possibly related to DEET (seizure, other neurological, dermal, and other) and one case of major severity was probably related to DEET (non-neurological). Fifty-nine cases with seizures were reported with 90% of the seizure cases of major or moderate severity. People with underlying seizure disorder were not disproportionately represented (6.8%) in these 59 cases. It was concluded in the report that most of the seizures were probably idiopathic since these are not uncommon, especially in children. Furthermore it was also concluded in the report that because over 5 billion applications of DEET occurred in the population during the 7 year span the overall risk of clinically significant adverse events is extremely low.*

*Setting of an ADI is not considered necessary, since exposure to DEET is via direct application to skin.*

*The ARfD of a chemical can be defined as "an estimate of a substance in food and/or drinking water, normally expressed on a body weight basis, that can be ingested in a period of 24 hours or less, without appreciable health risk to the consumer on the basis of all the known facts at the time of evaluation” (EU guidance, 7199/VI/99/rev 6). By this definition, the setting of ARfD for DEET which is used as an insect repellent directly applied to the skin (PT19) is considered not to be relevant by RMS, since there will be no exposure of DEET via food or drinking water. However since the use of DEET containing repellents include application to the skin on hands and on clothing, there is a risk of ingestion by hand to mouth behaviour, especially in children and an AELacute is proposed to be set. According to the data base on toxicological effects there is a possibility of acute toxicity manifested as neurotoxicity. The lowest relevant NOAEL for neurotoxicity is based on clinical signs of neurotoxicity. An 8-week oral capsule study in dogs, terminated at day 5 due to severe toxicity, yielded a NOAEL of 75 mg/kg/day based on clinical signs of neurotoxicity (abnormal head movements and ptyalism, emesis, ptosis, ataxia, convulsions). Division by a standard assessment factor of 100, gives an AELacute of 0.75 mg/kg bw/day.*

*DEET is used as an insect repellent directly applied to the skin. Furthermore, there is according to the applicant currently no production of DEET within the European Union. The setting of an AOEL for professional use, bystanders and re-entry workers is therefore not considered relevant. For risk assessment in consumers an AELrepeated of 8.2 mg/kg bw/day is set based on the 90 day dermal study in rats with a NOAEL of 1000 mg/kg bw/day, the highest achievable dose and using a standard assessment factor of 100 and correction of a dermal absorption of approximately 82% in the rat. It was decided at TM II 2009, to use the dermal study in rats, even though rat was clearly not the most sensitive species with respect to neurotoxic effects. It was discussed to use an additional factor for correcting for the difference in species sensitivity. At the same time it was also discussed that the assessment factor could be reduced due to the availability of human plasma data and plasma data in both rats and dogs, as well as metabolism data in humans and rats. The use of a standard assessment factor of 100 was therefore considered appropriate.*

The current harmonised classification for toxicological properties of the active substance is the following:

|  |  |
| --- | --- |
| Classification under directive 67/548/EEC | Classification under regulation (EC) 1272/2008 |
| Xn, R22  Xi, R36/38  No specific concentration limit | Acute Tox. 4 H302  Eye Irrit. 2 H319  Skin Irrit. 2 H315  No specific concentration limit |

#### Toxicology of the substance(s) of concern

Considering the following definition of a substance of concern set in the TNsG on data requirement chapter 4 (2000), “*the substance is regarded as a substance of concern if [...] it is classified as dangerous and its concentration in the product exceeds the classification limit set in the Council Directive 88/379/EEC, as amended by Directive 1999/45/EC, for a particular dangerous property or the other classification limit indicated for the substance in a preparation set in Annex I of Council Directive 67/548/EEC or causes that the overall sum of the concentrations of dangerous substances in the product exceeds the limit for classification of the preparation set in Council Directive 88/379/EEC, as amended by Directive 1999/45/EC, for a particular dangerous property*”, INSECT ECRAN ZONES INFESTEES does not contain any substance of concern.

#### Toxicology of the biocidal product

The toxicology of the biocidal product was examined appropriately according to standard requirements. The product was not a dummy product in the EU- review program for inclusion of the active substance in Annex I of Directive 98/8/EC.

The basis for the health assessment of the biocidal product is laid out in Annex 5 ”Toxicology – biocidal product”

Most toxicity studies submitted were performed with an older formulation of INSECT ECRAN ZONES INFESTEES. Based on their concentrations in INSECT ECRAN ZONES INFESTEES, no impact on the classification of the product is expected. Therefore, since it is not expected that these differences of composition between the old and the current formulation impact the acute toxicity, the extrapolation of study results from the old formulation of INSECT ECRAN ZONES INFESTEES was accepted.

##### Percutaneous absorption

The dermal absorption of DEET formulated in INSECT ECRAN ZONES INFESTEES (containing analyzed 51.51% w/w DEET) was investigated using human skin *in vitro*. The average percentage of absorbed DEET (total % at dose site without tape strips 1&2 + total % directly absorbed (receptor fluid + receptor fluid terminal + receptor chamber)) was 5.84±2.34% and the total recovery of DEET was 98.35±2.16% when skin discs were exposed for 24 hours to 6.4 µL of INSECT ECRAN ZONES INFESTEES (old formulation) corresponding to 5.4 mg a.s/cm2. According to the Scientific Opinion of EFSA on “Guidance on Dermal Absorption” (EFSA Journal 2012; 10(4):2665)”, the standard deviation to the mean value was added since a significant variation between replicates was noted (standard deviation larger than 25% of the mean of absorption). Therefore, a dermal absorption of 8.2% was used for the risk assessment.

##### Acute toxicity

ORAL ROUTE:

| Route | Method Guideline | Test material | Species, Strain Sex, no/group | dose levels | Value LD50 | Reference |
| --- | --- | --- | --- | --- | --- | --- |
| Oral | OECD 425  G | IE-DEET-A50 (old formulation) | Sprague Dawley  6 Females | 990, 1750, 3100 mg/kg bw | 1750 mg/kg bw (95% confidence interval between 871.5 and 4260 mg/kg body weight) | Richeux. F. 2012 |
| The reliability of the estimated LD50 is low. Acceptable only as additional data | | | | | | |
| Oral | OECD 423  G | IE-DEET-A50 (old formulation) | Sprague Dawley  6 Females | 2000mg/kg bw | > 2000mg/kg bw | Richeux. F. 2012 |
| One mortality was noted. The macroscopical examination revealed a thinning of the forestomach and a thinning of the corpus associated with a smooth aspect and red foci.  In survival animals, decrease in spontaneous activity and in muscle tone, mydriasis, piloerection and noisy respiration were noted. The animals recovered a normal behaviour between 24 hours and 48 hours post dose. | | | | | | |
| Acceptable: Yes | | | | | | |

Based on these results, no classification is required for this endpoint for INSECT ECRAN ZONES INFESTEES.

DERMAL ROUTE:

| Route | Method Guideline | Test material | Species, Strain Sex, no/group | dose levels | Value LD50 | Reference |
| --- | --- | --- | --- | --- | --- | --- |
| Dermal | OECD 402  G | IE-DEET-A50 | Sprague Dawley  5 males/5 females | 2000mg/kg bw | > 2000mg/kg bw | Richeux. F. 2012 |
| No mortality occurred during the study. Neither cutaneous reactions nor systemic clinical signs related to the administration of the test item were observed. | | | | | | |
| Acceptable: Yes | | | | | | |

Based on these results, no classification is required for this endpoint for INSECT ECRAN ZONES INFESTEES.

INHALATION ROUTE:

No study was performed on the product. Considering the intended use and that only 1% of particles were inferior to 16 µm, exposure via inhalation route is considered negligible compared to dermal exposure to INSECT ECRAN ZONES INFESTEES.

Based on the composition of INSECT ECRAN ZONES INFESTEES and according to the EC Directive 1999/45, the product is not classified for this endpoint.

##### Irritation and corrosivity

SKIN IRRITATION:

A single patch test was performed on adult subjects. Only two women showed a very slight erythema 30 minutes after the removal of the patch. No irritation was observed 24 hours after the removal of the patch in any subject. Therefore, although not fully reliable, this study did not show any dermal irritation potential of INSECT ECRAN ZONES INFESTEES.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Species | Method | Test material | Result | Reference |
| Adult human volunteers  2 men and 8 women (18 – 59 years, phototype II/III) | Patch-test  48 hours, semi-occlusive | INSECT ECRAN PEAU ADULTE (old formulation) 50 µl pur | MII (Mean irritation index) = 0.10 (30 minutes after patch removal); 0.00 (24 hours after patch removal) | Nowakowska (2004) |
| Acceptable: Yes | | | | |

* Considering the results above, no classification is proposed for this endpoint for INSECT ECRAN ZONES INFESTEES.
* EYE IRRITATION TEST:
* The first test performed with the old formulation of INSECT ECRAN ZONES INFESTEES results in irreversible ocular lesions. Reversible eye irritation was observed when the test was performed with the current formulation of INSECT ECRAN ZONES INFESTEES.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Species | Method | Test material | Average Score (24h, 48h, 72h) | | | | Result | Reversibility yes/no | Reference |
| Cornea | Iris | Redness  Conjunctiva | Chemosis |
| Albino NZW rabbit  1 male | OECD 405 | IE-DEET-A50 (old formulation) | 2 | 1 | 2 | 2.7 | Irreversible irritation | Opacity and corneal vascularisation remaining on D21. | Richeux. F. 2012 |
| Albino NZW rabbit  3 females | OECD 405 | IE-DEET-A50-NF (current formulation) | 1.2 | 0 | 1.6 | 1.9 | Irritant | 14 days after instillation, no ocular reaction persisted in any animal. | Gitton. I. 2012 |
| Acceptable: Yes | | | | | | | | | |

* Based on the results of the second assay, no classification is required for this endpoint for INSECT ECRAN ZONES INFESTEES according to the Directive 67/548/EEC but a classification Eye Irrit Cat 2 H319 is required according to the Regulation (EC) no. 1272/2008.

##### Sensitisation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Species | Method | Number of animals sensitized/total number of animals | Result | Reference |
| Dunkin, Hartley guinea pigs  15 females | OECD 406 (guinea pig maximisation test)  IE-DEET-A50 (old formulation)  Intradermal injection: 3.125%  Epicutaneous induction: 100%  Challenge: 100% - 50% | 0% | Not sensitizing | Richeux. F. 2012 |
| Acceptable: Yes  Positive control studies are regularly performed on guinea pigs with α-hexylcinnamaldehyde | | | | |

Based on these results, no classification is required for this endpoint for INSECT ECRAN ZONES INFESTEES.

##### Other studies

An *in vitro* tool for measuring taste (Astree Electronic Tongue) was submitted by the applicant. This assay showed that optimum denatonium benzoate concentrations that can match the taste of INSECT ECRAN ZONES INFESTEES (current formulation) spray were estimated at a level greater than 0.25 mg/mL (0.025% - 250 ppm), which could be considered as bitter enough to induce aversion.

### Human exposure assessment

INSECT ECRAN ZONES INFESTEES is a ready-to-use product containing 50% DEET as active substance and intended to be applied to human skin. The intended use is the dermal spraying on adults and children from 1 year-old. The applicant considers that the product can be used by pregnant women in case of risk of disease transmission. According to the applicant, two applications per day must not be exceeded.

|  |  |  |
| --- | --- | --- |
| MG/PT | Field of uses envisaged | Likely concentrations at which a.s. will be used |
| Main Group 03; Pest Control  PT19:  Repellents and attractants | Professional uses | |
| No | Not relevant |
| Non-professional uses | |
| Repellent for use by consumers (non-professional users/adults and children, dermal application) against arthropods' attacks (mosquitoes, ticks and sand flies). | 50% (w/w) |

**Method of application**

The product is intended to be applied on human skin to repel mosquitoes, sand flies and ticks. The product is sprayed in the hand and then spread on the exposed area of the skin (i.e. face, neck, three quarter arms, hands and half-legs) to protect people. Since the product is formulated as a ready-for-use product, no dilution or other preparation is necessary. The size of the bottle is 100 mL. The ready-for-use spray bottle dispenses a spray dose of 120 µL (e.g. 115 mg) per spray.

#### Identification of main paths of human exposure towards active substance from its use in biocidal product

**Inhalation exposure:**

Since INSECT ECRAN ZONES INFESTEES is applied by spraying, an exposure by inhalation could be considered as possible from respiring aerosols during spraying.

Based on a study, the mass median aerodynamic diameter (MMAD) of the aerosol droplets generated by INSECT ECRAN ZONES INFESTEES is 59 μm. Only 10% of particles were < 33 μm and 1% < 16 μm.

In this context, the product is not expected to generate significant number of particles which are deposited in tracheobronchial and alveolar regions. Therefore exposure to respirable aerosol could be considered as negligible. Although this product was not considered as respirable, it could be swallowed after reflex of the body to remove product from the body by natural clearance (coughing, sneezing etc).

Finally, according to fugacity model, DEET concentration in atmosphere is expected to be less than 1% (0.6% DEET). Hence, after application, limited exposure is expected by inhalation for consumers.

**Oral exposure:**

As mentionned above, the non respirable fraction of the inhalable dose should be considered as swallowed during spraying of INSECT ECRAN ZONES INFESTEES.

Oral exposure to INSECT ECRAN ZONES INFESTEES, especially by hand-to-mouth transfer, is not expected to be a significant route of exposure. Indeed, the product INSECT ECRAN ZONES INFESTEES contains the active substance (DEET) that acts as a self deterrent because of its smell and taste and a co-formulant which is a strong deterrent for ingestion.

Hand-to-mouth transfer behaviour is more frequent in small children and concerns mainly infants until 2-3 years. However, children from 3 years of age and adults may be accidentally exposed orally to the product. In this context, a reverse scenario calculation was included to show the importance of deterrents for ingestion in the product. This scenario was assessed as an acute exposure.

**Dermal exposure:**

Dermal exposure is the primary route of exposure as the product is directly applied to the skin. According to the applicant, the product can be used on children from 1 year-old. In this context, the assessment of the scenario of a person who applies the product on another person is considered as relevant in order to consider a parent applying the product on his/her children.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Exposure path** | **Industrial use** | **Professional use** | **General public** | ***via* the environment** |
| Inhalation | Not relevant | Not relevant | Negligible | Not relevant |
| Dermal | Not relevant | Not relevant | Yes | Not relevant |
| Oral | Not relevant | Not relevant | Yes | Not relevant |

#### Direct exposure as a result of use of the active substance in biocidal product

##### Exposure of professional users

Not relevant since INSECT ECRAN ZONES INFESTEES is a consumer product applied on the skin.

##### Exposure of non-professional users

Primary exposure to INSECT ECRAN ZONES INFESTEES consists on the application of the product by spraying (2 applications per day are recommended by the applicant).

For inhalation exposure, as quoted above, considering the aerosol droplet diameter, the amount of substance is considered as mainly swallowed. As a worst case, it was considered that all the amount of substance is swallowed without taken into consideration the respirable fraction. An absorption of 100% is used for oral route.

To assess this exposure, hand held trigger spray model 2 of the TNG 2002 part 2, updated with the user guidance, was used.

| **Tier** | **Inhalation exposure – amount of substance mainly swallowed** |
| --- | --- |
| Without PPE | Systemic dose |
|  | mg a.s. / kg bw /day |
| **Task – time frame:** | **Scenario : exposure during application – two applications** |
| Adult woman | 1.79 x10-3 |
| Adult man | 1.48 x10-3 |
| 9 -14 years-old | 2.14 x10-3 |
| 3 – 9 years-old | 2.68 x10-3 |
| 1.5-3 years-old | 2.13 x10-3 |
| 12-18 months | 2.22 x10-3 |

Based on these results, the exposure by inhalation could be considered as negligible.

The exposure by dermal route was 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 male and female adults and to children. ARp, CDEET, Dermal absorption and N remain the same, the body surface exposed to the product and the body weight vary according to gender and to age range.

The product is not intended to be applied on the total body surface but on the following body segments which correspond to uncovered parts: head + neck + ¾ arms + ½ legs + hands.

According to the applicant, two applications per day must not be exceeded.

Table 2.7.2.2.2-1: Parameters for the calculation of consumer exposure to INSECT ECRAN ZONES INFESTEES.

|  |  |  |
| --- | --- | --- |
| Parameter | Value | Source |
| Average dose of product applied on skin (mg/cm²) | 0.41 | Applicant data |
| Average concentration of substance in product | 50 % w/w | Applicant data |
| Body surface exposed to the product (cm²) | See Table below | RIVM General Fact Sheet |
| Dermal absorption (%) | 8.2 | See IIIB6.4 |
| Number of product applications per day (/day) | 2 | Applicant data |
| Body weight (%) | See Table below | RIVM General Fact Sheet |

Table 2.7.2.2.2-2: Results of exposure by dermal route after application of INSECT ECRAN ZONES INFESTEES at 0.4 mg/cm2

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | BS  Body surface area cm2 (head + 3/4 arm + hands + 1/2 legs) | BW  Body weight (kg) | Mass of applied product (mg) | CDEET  Active substance concentration (%) | Mass of applied active substance (mg) | Dermal absorption (%) | Mass of absorbed active substance (mg) | ID  Active substance mg/kg |
| man | 7215 | 74 | 5916.3 | 50 | 2958.2 | 8.20 | 242.6 | 3.3 |
| woman | 6451 | 61 | 5289.8 | 50 | 2644.9 | 8.20 | 216.9 | 3.6 |
| 9-14 years-old | 5361 | 39,3 | 4396.0 | 50 | 2198.0 | 8.20 | 180.2 | 4.6 |
| 3-9 years-old (mean 4.5 years-old) | 3040 | 16.3 | 2492.8 | 50 | 1246.4 | 8.20 | 102.2 | 6.3 |
| 1.5-3 years-old | 2094 | 9.85 | 1717.1 | 50 | 858.5 | 8.20 | 70.4 | 7.1 |
| 12-18 months | 2034 | 9.47 | 1667.9 | 50 | 833.9 | 8.20 | 68.4 | 7.2 |

*In Annex 7 “Safety for non-professional operators and the general public”, the results of the exposure calculations for the active substance and the substance of concern for the non-professional user and the general public are laid out.*

#### Indirect exposure as a result of use of the active substance in biocidal product

**Hand-to-mouth behaviour**

Consumers may be incidentally exposed orally to INSECT ECRAN ZONES INFESTEES via hand-to-mouth behaviour. Even if the product contains a bittering agent, a reverse scenario calculation was included.

Table 2.7.2.3-1: Parameters for the reverse scenario calculation - hand-to-mouth transfer

|  |  |  |
| --- | --- | --- |
| Parameter | Value | Source |
| Average dose of product applied on skin (mg/cm²) | 0.41 | Applicant data |
| Average concentration of substance in product | 50% w/w | Applicant data |
| Hand or finger surface exposed to the product (cm²) | See Table below | RIVM General Fact Sheet |
| Oral absorption (%) | 100 | Assessment Report |
| Body weight (%) | See Table below | RIVM General Fact Sheet |
| Number of product applications per day (/day) | 2 | Applicant data |

The results are summarized in the table below.

Table 2.7.2.3-2: Results of the reverse scenario calculation - hand-to-mouth transfer of INSECT ECRAN ZONES INFESTEES

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Surface of one hand (cm2) | Body weight (kg) | AEL (mg/kg bw/day) | mass of substance active needed to reach the AEL (mg) | mass of product needed to reach the AEL (mg) | Skin surface put in the mouth needed to reach the AEL (cm2) | Hand surface put in the mouth to reach the AEL (%) |
| man | 468 | 74 | 0.75 | 55.5 | 111 | 135 | 28.9 |
| woman | 411.5 | 61 | 0.75 | 45.8 | 92 | 112 | 27.1 |
| 9-14 years-old | 373.4 | 39.3 | 0.75 | 29.5 | 59 | 72 | 19.3 |
| 3-9 years-old | 195.0 | 16.3 | 0.75 | 12.2 | 24 | 30 | 15.3 |
| 1.5-3 years-old | 123.6 | 9.9 | 0.75 | 7.4 | 15 | 18 | 14.6 |
| 12-18 months | 123.8 | 9.5 | 0.75 | 7.1 | 14 | 17 | 14.0 |

Based on the short-term AEL of 0.75 mg/kg bw/day, the lowest percentage of hand surface to put in the mouth to reach the AEL is 28.9% (man) or 27.1% (woman) of the surface of one hand of an adult. For children, the lowest percentage of hand surface to put in the mouth to reach the AEL is 14.0% (child between 12 and 18 months), 14.6% (children between 1.5 and 3 years old), 15.3% (child 3-9 years old) or 19.3% (child 9-14 years old) of the surface of one hand.

#### Indirect exposure via residues in food

No specific residue data were submitted in the context of this dossier. The product INSECT ECRAN ZONES INFESTEES will be used as an insect repellent directly applied to the skin. However since the use of DEET includes application to the skin (incl. hands), there is a risk to contaminate the food ingested after an application of the product in the palm surface of hands.

* Although not defined at the European level, an ARfD was proposed by ANSES in purpose of acute risk assesment. This ARfD is based on concluded AEL of 0.75 mg/kg bw/day (EU 2011) derived from an 8-weeks study on dogs (oral capsule). This 8-weeks study on dogs is not considered as the most appropriate to derive an ADI and in addition the smell and taste of the product can act as a self deterrent against repetitive ingestion (the product contains an ingredient that acts as a strong deterrent for ingestion (BITREX)).

A worst case calculation for the product INSECT ECRAN ZONES INFESTEES was realized based on proposed and acceptable conditions of use following primary exposure assesment (i.e. from 2 years old).



**Comment** : this calculation includes a dilution factor of “3” following a washing hand preconised as a restriction of use to be realized after application and before eating food. This default value was collected from the ConsExpo model[[13]](#footnote-13). This dilution factor is not deemed to be an overestimation according to physico-chemical properties of the active substance with water :

* water solubility of 11.2 g/L with no pH control (EU 2011)
* log Pow of 2.4 at pH 6 (EU 2011).

Resulted acute exposure is below 100% for adults and slightly above 100% for children. There is curently no data to refine this assesment This assessment includes several worst case estimations (transfer factor of 100% from hand to food and food to mouth) which in all likelihood are overestimations. It can be considered also that the smell and taste of the product can act as a self deterrent against repetitive ingestion.

In addition, it can be underlined that a cumulative effect following a second application would be negligible since the proposed label statement should indicate to wash hands after each application and to not applicate the product on children’s hands (which consequently highly reduce the possibility for children to ingest the product and therefore induce a non-exposure situation).

After completing a comprehensive re-assessment of DEET, US-EPA also concluded that, as long as consumers follow label directions and take proper precautions, insect repellents containing DEET do not present a health concern. Human exposure is expected to be brief, and long-term exposure is not expected. Based on extensive toxicity testing, US-EPA believes that the normal use of DEET does not present a health concern for the general population. EPA completed this review and issued its re-registration decision (called a RED) in 1998.[[14]](#footnote-14)

U.S. EPA label requirements state that[[15]](#footnote-15) :

* DEET sprays should not be applied near food
* DEET-contaminated hands should be washed prior to eating.
* DEET should not be applied to children’s hands.

Consequently

Following assessment based on supported uses for the product INSECT ECRAN ZONES INFESTEES and EPA label requirements, the following restrictions of use are proposed:

* Do not applied near food
* Do not apply to children’s hands and for other people avoid palm hand contamination or

DEET-contaminated hands should be washed carefully prior to eating.

No unacceptable risk for the consumer from residues of DEET on food is awaited.

#### Combined exposure

The assessment of the scenario of a person applying the product on another person, such as children, is considered as relevant. A reverse scenario was calculated (see section 2.7.3.4).

The secondary exposure by oral route cannot be combined to exposure by dermal route, considering that it is more appropriate to compare the relevant routes for human exposure to the AELs derived for the corresponding specific routes. Indeed, according to the CAR for DEET and the final minutes of TMII09, the dermal rat study is considered as the most appropriate study to set the AELrepeated since the dermal route is the relevant one for human exposure to DEET. In addition, since child poisoning can occur after oral exposure to DEET, inducing neurotoxic effects (seizures), it was considered more appropriate to compare the oral exposure to an AELacute based on an oral study in dogs, in which neurotoxicity was observed as an acute effect of DEET.

### Risk assessment for human health

#### Risk for direct exposure

##### Professional users

Not applicable.

##### Non-professional users

Exposure to DEET for consumer application is exclusively dermal. Contributions via other routes (inhalation and oral) are considered as negligible and not taken into account in the risk assessment.

Exposure was compared with the AELrepeated set in the Assessment Report of the active substance. The AELrepeated of 8.2 mg/kg b.w./day was based on the 90-day dermal study in rats with a NOAEL of 1000 mg/kg b.w./day, the highest achievable dose and using an assessment factor of 100 and correction for a dermal absorption of approximately 82% in the rat.

Table 2.7.3.1.2-1: Risk characterisation for non-users – direct exposure

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Systemic exposure  active substance (mg/kg) | AEL (mg/kg/d) | % AEL (%) | Number of acceptable applications per day |
| man | 3.3 | 8.2 | 40 | 5.00 |
| woman | 3.6 | 8.2 | 43 | 4.61 |
| 9-14 years-old | 4.6 | 8.2 | 56 | 3.58 |
| 3 – 9 years-old | 6.3 | 8.2 | 76 | 2.62 |
| 1.5-3 years-old | 7.1 | 8.2 | 87 | 2.29 |
| 12-18 months | 7.2 | 8.2 | 88 | 2.27 |

The results show that the % AEL for adults and children from 12 months is below 100 %. The risk is thus acceptable for adults and children from 12 months using the product INSECT ECRAN ZONES INFESTEES twice a day.

Concerning pregnant women, no exposure model is available to assess the risk for the foetus. Although no developmental effect was observed in experimental studies performed with DEET, no conclusion can be made for this population using INSECT ECRAN ZONES INFESTEES.

Finally, considering the inclusion directive for DEET, INSECT ECRAN ZONES INFESTEES must not be used on children less than two years old, and use should be restricted for children between two and twelve years old, except where motivated by the risk for human health through e.g. outbreaks of insect-borne diseases.

#### Risk for indirect exposure

Based on the reverse scenario calculation and the presence of a bittering agent in the product, adults and children with hand-to-mouth behaviour are not at significant risk of poisoning. However, hand-to-mouth transfer behaviour is more frequent in small children and concerns mainly infants until 2-3 years. Therefore, as stated in the CAR of the active substance, the product must not be intended for use on children less than 2 years-old.

#### Risk for consumers via residues in food

Based on proposed conditions of use from acceptable primary exposure and as long as consumers follow label directions detailed above and take proper precautions, acute exposure to residues in food resulting from the intended uses for INSECT ECRAN ZONES INFESTEES is unlikely to cause a significant dietary risk to the categories of users from 24 months old and adults.

#### Risk for combined exposure

The assessment of the scenario of a person applying the product on another person, such as children, is considered as relevant. Considering an AELrepeated of 8.2 mg/kg bw/day, it is calculated that about 4 applications per day are needed to exceed this AEL. This is a worst case for the scenario of an adult applying the product on a child since the calculation was made considering the amount applied on an adult (which is higher than for children).

The secondary exposure by oral route cannot be combined to exposure by dermal route, considering that it is more appropriate to compare the relevant routes for human exposure to the AELs derived for the corresponding specific routes. Indeed, according to the CAR for DEET and the final minutes of TMII09, the dermal rat study is considered as the most appropriate study to set the AELrepeated since the dermal route is the relevant one for human exposure to DEET. In addition, since child poisoning can occur after oral exposure to DEET, inducing neurotoxic effects (seizures), it was considered more appropriate to compare the oral exposure to an AELacute based on an oral study in dogs, in which neurotoxicity was observed as an acute effect of DEET.

#### Conclusion of risks assessment for human health

Acceptable risks were identified for adults and children from 1 year-old dermally exposed during the use of the product INSECT ECRAN ZONES INFESTEES twice a day.

Concerning pregnant women, no exposure model is available to assess the risk for the foetus. Although no developmental effect was observed in experimental studies performed with DEET, no conclusion can be made for this population using INSECT ECRAN ZONES INFESTEES.

Based on the reverse scenario calculation and the presence of a bittering agent in the product, adults and children with hand-to-mouth behaviour are not at significant risk of poisoning. However, hand-to-mouth transfer behaviour is more frequent in small children and concerns mainly infants until 2-3 years. Therefore, as stated in the CAR of the active substance, the product must not be intended for use on children less than 2 years-old.

Finally, considering the inclusion directive for DEET, INSECT ECRAN ZONES INFESTEES must not be used on children less than two years old, and use should be restricted for children between two and twelve years old, except where motivated by the risk for human health through e.g. outbreaks of insect-borne diseases.

When the product is not applied on young children’s hands and the palm of other users hands are washed after application, acute exposure to residues in food resulting from the intended uses for INSECT ECRAN ZONES INFESTEES is unlikely to cause a significant risk to the categories of users supported.

***Risk mitigation measures linked to risk assessment for human health***

* Do not use on children less than two years old
* Use should be restricted for children between two and twelve years old, except where motivated by the risk for human health through e.g. outbreaks of insect-borne diseases.
* Do not exceed two applications per day
* Only apply on uncovered skin
* Do not put hands in mouth after application
* Keep out of the reach of children
* Do not spray directly in the face
* Do not apply on young children’s hands. For other users, wash the palm of hands after application.
* Do not use the spray near food and surfaces that may come into contact with food or drink intended for human consumption.

## Risk assessment for the environment

### Fate and distribution in the environment of the active substance DEET

The summary of information about the active substance DEET is carried out with the data from the CAR of DEET supplied by the notifier 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).

#### 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). 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 (cf 2.8.1.1.1.4). 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 notifier 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.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **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 concentrations

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).

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **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 does 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 Pow, 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):

**PNECsoilEP = 0.0379 mg/kg wet weight soil**

#### 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 |

#### 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 Assessment

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

### Effects on environmental organisms for biocidal product

The biocidal product INSECT ECRAN ZONES INFESTEES 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 provides ecotoxicological data on algae which is the most sensitive species for the active substance DEET and activated sludge exposed to the biocidal product INSECT ECRAN ZONES INFESTEES. All the other available data are 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 is classified as “Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment” in the frame of the Directive 91/414/EEC. Nevertheless at the concentration used in INSECT ECRAN ZONES INFESTEES, the substance does not contribute to the classification of the biocidal product.

No other substance used in the biocidal product is classified for the environment.

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

##### Aquatic organisms

The product INSECT ECRAN ZONES INFESTEES is not toxic to algae (ErC50 >100 mg/L).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Test item** | **Species** | **Guideline** | **Endpoints** | **Toxicity (mg product/L)** | **Reference** |
| ***Algae*** | | | | | |
| **IE-DEET-A50 (INSECT ECRAN ZONES INFESTEES)** | *Pseudokirchneriella subcapitata* | OECD 201  Static conditions | ErC50 – 72h  EbC50 – 72h | >1001  42 | III-B 7.2.2.2 |

1 Nominal concentration

A new study with the product INSECT ECRAN ZONES INFESTEES was submitted by the applicant. A summary is presented in the table below:

|  |  |  |
| --- | --- | --- |
| **Title** | **Growth inhibition test on *Pseudokirchneriella subcapitata* with IE-DEET-A50** | |
| Author, date, N° reference | Tobor-Kaplon, M.A., 2012. Study reference 499243 | |
| GLP | Yes | |
| Deviation | No | |
| Validity/ Acceptability | * In the controls, cell density increased by an average factor of > 16 within three days. * The mean coefficient of variation for section-by-section specific growth rates in the control cultures did not exceed 35%. * The coefficient of variation of average specific growth rates during the whole test period in replicate control cultures did not exceed 7%. | |
| Method | Guideline | -OECD Guideline No.201, 2006; Annex 5 corrected 28/07/2011  -Commission Regulation (EC) No.440/2008, Part C.3, 2008; amended by EC No.761/2009.  - ISO International Standard 8692, 2004. |
|  | Organisms | *Pseudokirchneriella subcapitata* |
|  | Test item | Trade name: Insect Ecran Zones Infestées  Chemical name: N,N-diethyl-m-toluamide (DEET)  CAS No 134-62-3 |
|  | Treatments | - 3 replicates of each test concentrations: 1.0, 3.2, 10, 32 and 100 mg IE-DEET-A50 /L, i.e. 0.5, 1.6, 5.0, 16 and 50 mg DEET/L (nominal).  - 6 replicates of the control.  - 1 replicate of each concentration without algae. |
|  | Exposure | 100 mL test vessels, all-glass, containing 50 mL of test solution placed in incubator where algal cells were kept in suspension by continuous shaking, under continuous light (400-700nm) and static conditions during 72 h. |
| Results | Analysis | Growth rate inhibition and yield inhibition at 0h - 24h and 72h.  EC50 and EC10 values was based on log-linear regression analysis of the percentages of growth rate reduction and the percentages of yield inhibition *versus* the logarithms of the corresponding nominal concentrations of IE-DEET-A50. |
|  | Lethal effects | N.D. |
|  | Sub-lethal effects | The EC50 for growth rate reduction (ErC50: 0-72h) was beyond the range tested, *i.e.* exceeded 100 mg IE-DEET-A50/L (50 mg DEET/L).  The EC50 for yield inhibition (EyC50: 0-72h) was 42 mg IE-DEET-A50/L (21 mg DEET/L) with a 95% confidence interval ranging from 17 to 104 mg IE-DEET-A50/L (8.5 - 52 mg DEET/L).  The NOEC for both growth rate reduction and yield inhibition was 10 mg IE-DEET-A50/L (5.0 mg DEET/L). |
| Conclusion | Endpoints | **ErC50 > 100 mg IE-DEET-A50/L (>50 mg DEET/L).** |
| Reliability index | 1 | This study is considered as acceptable by RMS |

This study is used for the proposed classification of the product.

##### Sediment dwelling organisms

Refer to section 2.8.2.1.2

##### STP micro-organisms

A new study with the product INSECT ECRAN ZONES INFESTEES was submitted by the applicant. A summary is presented in the table below:

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Test item** | **Guideline/Test method** | **Species/inoculums** | **Endpoint / type of test** | **Exposure design duration** | **Result [mg Product/L]** | | | **reference** |
| EC20 | EC50 | EC80 |
| **IE-DEET-A50 (INSECT ECRAN ZONES INFESTEES)** | OECD 209; EEC Method C11; ISO Standard 8192 | Activated sludge | Inhibition of oxygen consumption | 3h | N.D.1 | >1000 | N.D. | III-B 7.2.3 |

1 at 100 mg/L there was 0% inhibition

|  |  |  |
| --- | --- | --- |
| **Title** | **Activated sludge respiration inhibition test (Carbon and ammonium oxidation with IE-DEET-A50** | |
| Author, date, N° reference | Desmares-Koopmans, M.J.E., 2013. Study reference 499244 | |
| GLP | Yes | |
| Deviation | No deviation | |
| Validity/ Acceptability | Study in compliance with the OECD 209 guideline quality criteria:   * The blank controls oxygen uptake rate exceeded 20 mg oxygen per one gram of activated sludge (dry weight of suspended solids) in an hour. The coefficient of variation of oxygen uptake in control replicates did not exceed 30% at the end of the definitive test. * The EC50 of 3,5-dichlorophenol was in the accepted range of 2 to 25 mg/L for total respiration (4.6 mg/L). | |
| Method | Guideline | * OECD 209 guideline, adopted 22/07/2010 –"Activated Sludge, Respiration Inhibition Test (Carbon and Ammonium Oxidation) " * Methods of Council Regulation (EC) No.440/2008 of 30/05/2008, Publication No.L142, Part C11 * ISO 8192 (2007). |
|  | Organisms | The inoculum comes from an activated sludge of the biological wastewater treatment plant. |
|  | Test item | Trade name: Insect Ecran Zones Infestées  Chemical name: N,N-diethyl-m-toluamide (DEET)  CAS No 134-62-3 |
|  | Treatments | * Blank-control; * Nitrification control (sludge + ATU (11.6 mg.L-1)) * Abiotic control; * Reference substance: 3,5-dichlorophénol (5, 12 and 30 mg.L-1); * Test item (10 mg.L-1 (1 replicate), 100 mg.L-1 (1 replicate) and 1000 mg.L-1 (3 replicates)) * Test item + ATU; |
|  | Exposure | 16 mL of synthetic medium and IE-DEET-A50 or 3,5-dichlorophénol and/or ATU made up to 250 mL with water are mixed in 1L bottle. 250 mL activated sludge are added and stirred at around 20°C and at pH 7.3-7.6 during 3 hours. |
| Results | Analysis | Respiration rate (mg O2 /L.h) |
|  | Lethal effects | N.D. |
|  | Sub-lethal effects | The combined limit / range-finding test showed 2%, 0% and an average of 23% inhibition of the respiration rate at 10, 100 and 1000 mg IE-DEET-A50/L, respectively. The inhibition observed at 1 000 mg/L was statistically significant (Two Sample t-Test: α = 0.05 Toxstat). However, no inhibition of the respiration rate was observed at 100 mg IE-DEET-A50/L. Therefore the applicant proposed that the NOEC is based on the biological effect at 100 mg/L. Nevertheless, RMS disagrees with this conclusion since only 1 replicate is used for the tested concentration of 100 mg.L-1. Therefore, no variation could be observed.  The EC50 was above the highest concentration rate tested (1 000 mg.L-1).  There was no oxygen uptake from abiotic processes and the results at 1000 mg.L-1 with a nitrification inhibitor showed that the heterotrophic inhibition of the respiration rate was slightly higher than the total inhibition. |
| Conclusion | Endpoints | IE-DEET-A50 was slightly toxic to waste water bacteria at a concentration higher than 1 000 mg.L-1. **EC50 > 1000 mg.L-1 (500 DEET mg.L-1).** |
| Reliability index | 1 | This study is considered as acceptable by RMS |

#### Atmosphere

See section 2.8.2.2

#### Terrestrial compartment

See section 2.8.2.3

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

See section 2.8.2.5

#### Summary of PNECs for product INSECT ECRAN ZONES INFESTEES

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Compartment | Species | Endpoint (mg DEET/L) | Safety factor | PNEC |
| Surface water | *Pseudokirchneriella subcapitata* | ErC50 = 50 | 1000 | 0.05 mg/L |

This PNEC value for product has not been used for risk assessment.

### Environmental exposure assessment

#### Assessment of exposure to the environment

The product INSECT ECRAN ZONES INFESTEES containing 50% DEET is used in personal insect repellent (PT19) that is applied on uncovered **human skin**. It is sprayed in the hand and then spread on the exposed area of the skin (*i.e.* face, neck, three-quarter arms, hands and half-legs). The recommended application rate is **0.4 mg product.cm-2** of skin. The application can be renewed if necessary, without exceeding two applications per day. The resistance of the product to water has not been demonstrated, therefore it is not recommended to use the product before bathing or showering.

The first route of entry in the environment is assumed to be indirect, DEET reaching the water compartment *via* STP effluents, when people bathe or take a shower after DEET application. According to Simple Treat model, the emissions will primarily affect the water compartment of aquatic environments. Contamination of soil and groundwater compartments must also be assessed as they could be indirectly exposed to the biocidal product *via* contaminated STP sludge.

The direct outdoor emissions to surface water *via* some direct flow of DEET from skin during direct contact with water while swimming can be assumed. The recommendations proposed by the applicant (it is not recommended to use the product before bathing or showering) can not be considered sufficient to waive the evaluation of direct contamination of the water compartement ; this route of direct entry in the aquatic compartment must be assessed.For both routes (direct and indirect), sediment compartment is not considered as relevant for DEET due to its low adsoprtion potential (log Pow<3).

In the following sections, PEC values for indirect exposure are derived by using the Emission Scenario Document (ESD) for PT01 (Human hygiene products)[[16]](#footnote-16) and equations from the TGD Part II (since there is no specific ESD developed for PT 19). These calculations are based on maximum amount of product consumed by individual per day as described in the intended uses. The PEC values for groundwater are calculated using FOCUS-PEARL modelling performed on the submitted information on the EU tonnage of DEET as described in the CAR for the active substance.

Direct releases to surface water are estimated according to the DE proposed ”swimming scenario” (Klein, 2011[[17]](#footnote-17)) with some modifications in order to be conservative enough.

#### Environmental emission calculations and PEC derivations

##### Indirect emission through the STP (“Scenario ESD PT01”)

**Consumption based approach for PEC STP, surface water, soil**

According to the ESD for PT01, Elocalwater (kg.d-1), *i.e.* the inflow of DEET to an STP during an emission episode, can be calculated from the formula:

**Elocalwater = Nlocal \* Finh \* Fwater \* Qforminh \* Cformweight \* Fpenetr \* 10-6**

Where

NlocalNumber of inhabitants feeding one STP (default ESD PT01 = 10 000)

Finh Fraction of inhabitants using an insect repellent (CAR value = 0.37)

Fwater Fraction released to wastewater during skin cleaning (adapted CAR value for DEET applied on skin only = 0.874 considering a dermal absorption of 8%)

Qforminh Consumption per inhabitant per day (g.day-1; Nappl\* Qformappl\*BS)

Cformweight Concentration of the active substance in the product (specific value for INSECT ECRAN ZONES INFESTEES = 500 g.kg-1)

FpenetrMarket share for DEET-containing repellent products (CAR value for DEET based products = 0.28)

Nappl Number of applications (specific value for INSECT ECRAN ZONES INFESTEES = 2 day-1)

Qformappl Consumption per application (specific value for INSECT ECRAN ZONES INFESTEES = 0.4 mg product.cm-2)

BS Body surface treated (7215 cm2; see Human Exposure Section)

According to the survey presented in the CAR regarding the uses of DEET based products (Boomsma and Parathasarathy, 1990), 37% (*Finh* 0.37) of the population use an insect repellent. This value was applied to carry out the risk assessment of the representative product presented to support DEET inclusion. It is therefore considered also applicable to INSECT ECRAN ZONES INFESTEES. It is worth noting that this value is more conservative than the value proposed in the PT01 ESD for aerosol deodorants (0.2).

A fraction of 0.874 released to wastewater (Fwater) is considered for the exposure assessment of INSECT ECRAN ZONES INFESTEES. The evaporation reported in the CAR (5%) and the dermal absorption rate specific to INSECT ECRAN ZONES INFESTEES (8%) are subtracted from the total amount of DEET applied. In fact, since the product INSECT ECRAN ZONES INFESTEES is used on skin only, applications on clothes are not considered and the emission reduction due to dermal penetration can be applied on the total quantity of INSECT ECRAN ZONES INFESTEES used.

The applicant supplied a document justifying the use of a market share (Fpenetr) specific to INSECT ECRAN ZONES INFESTEES product, instead of the default value of 0.5 from the ESD. No detailed information on the methods applied to calculate this market share is available and it is therefore not possible to consider this value for the risk assessment. A market share of 0.28 for DEET-containing repellents is considered according to the same survey study reported in the CAR and used to conclude on the Finh. Following analysis of confidential data on the market of insect repellents in France, it can be concluded that the CAR value of 0.28 covers the market share of all the DEET-containing products put on the French market.

It is worth noting that the average amount of DEET consumed per application (skin only) used in the CAR (0.9 g) is covered by the amount of DEET per application calculated as presented above on the basis of the intended uses for INSECT ECRAN ZONES INFESTEES (Qformappl × Cformweight × BS x 10-6= 1.44 g). For the comparison, the average amount of DEET consumed by the general population (0.9 g/application on skin only) has to be chosen rather than the 75th percentile of dermal exposure estimated for subgroups (for instance male adult, female adult, children...), since this value is more relevant in the context of the environmental exposure assessment conducted at the STP scale. However, it was verified that the estimation of emissions using the 75th percentile approach (1.5 g or 1.66 g of DEET per skin application for male adult or children respectively), and 2 applications per day as a mean application rate, led to the same conclusions.

Then,

**Elocalwater = 2.61 kg DEET.d-1**

The concentration in the untreated wastewater, Clocalinf, is calculated considering a daily sewage volume of 2 × 106 L (TGD II, eq.32), therefore,

**Clocalinf = 1.31 mg DEET.L-1**

According to the SimpleTreat model integrated in EUSES, the fractions to surface water and sludge in the STP considering the physico-chemical parameters of DEET are presented in the Table below:

Table 4.8.4.2‑1: Fractions of emission by the STP

|  |  |  |  |
| --- | --- | --- | --- |
| **Symbol** | **Parameter** | **Value** | **Unit** |
| **INPUTS** | | | |
|  | Characterisation of biodegradability | Readily biodegradable | [-] |
| VP | Vapour pressure | 0.23 (at 20°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 | [%] |

DEET concentrations in the STP effluent and in surface water are calculated according to the TGD equations considering the Elocalwater calculated above and the different parameters presented in the following Table:

Table 4.8.4.2‑2: Input and output values for calculation of concentrations in STP and surface water

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| ***Local emission of active substance to waste water during episode:*** | | **Value** | **Unit** | **Reference** |
| **INPUTS** | | | |  |
| Elocalwater | Emission rate to wastewater | 2.61 | [kg.d-1] | - |
| Clocalinf | Concentration in sewage water to default STP | 1.31 | [mg.L-1] | TGD Eq. 32 |
| Fstp water | Fraction emitted to water by STP | 12.6 | [%] | Table 4.8.4.2‑1 |
| Koc | Partition coefficient organic carbon-water | 43.3 | [L.kg-1] | - |
| Kpsusp | Solids-water partitioning coefficient | 4.33 | [L.kg-1] | TGD Eq. 23 |
| **OUTPUTS** | | | |  |
| PECSTP | PEC in the treated wastewater | 0.16 | [mg.L-1] | TGD Eq. 33 |
| PEClocalwater | PEC in water during emission episode | 1.65E-02 | [mg.L-1] | TGD Eq. 45 |

The concentrations in agricultural soil, following the spreading of contaminated STP sludge, are calculated according to the TGD equations considering the emissions Elocalwater and the different parameters presented in Table 4.8.4.2‑3. Degradation of the substance in soil is considered based on its ready biodegradability (DT50 sol = 30 days at 12°C); dissipation by leaching and volatilisation is also taken into account based on the TGD equations.

Table 4.8.4.2‑3: Input values and output values for the calculation of soil concentrations

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| ***Local emission of active substance to soil during episode:*** | | **Value** | **Unit** | **Reference** |
| **INPUTS** | | | | |
| Elocalwater | Emission rate to wastewater | 2.61 | [kg.d-1] | - |
| Fstp sludge | Fraction emitted to sludge by STP | 0.407 | [%] | Table 2.8.4.2-1 |
| ksoil | Rate constant for removal in soil based on biodegradation and dissipation | 0.0249 | [-] | TGD Eq. 56  TGD Eq. 57 |
| Koc | Partition coefficient organic carbon-water | 43.3 | [L.kg-1] | - |
| SLUDGERATE | Rate of sewage sludge production | 710 | [kg.d-1] | TGD Eq. 37 |
| Ksoil water | Soil-water partitioning coefficient | 1.5 | [m3.m-3] | TGD Eq. 24 |
| **OUTPUTS** | | | | |
| Csludge | Concentration in dry sewage sludge | 14.98 | [mg.kg-1dwt] | TGD Eq. 36 |
| PEC local soil | PEC in soil after 10 years of application - Twa over 30 d | 1.55E-02 | [mg.kg-1wwt] | TGD Eq. 55 |

**Tonnage based approach for PEC groundwater**

DEET concentrations in groundwater are estimated using the leaching model FOCUS-PEARL 4.4.4., which integrate transformation and dilution of the active substance in deeper soil layers. Modelling is based on the annual tonnage of DEET placed on the EU market as proposed in the CAR for the active substance inclusion, 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.

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[[18]](#footnote-18)). 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 TGD, Part II 2.3.8.5), 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/TGD, Part II 2.3.6.5, for readily biodegradable substances (30 days at 12°C).

Table 4.8.4.2‑4: Summary of data used and assumptions made to calculate PECgw for DEET in FOCUS scenariosParameters

|  |  |  |
| --- | --- | --- |
|  | **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 & Winter Cereals | Grass/alfalfa |
| Molar mass | 191.3 g/mol | 191.3 g/mol |
| Vapour pressure | 0.23 Pa | 0.23 Pa |
| Water solubility | 11200 mg/L, 25°C | 11200 mg/L, 25°C |
| Kom | 25.1 L/kg | 25.1 L/kg |
| Freundlich exponent | 0.9 (FOCUS Default) | 0.9 (FOCUS Default) |
| DT50soil | 30d | 30d |
| Coefficient for uptake by plant | 0 | 0 |

Results in **Erreur ! Source du renvoi introuvable.** show that the predicted groundwater concentrations of DEET are all below the threshold value of 0,1 µg.L-1 for all the tested conditions.

Table 4.8.4.2‑5: 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 DEET/L)** | | |
|  | **Maize** | **WinterCereals** | **Grass/alfalfa** |
| **Chateaudun** | < 0.001 | 0.001 | < 0.001 |
| **Hamburg** | 0.003 | 0.026 | < 0.001 |
| **Jokioinen** | - | 0.011 | < 0.001 |
| **Kremsmuenster** | 0.003 | 0.017 | < 0.001 |
| **Okehampton** | 0.006 | 0.032 | < 0.001 |
| **Piacenza** | 0.001 | 0.011 | < 0.001 |
| **Porto** | < 0.001 | 0.014 | < 0.001 |
| **Sevilla** | < 0.001 | < 0.001 | < 0.001 |
| **Thiva** | < 0.001 | < 0.001 | < 0.001 |

##### Direct exposure - ”swimming scenario”

No scenario for a direct exposure of surface water during recreactional activities has been proposed by the applicant in the product authorisation dossier, as a harmonized approach does not exist yet for this type of exposure. In the frame of the review program of the active substance, the direct release to surface water during swimming etc. was also not considered on reasons of missing scenario and the issue reported to the authorisation phase. A “swimming scenario” was therefore developed by the German Federal Environment Agency. This scenario is still under discussion after its presentation during the TM II/2011.

The proposed emission calculation is based on equations of EU TGD II (2003) and on the specific scenario developed by DE that simulates the release of active substance into natural and artificial lakes by swimming of people treated with a PT19 biocidal product. Some modifications of the receiving aquatic compartment volume and the number of swimmers are further proposed for the assessment of the product INSECT ECRAN ZONES INFESTEES in order to be more conservative and to better cover local conditions.

* In the proposed DE scenario, the assumed volume of a lake is set to 1 million m3 (1 000 000 000 L) as a worst case assumption, which is seen representative for a medium quarry pond and for small natural and other freshwater lakes for swimming, based on some inquiries of ponds and lakes near to urban areas in Saxony and Bavaria, known to be used by the public for swimming during bathing season.

This volume seems to be applicable to the total volume of a pond and is further used in the long-term assessment of the product INSECT ECRAN ZONES INFESTEES over the bathing season.

Nevertheless, this proposed volume of 1 million m3 seems underestimated if the risk is evaluated at short term in the bathing area, which can be reduced compared to the total volume of a water body. Considering published data on the attendance ratio of several lakes located in France[[19]](#footnote-19),[[20]](#footnote-20), a more realistic water volume of 70 000 m3, which corresponds to the specific swimming area, has been chosen for the short term assessment.

* According to DE proposal, the average number of people who are swimming at the same day in one lake or pond while using the biocidal product is set to 20 persons based on the TGD fraction of main source (Fmain source) of 0.002 for dispersive uses; this corresponds to 20 persons out of 10 000 inhabitants.

Published data on the attendance ratio of several lakes located in France showed that the maximum average number of swimmers is 780 per day. Considering the fraction of inhabitants (Finh) using a repellent product of 0.37 and the market share (Fpenetr) of 0.28 (see indirect exposure section), the number of swimmers using the repellent product INSECT ECRAN ZONES INFESTEES per day should be:

Nswim = 780 \* 0.37 \* 0.28

Nswim = 81 swimmers.day-1

* The fraction of the product which is emitted to the swimming water is set as default to Fwater = 0.874. The same emission factor as in the scenario for body cleaning is used.
* The rate constant for biodegradability in surface water is set according to Table 7 (EU TGD, 2003) considering the ready biodegradability of the active substance: k=0.047 d-1 (DT50 water = 15 days at 12°C).
* The time of swimming during the year is limited by the temperature of the air and the water, therefore it was estimated that swimming will take place once a day on 150 days per year as a maximum limit. The assessment time is set as T1d for a short term assessment and Temission for a long-term emission corresponding to 150 days.
* For PEC localwater, two situations are calculated: Clocalwater after 1 day in the bathing area (without considering degradation) and Clocalwater\_annual over 150 days in the total volume of the lake considering the constant release of the product and the degradation over time, which can be considered as a background concentration.

A cumulative assessment is further conducted for the bathing area in order to consider the release during one day in this restricted zone with the background calculated over 150 days.

Calculation steps:

1. The daily emission to the lake, Elocalwater (kg.d-1), is estimated from the formula:

**Elocalwater = Nswim \* Fwater \* Qforminh \* Cformweight \* 10-6**

Where

NswimNumber of swimmers using the repellent product INSECT ECRAN ZONES INFESTEES per day (81 d-1)

Qforminh Consumption per inhabitant per day (g.d-1; Nappl\* Qformappl\*BS)

Cformweight Concentration of the active substance in the product (specific value for INSECT ECRAN ZONES INFESTEES = 500 g.kg-1)

Nappl Number of applications (specific value for INSECT ECRAN ZONES INFESTEES = 2 day-1)

Qformappl Consumption per application (specific value for INSECT ECRAN ZONES INFESTEES = 0.4 mg product.cm-2)

BS Body surface treated (7215 cm2; see Section Human exposure)

Fwater Fraction of the product emitted to the swimming water (0.874)

**Then,**

**Elocalwater = 0.20 kg DEET.d-1**

1. **Short-term assessment**:

Calculation of Clocalwater is done considering with the volume of Vbathing area = 70 000 000 L for the bathing area, after the first day of bathing, without taking into account the degradation in surface water.

**Clocalwater= Elocalwater\*10-6 / Vbathing area**

**Then,**

**Clocalwater = 2.91E-03 mg DEET.L-1**

1. **Long-term assessment**:

Calculation of Clocalwater\_annual according to the modified equation no. 7.16 from the OECD emission scenario document for PT 8 (wood preservatives) for the constant release into a static water body (continuously input of a.s., time-weighted average concentration over one bathing season considering degradation):

With

k = rate constant for biodegradation in surface water (readily biodegradable substance = 0.047 d-1)

Vwaterbody = 1 000 000 000 L

Temission = 150 days

Then,

**Clocalwater\_annual = 3.78E-03 mg DEET.L**-1

1. **Cumulative assessment**:

Calculation of the total concentration in the bathing area considering the Clocalwater and the Clocalwater\_annual as a background concentration.

**Total Clocalwater = Clocalwater\_annual + Clocalwater**

Where

Clocalwater\_annual Background water concentration after a season

Clocalwater Local concentration at the last swimming day in the bathing area

Then,

**Total Clocalwater = 6.69E-03 mg DEET.L-1**

For the ’swimmer scenario’, the exposure of the terrestrial compartment was considered negligible.

#### Summary of PEC values

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

Table 4.8.4.3‑1: Summary of PEC values for DEET considering the indirect and direct emissions to the aquatic compartment

|  |  |  |
| --- | --- | --- |
|  | **PEC** | **Unit** |
| **Indirect emissions (via the STP – ESD PT01)** | | |
| STP | 0.16 | [mg.L-1] |
| Surface water | 1.65E-02 | [mg.L-1] |
| **Direct emissions (Swimming scenario)** | | |
| Surface water – Clocalwater  Short term assessment in the bathing area | 2.91E-03 | [mg.L-1] |
| Surface water – Clocalwater\_annual  Long term assessment in the lake | 3.78E-03 | [mg.L-1] |
| Surface water – Total Clocalwater  Cumulative assessment | 6.69E-03 | [mg.L-1] |

##### Atmospheric compartment

For DEET, the estimated half-life for the hydroxyl reaction in air is 0.63 days or 15.2 hours, the vapour pressure is 0.23 Pa (25°C) and the Henry's law constant is 3.93 x 10-3 Pa.m3.mol-1. Thus, an extensive accumulation of DEET in air and long range transport is unlikely.

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

Table 4.8.4.3‑2: Summary of PEC values for DEET for the terrestrial compartment only for indirect emissions (via the STP)

|  |  |  |
| --- | --- | --- |
|  | **PEC** | **Unit** |
| **Indirect emissions (via the STP)** | | |
| Soil | 1.55E-02 | [mg.kg-1wwt] |
| Groundwater  Focus PEARL 4.4.4 | < 0.1 | [µg.L-1] |

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

The low calculated BCF values of DEET suggest that INSECT ECRAN ZONES INFESTEES has a low potential to bioaccumulate into aquatic and terrestrial organisms.

### Risk characterisation for the environment

#### Skin application

Risk characterization for the environment is done quantitatively by comparing predicted environmental concentrations (PEC) and the concentrations below which effects on organism will not occur (PNEC) according to the Technical guidance document (TGD, 2003) and 'Emission scenario document for PT01 (Human Hygiene products)’ and equations in the TGD Part II (since there is no specific ESD available for PT19). The environmental risk characterization has been carried out for DEET.

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

The table below summarizes the risk characterization ratio for the aquatic compartment and STP.

Table 4.8.5.1‑1: Risk characterization in the aquatic compartment

|  |  |  |  |
| --- | --- | --- | --- |
|  | **PEC (mg.L-1)** | **PEC/PNEC** | |
| **Indirect emissions (*via* the STP)** | | | |
| STP | PNECSTP microorganisms = 10 mg/L | | |
| 0.16 | | 1.65E-02 |
| Surface water | PNECwater = 0.043 mg/L | | |
| 1.65E-02 | 0.38 | |
| **Direct emissions (swimming scenario)** | | | |
| Surface water | PNECwater = 0.043 mg/L | | |
| Short term assessment in the bathing area | 2.91E-03 | 6.77E-02 | |
| Long term assessment in the lake | 3.78E-03 | 8.78E-02 | |
| Cumulative assessment | 6.69E-03 | 0.16 | |

The PEC/PNEC ratios are all below the trigger value of 1. Then, risks for aquatic organisms and for STP microorganisms are acceptable for both indirect and direct emissions and after 2 daily skin applications of INSECT ECRAN ZONES INFESTEES at 0.4 mg.cm-2.

##### Atmospheric compartment

According to the characteristics of DEET, the risk to the atmospheric compartment is considered negligible.

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

The table below summarizes the PEC/PNEC ratios for terrestrial compartment including soil and the threshold values for groundwater.

Table 4.8.5.1‑2: Risk characterization in the terrestrial compartment only for indirect emissions (via the STP)

|  |  |  |
| --- | --- | --- |
|  | **PEC** | **PEC/PNEC** |
| **Indirect emissions (via the STP)** | | |
| Soil | PNECsoilEP = 0.0379 mg.kg-1wwt | |
| 1.55E-02 mg.kg-1wwt | 0.41 |
| Groundwater  Focus PEARL 4.4.4 | < 0.1 µg.L-1  Threshold value in groundwater | |

The PEC/PNEC ratio for soil compartiment is below the trigger value of 1. Then, risks for terrestrial organisms acceptable after 2 daily skin applications of INSECT ECRAN ZONES INFESTEES at 0.4 mg.cm-2.

The predicted groundwater concentrations of DEET are lower than the trigger value of 0.1 µg.L-1 for all the conditions tested in Focus PEARL 4.4.4. Consequently, the risk for groundwater is acceptable.

FR underlines that the presence of DEET in the groundwater compartment has been demonstrated in several monitoring studies performed all around the world. Although not peer reviewed, groundwater monitoring data from The Netherland (149 molecules at 189 locations), showed that in 1.6% of the samples, DEET concentrations ranged between 0.36-1.48 μg.L-1 (CAR, 2010). Therefore, monitoring data of DEET should be performed and included in national programs

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

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 is expected.

##### Conclusions

Considering indirect emissions through the STP, and according to the applicant intended uses for INSECT ECRAN ZONES INFESTEES, risks for aquatic (including water and STP), soil and groundwater are acceptable.

Considering direct emissions through bathing activities and according to the applicant intended uses for INSECT ECRAN ZONES INFESTEES, the risk for surface water is acceptable.

According to DEET properties, no risks to the atmospheric compartment and no secondary poisoning are expected.

**Therefore, it can be concluded** on acceptable environmental risks for the biocidal product INSECT ECRAN ZONES INFESTEES.

According to the recommendation in the European dossier regarding the presence of the active substance in several groundwater monitoring studies in Europe and in the world, and considering the lack of recent data in France, ANSES recommends that monitoring of DEET concentrations in groundwater have to be performed and included in national programs.

***Risk mitigation measures linked to risk assessment for environment***

* Do not use the product before bathing or showering.
* Do not exceed 2 applications of the product per day.

## Measures to protect man, animals and the environment

*See Summary of product characteristics.*

# Appendices

Annex 0a: Practical use claimed by the applicant

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Name of the product and type of formulation (gel, paste, spray, dust, powder, …)** | **Target organisms (common species and genus) and development stages (larvae, nymph, adults, female or male…)\*** | **User category (professional/non professional)\*** | **Application aim (human or animal protection)** | **Area of use (dermal, clothes, indoor or outdoor buildings…)** | **Method of application including description of system used (spraying, padding treatment….)** | **Application rate (expressed in g/m3, g/m2, ml/m2…)**  **Maximum and minimum dosage (if appropriate)** | **Mode of action including time delay (repellent or attractant)** | **Time delay of residual efficacy (hours, days, weeks and months)** | **Time delay for human , food and animals reentrance after treatment (if appropriate)** | **Frequency and duration of application (number of application, time between each application…)** | **Package details : Individual packaging (yes/no)\*\*** | **Primary packaging : type : bulk, individual wrapping…/ nature: bucket, bottle, sachet…/ material: paper, polyethylene…/** | **Size of each packaging** | **Secondary packaging** |
| **INSECT ECRAN ZONE INFESTEES**  Formulation: INSECT ECRAN ZONES INFESTEES | I.1.1.1 Ixodidae  II.1.3 Nymphs  II.1.5 Adults | V.1 Non professional user / consumer | VII.2 Health protection (human) | IV.3 Use on skin | VI.1 Spraying | 0,4 mg/cm²  Max 2 applications per day | III.2.6 Repellent | Not applicable | Not appropriate | Duration of efficacy : 8 hours | Yes | Polypropylene bottle | 125 mL bottle filled in with 100 mL of product | None |
| I.3.12.1 Culicidae  II.1.5 Adults |  |  |  |  |  | III.4.2 Residual activity (long time effect) |  |  | Number of applications : max 2 per day |  |  |  |  |
| I.3.12.4 Psychodidae  II.1.5 Adults |  |  |  |  |  | Time delay : none |  |  |  |  |  |  |  |

Annex 0b: Proposed uses for authorisation

*This table reflects the results of the risk assessment. In case of differences between the uses suggested by Anses to be authorised and the uses contained in the decision taken by the French ministry, only the original and signed decision has a legal value.*

|  |  |  |
| --- | --- | --- |
| Users | Field of uses envisaged | Likely doses at which product will be used |
| Public - Adults and children from 2 years | Repellent against mosquitoes  *Aedes aegypti, Anopheles gambiae, Aedes albopictus*and *Culex pipiens* | 0.40 mg/cm2 of skin, protection up to 8 hours  Max. 2 applications per day |
| Repellent against sand flies  *Phlebotomus duboscqi* |
| Repellent against ticks  *Ixodes ricinus* | 0.41 mg/cm2 of skin, protection up to 7 hours  Max. 2 applications per day |

Annex 1: Summary of product characteristics

*See separated file.*

Annex 2: List of studies reviewed

****



* **Minor change (2016)**

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

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Section** | **Reference N°** | **Author** | **year** | **Title** | **Owner of data** | **Letter of access** | **Data protection claimed** | **Essential for the assessment** |
|  |  |  |  | . |  | No | No | Yes |
| B | B3-B4 | Laurent E | 2014 | Longterm stability study. Guideline ICH Q1A (R1): Stability testing of New drug substances and products | COOPER |  |  |  |

* **Minor Change Application for INSECT ECRAN ZONES INFESTEES – 2018 :**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Section** | **Reference N°** | **Author** | **year** | **Title** | **Owner of data** | **Letter of access** | **Data protection claimed** | **Essential for the assessment** |
|  |  |  |  | . |  | No | Yes | Yes |
| S3 IUCLID | 3.4.1 Iuclid | Laurent. E | 2018 | IE-DEET-A50 Insect Ecran Zones Infestées  (Format Pocket 50mL), Stability study, Report No.  2779, Cooper | COOPER |  |  |  |

* **Minor Change Application for INSECT ECRAN ZONES INFESTEES – 2019 :**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Section** | **Reference N°** | **Author** | **year** | **Title** | **Owner of data** | **Letter of access** | **Data protection claimed** | **Essential for the assessment** |
|  |  |  |  | . |  | No | Yes | Yes |
| S3 IUCLID | 3.4.1 Iuclid | Laurent. E | 2019 | IE-DEET-A50 Insect Ecran Zones Infestées  (Format Pocket 250mL), Stability study, Report No.  2779, Cooper | COOPER |  |  |  |

* **Minor change application for INSECT ECRAN ZONES INFESTEES – 2022:**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Section** | **Reference N°** | **Author** | **year** | **Title** | **Owner of data** | **Letter of access** | **Data protection claimed** | **Essential for the assessment** |
|  |  |  |  |  |  |  |  |  |
| S3 iuclid | 3.4.1 iuclid | Laurent E. | 2021 | IE-DEET-A50 Insect Ecran Zones Infestées (Format 100 ml), Stability study, Report No. 3468/2, | COOPER | **no** | **Yes** | **Yes** |

Annex 3: Analytical methods residues – active substance

**DEET**

**Matrix, action levels, relevant residue and reference**

|  |  |  |  |
| --- | --- | --- | --- |
| matrix | limit | relevant residue | reference or comment |
| plant products | - | - | No exposure expected |
| food of animal origin | - | - | No exposure expected |
| soil | 0.05 mg/kg | DEET |  |
| drinking water | 0.1µg/L | DEET |  |
| surface water | 0.1 µg/L | DEET |  |
| air | - | - | No exposure expected |
| body fluids / tissues | - | - | Not required |

**Methods suitable for the determination of residues (monitoring methods)**

**Methods for products of plant origin**

Not required as the use pattern of DEET will not results in any contact with food or feeding stuffs

**Methods for foodstuffs of animal origin**

Not required as the use pattern of DEET will not results in any contact with food or feeding stuffs

**Methods for soil**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| reference | LOQ (mg/kg) | principle | comment | owner |
| Study No. DCP004/052633 | 0.01 mg/kg | LC-MS/MS | 1 transition | EUJV |

**Methods for drinking water and surface water**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| reference | LOQ (mg/kg) | principle | comment | owner |
| Study No.  103231 | 1 ng/L | LC-MS/MS | 2 transition | EUJV |

**Methods for air**

No method required based on the use pattern and properties of DEET and the biocidal product.

**Methods for body fluids/tissue**

No data required as DEET is not classified as toxic or highly toxic.

Annex 4 : Toxicology and metabolism –active substance

**<DEET>**

**Threshold Limits and other Values for Human Health Risk Assessment**

| **Summary** | | | |
| --- | --- | --- | --- |
|  | Value | Study | SF |
| AEL long-term | Not relevant |  |  |
| AEL medium-term | 8.2 mg/kg/d | 90 day study (rat, dermal) | 100 |
| AEL acute  ADI Not applicable  ARfD Not applicable | 0.75 mg/kg/d | 8 week study (dogs, oral)[[21]](#footnote-21) | 100 |
|  | | | |

|  |  |
| --- | --- |
| Inhalative absorption | No data |
| Oral absorption | > 80 % |
| Dermal absorption | Rat: 82%  Human: <20% |

| **Classification** | |
| --- | --- |
| with regard to toxicological data (according to the criteria in Dir. 67/548/EEC) | Xn  R22 R36/38 |
| with regard to toxicological data (according to the criteria in Reg. 1272/2008) | Acute Tox. 4 H302: Harmful if swallowed  Eye Irrit. 2 H319: Causes serious eye irritation  Skin Irrit. 2 H315: Causes skin irritation. |

Annex 5 : Toxicology – biocidal product

**< INSECT ECRAN ZONES INFESTEES>**

|  |  |
| --- | --- |
| General information | |
| Formulation Type | Spray |
| Active substance(s) (incl. content) | DEET (48.50%) |
| Category | PT19 |

| Acute toxicity, irritancy and skin sensitisation of the preparation (Annex IIIB, point 6.1, 6.2, 6.3) | | | | |
| --- | --- | --- | --- | --- |
| Rat LD50 oral (OECD 423) | > 2000 mg/kg bw/day |  |  |  |
| Rat LD50 dermal (OECD 402) | > 2000 mg/kg bw/day |  |  |  |
| Rat LC50 inhalation | Justification for non submission |  |  |  |
| Skin irritation (patch test on volunteers) | Not irritating to skin |  |  |  |
| Eye irritation (OECD 405) | Irritant |  |  |  |
| Skin sensitisation (OECD 406) | Non sensitizing |  |  |  |

| Additional toxicological information (e.g. Annex IIIB, point 6.5, 6.7) | | | | |
| --- | --- | --- | --- | --- |
| Short-term toxicity studies | Not relevant |  |  |  |
| Toxicological data on active substance(s) (not tested with the preparation) |  |  |  |  |
|  |  |  |  |  |
| Toxicological data on non-active substance(s) (not tested with the preparation) |  |  |  |  |
|  |  |  |  |  |
| Further toxicological information |  | | | |

|  |  |
| --- | --- |
| Classification and labelling proposed for the preparation with regard to toxicological properties (Annex IIIB, point 9) | |
| Directive 1999/45/EC | None |
| Regulation 1272/2008/EC | Eye Irrit Cat 2 H319: Cause serious eye irritation |

Annex 6 : Safety for professional operators

**< INSECT ECRAN ZONES INFESTEES>**

**Exposure assessment**

| **Exposure scenarios for intended uses (Annex IIIB, point 6.6 )** |
| --- |

Primary exposure of professionals: not relevant

Risk assessment: not relevant

Annex 7 : Safety for non-professional operators and the general public

**< INSECT ECRAN ZONES INFESTEES>**

| General information | |
| --- | --- |
| Formulation Type | Spray |
| Active substance(s) (incl. content) | DEET (50%) |
| Category | PT19 |
| Authorisation number |  |

| **<DEET>** |
| --- |

| Data base for exposure estimation | |
| --- | --- |
| according to | Appendix: Toxicology and metabolism – active substance/CAR |

| Exposure scenarios for intended uses (Annex IIIB, point 6.6 ) | |
| --- | --- |
| Primary exposure | Spraying |
| Secondary exposure, acute | Hand-to-mouth behaviour |
| Secondary exposure, chronic | Not relevant |

Conclusion:

Primary exposure:

Dermal exposure of adults and children from 1 year-old to the biocidal product containing DEET as active substance induces acceptable risk, if the biocidal product is used as intended and all safety advices are followed.

Secondary exposure:

Based on the reverse scenario calculation and the presence of bittering agent, adults and children with hand-to-mouth behaviour are not at significant risk of poisoning.

Details for the exposure estimates – Direct exposure:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Component** | **CAS** | **Dermal  Exposure**  **[mg/kg/d]** | **Inhalation Exposure**  **[mg/kg/d]** |
| Man | DEET | 134-62-3 | 3.3 | 1.5 x10-3 |
| Woman | DEET | 134-62-3 | 3.6 | 1.8 x10-3 |
| 9-14 y-o | DEET | 134-62-3 | 4.6 | 2.1 x10-3 |
| 3-9 y-o (mean 4.5 yo) | DEET | 134-62-3 | 6.3 | 2.7 x10-3 |
| 1.5-3 y-o | DEET | 134-62-3 | 7.1 | 2.1 x10-3 |
| 12-18 months | DEET | 134-62-3 | 7.2 | 2.2 x10-3 |

Inhalation exposure is considered as negligible and was not taken into account in the risk characterization.

Risk assessment – dermal exposure

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Component** | **CAS** | **AEL [mg/kg/d]** | **Absorption [%]** | **Total syst exposure**  **[mg/kg bw/d]** | **% AEL** | **Risk** |
|  |  |  |  | dermal |  |  |  |
| Man | DEET | 134-62-3 | 8.2 | 8.2 | 3.3 | 40 | Acceptable |
| Woman | DEET | 134-62-3 | 8.2 | 8.2 | 3.6 | 43 | Acceptable |
| 9-14 y-o | DEET | 134-62-3 | 8.2 | 8.2 | 4.6 | 56 | Acceptable |
| 3-9 y-o | DEET | 134-62-3 | 8.2 | 8.2 | 6.3 | 76 | Acceptable |
| 1.5-3 y-o | DEET | 134-62-3 | 8.2 | 8.2 | 7.1 | 87 | Acceptable |
| 12-18 months | DEET | 134-62-3 | 8.2 | 8.2 | 7.2 | 88 | Acceptable |

Annex 8 : Efficacy of the active substance from its use in the biocidal product (\*)

| Test substance | Test organisms | Test system / Concentrations applied / exposure time | Test conditions | Test results: effects, mode of action, resistance | Reference | RI |
| --- | --- | --- | --- | --- | --- | --- |
| INSECT ECRAN ZONES INFESTEES (less than one year old), DEET 50 % w/w | *Aedes aegypti*  *Anopheles gambiae*  *Aedes albopictus*  *Culex pipiens*  *Phlebotomus duboscqi*  For each test organism, 200 ± 10 females (5 to 7 days old) for each replicate. | Laboratory test.  Arm-in-cage study.  10 volunteers (5 men and 5 women).  Product applied on one forearm of each volunteer, the other untreated one being used as a control. Dose of product 0.40 mg/cm² (± 0.01), *i.e.* 2 sprays for a forearm which corresponds to an average area of 600 cm².  The trial began 30 minutes after the product had been applied. The control forearm was inserted into the cage for 30 seconds, and after validation of this control (10 landings of test organism), the treated forearm was inserted into the cage for 3 minutes (exposure time).  The same procedure was repeated every hour until 7 hours and then every 30 minutes, until inefficacy.  Landings and bites were counted during each exposure time. | 200 ± 10 insects in each cage, 10 volunteers for each test organism.  Ambient conditions in testing chamber were maintained during the period of testing at a temperature of 25 ± 2°C, a relative humidity of 65 ± 5% and with smooth ventilation (30 m3/h).  Throughout the duration of the trial, the cages were maintained at a temperature of 27 ± 2°C, a relative humidity of 70 ± 10%, with a light intensity of 700 lux. | Repellent efficacy = the ability to offer a subject total protection (100 %) against the bites of arthropods.  Duration of the repellent efficacy = time between application of the product and the first bite, followed by a second one.  The average duration of efficacy was 8 hours for the 4 species of mosquitoes and 8.05 hours for the sand fly tested. | Serrano B. (2012)  B5.10/01 | 1 |
| DEET 15 % w/w, dilution of INSECT ECRAN ZONES INFESTEES | *Aedes aegypti.*  *Anopheles gambiae.*  For each test organism, 200 ± 10 females (5 to 7 days old) for each replicate. | Laboratory test.  Arm-in-cage study.  10 volunteers (5 men and 5 women).  Product applied on one forearm of each volunteer, the other untreated one being used as a control. Dose of product 0.41 mg/cm² (± 0.02), *i.e.* 2 sprays for a forearm which corresponds to an average area of 600 cm².  The trial began 30 minutes after the product had been applied. The control forearm was inserted into the cage for 30 seconds, and after validation of this control (10 landings of test organism), the treated forearm was inserted into the cage for 3 minutes (exposure time).  The same procedure was repeated every 30 minutes until inefficacy.  Landings and bites were counted during each exposure time. | 200 ± 10 insects in each cage, 10 volunteers for each test organism.  Ambient conditions in testing chamber were maintained during the period of testing at a temperature of 25 ± 2°C, a relative humidity of 65 ± 5% and with smooth ventilation (30 m3/h).  Throughout the duration of the trial, the cages were maintained at a temperature of 27 ± 2°C, a relative humidity of 70 ± 10%, with a light intensity of 700 lux. | Repellent efficacy = the ability to offer a subject total protection (100%) against the bites of arthropods vectors.  Duration of the repellent efficacy = time between application of the product and the first bite, followed by a second one.  The average duration of repellency was 0.1 hours for the 2 species of mosquitoes. No relevant protection against mosquitoes demonstrated. | Serrano B. (2012)  B5.10/02 | 2 |
| INSECT ECRAN ZONES INFESTEES (less than one year old), DEET 50% w/w | *Ixodes ricinus* (sheep tick)  80 nymphs for each replicate. | Laboratory test.  Simulated-use test: run test.  10 volunteers (5 men and 5 women).  Dose of product 0.411 mg/cm² (± 0.021).  Product applied on one forearm of each volunteer, leaving the lowest 5 cm near the wrist untreated. 3 marks on the forearm: at the border between treated and untreated zone, 3 cm below and 3 cm within the treated area. The arm was held vertically (with the fingertips or palm placed on a horizontal surface) and a tick was placed on the first mark, 3 cm below the treated area. Each test run lasted a maximum of 3 minutes.  The test lasted for 8 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. | 8 hour periods \* 10 ticks \* 10 volunteers  Temperature and relative humidity continuously recorded, and ambient conditions maintained during the period of testing at an average temperature of 22.1 ± 0.7°C, relative humidity 41.8 ± 4.1% in the test room. | 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 INSECT ECRAN ZONES INFESTEES showed an efficacy period of 7 hours. | Dautel H. (2012)  B5.10/03 | 1 |

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2. Guide à l’intention des responsables de la mise sur le marché des produits biocides. Lignes directrices sur l’étiquetage des produits biocides mis sur le marché. Version du 28 août 2007. [↑](#footnote-ref-2)
3. Applies only to existing authorisations [↑](#footnote-ref-3)
4. Please insert additional columns as necessary [↑](#footnote-ref-4)
5. Please insert additional columns as necessary [↑](#footnote-ref-5)
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12. Guide à l’intention des responsables de la mise sur le marché des produits biocides. Lignes directrices sur l’étiquetage des produits biocides mis sur le marché. Version du 28 août 2007. [↑](#footnote-ref-12)
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