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 RENEWAL OF NATIONAL AUTHORISATION APPLICATIONS**

(submitted by the evaluating Competent Authority)



VAPO REPULSIF CORPOREL ANTI-MOUSTIQUE

Product type 19

DEET

Case Number of REPULSIF ANTI-MOUSTIQUE CORPOREL in R4BP: BC-KY010403-26

Major Change of VAPO REPULSIF CORPOREL ANTI-MOUSTIQUES in R4BP: BC-JM058595-20

Evaluating Competent Authority: FR

Date: December 2013

Updated May 2021

Contents

[1 GENERAL INFORMATION ABOUT THE PRODUCT APPLICATION 4](#_Toc370299705)

[1.1 Applicant 4](#_Toc370299706)

[1.1.1 Person authorised for communication on behalf of the applicant 4](#_Toc370299707)

[1.2 Current authorisation holder 4](#_Toc370299708)

[1.3 Proposed authorisation holder 5](#_Toc370299709)

[1.4 Information about the product application 5](#_Toc370299710)

[1.5 Information about the biocidal product 5](#_Toc370299711)

[1.5.1 General information 5](#_Toc370299712)

[1.5.2 Information on the intended use(s) 6](#_Toc370299713)

[1.5.3 Information on active substance(s) 6](#_Toc370299714)

[1.5.4 Information on the substance(s) of concern 7](#_Toc370299715)

[1.6 Documentation 7](#_Toc370299717)

[1.6.1 Data submitted in relation to product application 7](#_Toc370299718)

[1.6.2 Access to documentation 8](#_Toc370299722)

[2 Summary of the product assessment 9](#_Toc370299723)

[2.1 Identity related issues 9](#_Toc370299724)

[2.2 Classification, labelling and packaging 9](#_Toc370299725)

[2.2.1 Classification of the active substance 9](#_Toc370299726)

[2.2.2 Classification of the biocidal product 10](#_Toc370299727)

[2.2.3 Labelling of the biocidal product 10](#_Toc370299728)

[2.2.4 Packaging of the biocidal product 11](#_Toc370299729)

[2.3 Physical/chemical properties and analytical methods 11](#_Toc370299730)

[2.3.1 Active ingredient 11](#_Toc370299731)

[2.3.2 Biocidal product 11](#_Toc370299732)

[2.4 Risk assessment for Physico-chemical properties 19](#_Toc370299733)

[2.5 Effectiveness against target organisms 20](#_Toc370299734)

[2.5.1 Function 20](#_Toc370299735)

[2.5.2 Organisms to be controlled and products, organisms or objects to be protected 20](#_Toc370299736)

[2.5.3 Effects on target organisms and efficacy 21](#_Toc370299737)

[2.5.4 Mode of action including time delay 23](#_Toc370299741)

[2.5.5 Occurrence of resistance – resistance management / Unacceptable Effect 24](#_Toc370299742)

[2.5.6 Evaluation of the Label Claims 24](#_Toc370299743)

[2.5.7 Conclusion of the efficacy assessment 24](#_Toc370299744)

[2.6 Description of the intended use(s) 25](#_Toc370299745)

[2.7 Risk assessment for human health 27](#_Toc370299746)

[2.7.1 Hazard potential 27](#_Toc370299747)

[2.7.2 Human exposure assessment 32](#_Toc370299748)

[2.7.3 Risk assessment for human health 38](#_Toc370299749)

[2.8 Risk assessment for the environment 41](#_Toc370299750)

[2.8.1 Fate and distribution in the environment of the active substance DEET 41](#_Toc370299751)

[2.8.2 Effects on environmental organisms for active substance DEET 42](#_Toc370299752)

[2.8.3 Effects on environmental organisms for biocidal product 45](#_Toc370299753)

[2.8.4 Environmental exposure assessment 46](#_Toc370299754)

[2.8.5 Risk characterisation for the environment 55](#_Toc370299756)

[2.9 Measures to protect man, animals and the environment 59](#_Toc370299759)

[3 Proposal for decision to be adopted by the French CA (Ministry of Ecology) 60](#_Toc370299760)

[4 Annexes 63](#_Toc370299761)

[Annex 0a: Practical use claimed by the applicant 63](#_Toc340131674)

[Annex 0b : practical uses validated by RMS France 64](#_Toc340131675)

[Annex 1: Summary of product characteristics 65](#_Toc340131676)

[Annex 2: List of studies reviewed 66](#_Toc340131677)

[Annex 3: Analytical methods residues – active substance 70](#_Toc340131678)

[Annex 4: Toxicology and metabolism –active substance 72](#_Toc340131679)

[Annex 5: Toxicology – biocidal product 73](#_Toc340131680)

[Annex 6: Safety for professional operators 74](#_Toc340131681)

[Annex 7: Safety for non-professional operators and the general public 75](#_Toc340131682)

[Annex 8: Efficacy of the active substance from its use in the biocidal product 79](#_Toc340131684)

# Note to the reader

This consolidated PAR for the major change of the product authorisation of VAPO REPULSIF CORPOREL ANTI-MOUSTIQUES CORPOREL is based on the PAR of the first authorisation of the product REPULSIF ANTI-MOUSTIQUE CORPOREL, from which VAPO REPULSIF CORPOREL ANTI-MOUSTIQUES is a same product. All addenda have been included in this document.

In part 1.1 of this consolidated PAR, the summary of product characteristics is pointed out and corresponds to the decision for the major change application.

In part 2 of this consolidated PAR, each section contains the initial assessment and the subsequent successive assessments (major change), the assessments related to the major change of the product are at the end of each section and are highlighted in grey.

**History of the dossier**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Application type | refMS | Case number in the refMS | Decision date | Assessment carried out (i.e. first authorisation / amendment /renewal) |
| NA-APP | *FR* | BC-KY010403-26 | 21/11/2014 | First authorisation |
| NA-BBS | *FR* | BC-MT053126-21 | 08/10/2019 | Same application for the product VAPO REPULSIF CORPOREL ANTI-MOUSTIQUES |
| NA-MAC | *FR* | BC-JM058595-20 | 19 mai 2021 | Major Change :* Addition of target organism, ticks, *Ixodes ricinus*
* Extension of shelf life to 3 years.
* Change of co-formulant
* Change of classification
* Addition of trade names
* Modification of the application rate
 |

1. **CONCLUSION**

**Major change application for VAPO REPUSLIF CORPOREL ANTI-MOUSTQUE – 2020 :**

**Conclusion physico chemical properties and analytical methods :**

The major change consists in the replacement of a solvent by another at the same content. New physico chemical studies and analytical method have been provided to support the composition change and are acceptable. Following the composition change, the product is not anymore classified as flammable.

Based on the results of the accelerated storage study with the new formulation, a shelf life of 2 years can be granted. The previous composition was also found to be stable up to 2 years at ambient temperature. For this application, the applicant claims a shelf life of 3 years and a new storage stability study (3 years) is ongoing. eCA considers that the product is stable up to 2 years since results at 3 years are not yet available. The applicant will need to submit a minor change dossier to confirm the shelf life of 3 years including final results of the ongoing study.

**Conclusion on efficacy :**

The product product VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE provides a protection time against mosquitoes (Culex spp. and Aedes spp.) up to 8 hours in temperate conditions, mosquitoes (Anopheles spp.) up to 7 hours in tropical conditions, and ticks (Ixodes ricinus) up to 7 hours in temperate conditions, when used on skin at the application rate of 0.5 mg / cm².

**Conclusion on human health :**

The data submitted by applicant in the framework of this application for major change are considered acceptable. In particular, the data submitted to modify the classification are acceptable and the product is now classified H319 instead of H318.

**Conclusion for the environment :**

The major change consisting in the replacement of a solvent by another at the same content has no impact on the environmental risk assessment.

The reduction of the application rate has no impact on the initial risk assessment.risk assessment.

# GENERAL INFORMATION ABOUT THE PRODUCT APPLICATION

## Summary of the product assessment – Major change 2020

### Administrative information

#### Identifier of the product

| **Identifier** | VAPO REPULSIF CORPOREL ANTI-MOUSTIQUE  |
| --- | --- |
| Trade names | Répulsif Corporel Adultes 30% Répulsif Corporel Anti-Moustiques Ultra Répulsif Corporel Adultes Tropiques Répulsif Anti-Tiques Corporel Plus Répulsif Anti-Tiques Peaux Longue Durée Spray Répulsif Anti-Moustiques Anti-Tiques Répulsif Corporel Anti-Moustiques Choc |

#### Authorisation holder

|  |  |  |
| --- | --- | --- |
| **Name and address of the authorisation holder** | **Name** | SARL SPRING |
| **Address** | 4 Rue Blaise Pascal ZI du Bois de Leuze13310 Saint-Martin de CrauFrance |
| **Authorisation number** |  |
| **Date of the authorisation** |  |
| **Expiry date of the authorisation** |  |

#### Manufacturer(s) of the products

|  |  |
| --- | --- |
| **Name of manufacturer** | SARL SPRING |
| **Address of manufacturer** | 4 Rue Blaise Pascal ZI du Bois de Leuze13310 Saint-Martin de CrauFrance |
| **Location of manufacturing sites** | 4 Rue Blaise Pascal ZI du Bois de Leuze13310 Saint-Martin de CrauFrance |

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

|  |  |
| --- | --- |
| **Active substance** | N,N-diéthyl-méta-toluamide |
| **Name of manufacturer** | VERTELLUS PERFORMANCE MATERIALS |
| **Address of manufacturer** | 2110 High Point Road NC27403 GreensboroUSA |
| **Location of manufacturing sites** | 2110 High Point Road NC27403 GreensboroUSA |

### 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 [x]

#### 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[[1]](#footnote-2)

| **Common name** | **IUPAC name** | **Function** | **CAS number** | **EC number** | **Content (%)** |
| --- | --- | --- | --- | --- | --- |
| DEET (technical)Purity 97% | N, N'-diethyl-m-toluamide | Active substance | 134-62-3 | 205-149-7 | 30.93 |

#### Information on technical equivalence

Not relevant

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

Not relevant

#### Assessment of endocrine disruption (ED) properties of the biocidal product

Not relevant

#### Type of formulation

|  |
| --- |
| AL – Any other liquid |

### Hazard and precautionary statements[[2]](#footnote-3)

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

| **Classification** |
| --- |
| Hazard category | Eye Irrit. 2 |
| Hazard statement | H319 : Causes serious eye irritation  |
|  |
| **Labelling** |
| Signal words | Attention |
| Hazard statements | H319 : Causes serious eye irritation |
| Precautionary statements | P101 : If medical advice needed, have product container or label at hand.P102 : Keep out of reach of children.P103 : Read label before use.P233: Keep container tightly closed.P305+P351+P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsingP337+P313: If eye irritation persists: Get medical advice.P264: Wash… thoroughly after handling.P370+P378: In case of fire: Use carbon dioxide for extinction.P403+P235: Store in a well-ventilated place. Keep coolP501: Dispose of contents to CONTAINERS. |
|  |
| Note |  |

### Authorised use(s)

#### Use description[[3]](#footnote-4)

Table 1. Use # 1 – Repellent – Mosquitoes and ticks – Skin

|  |  |
| --- | --- |
| **Product Type** |  19 |
| **Where relevant, an exact description of the authorised use** |  |
| **Target organism (including development stage)** | Mosquitoes :*Aedes spp.**Anopheles spp.**Culex spp.*Development stage: adultsTicks:*Ixodes ricinus* |
| **Field of use** | Use on skin for health protection |
| **Application method(s)** | Spraying on human skinFor France only : The product is sprayed on the palm of the hands then spread on exposed skins (face, neck, ¾ arms, hands and ½ legs). |
| **Application rate(s) and frequency** | One daily application only of 0.5 mg product / cm² of skin equivalent to 2 sprays for an adult 600 cm² forearm, or 1 spray for a child (6-12 years) 386 cm² forearm. Temperate conditions:Mosquitoes (*Aedes spp. and Culex spp)*: Protection time up to 8 hoursTicks (*Ixodes ricinus*): Protection time up to 7 hours.Tropical conditions: Mosquitoes *(Anopheles spp):* Protection time up to 7 hours |
| **Category(ies) of users** | Non professional |
| **Pack sizes and packaging material** | Polypropylene flask with spray pump (PP/POM) with three different volumes (80 mL, 100 mL and 150 mL). |

#### Use-specific instructions for use[[4]](#footnote-5)

|  |
| --- |
| - |

#### 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[[5]](#footnote-6)

|  |
| --- |
| * Comply with the instructions for use.
* The product must be shaken before use.
* Only use in ventilated areas.
* Respect the recommended application doses.
* In case of need of sunscreen, wait at least 20 minutes after the application of this protection to apply the repellent.
* Protection time can be lowered by sweating, water wash off, rubbing, high temperature (>30°C), wind velocity, etc..
* The authorization holder should be informed in case of inefficiency of the treatment.
 |

#### Risk mitigation measures

|  |
| --- |
| * Do not use on children less than 6 years old.
* Do not use on children between 6 and 12 years old and for pregnant women, except where motivated by the risk for human health through e.g. outbreaks of insect-borne diseases.
* For children between 6 and 12 years old, the repellent should be applied by adults.
* Warning: For children between 6 and 12 years old: Wear long sleeved shirt and long trousers.
* Do not exceed one application per day.
* Only apply on uncovered skin (France specific : face, neck, three quarter arms, hands and half-legs).
* Do not spray directly on face but spray on hands and apply to face.
* Do not apply on eyelids and eyes
* Do not apply on damaged skin (skin lesions, sunburn, skin disease…)
* Do not put hands in mouth after application.
* To prevent contamination of food, avoid contact of treated skin with food.
* Do not use the spray near food and surfaces that may come into contact with food or drink intended for human consumption.
* Keep away from food, drink and animal feeding stuff.
* Do not use the product before bathing or showering.
 |

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

|  |
| --- |
| * If swallowed: Risk of dizziness and loss of consciousness. Ingestion may lead to acute poisoning. Immediately contact the 15 (or 112) or poison control center. Do not induce vomiting without medical advice.
* In case of contact with eyes: If necessary, remove contact lenses. Wash under tepid water for about ten minutes, eyes open, do not forget to wash under eyelids. If the eye remains red after two hours, consult a doctor.
* In case of skin lesions, red patches or persistent pain after applying the product, consult a doctor.
* The active substance in the product (DEET) is likely to introduce a nervous hyperexcitability especially with sensitive person (epileptic) or when co-exposure with a convulsant product.
 |

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

|  |
| --- |
| * Dispose of unused product, its packaging and all other waste (i.e. plastic sheet) in accordance with local regulations.
* Do not discharge unused product on the ground, into water courses, into pipes (sink, toilets...) nor down the drains.
* In case of accidental leaking of the product, collect the product using an absorbing material (i.e sand,etc..) and dispose it as a dangerous waste.
 |

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

|  |
| --- |
| * The product must not be stored more than 2 weeks at 54°C.
* Shelf-life: 2 years at 25°C.
 |

### Other information

|  |
| --- |
| - |

## Documentation

### Data submitted in relation to product application

**Identity, physicochemical and analytical method data**

Physico-chemical properties studies and analytical methods on the biocidal product REPULSIF ANTI-MOUSTIQUES CORPOREL were provided by the applicant.

* **Major change application for VAPO REPULSIF CORPOREL ANTI-MOUSTIQUE – 2020:**
* A storage stability study of 3 years with the old formulation has been received in January 2019 in the frame of the Mutual Recognition in Sequence. As the initial authorization was for a shelf life of 2 years, this information was not updated in the frame of the Mutual Recognition in Sequence and can only be updated in the frame of a minor change application. Data were reported in this dossier for information but they refer to the old formulation.
* A new accelerated storage stability study has been provided for the new formulation and is found acceptable. A long term storage stability 3 years at ambient temperature with the new formulation is also on going. Only a shelf life of 2 years can only been extrapolated from the results of the accelerated storage. If the applicant claims a shelf life of 3 years, a minor change dossier including results of the storage stability study with the new formulation should be provided.
* A new study for flammability with the new composition has been provided to remove the classification H226.

**Efficacy data**

* **First authorization - 2014**

## An arm-in-cage study conducted with three human volunteers with the product REPULSIF ANTI-MOUSTIQUES CORPOREL (30 % m/m DEET) applied on the skin against four mosquito species *(Aedes aegypti, Anopheles gambiae, Aedes albopictus and Culex pipiens).*

## An arm-in-cage study conducted with three human volunteers with the product REPULSIF ANTI-MOUSTIQUES CORPOREL (30 % m/m DEET) applied on the skin against four mosquito species *(Aedes aegypti, Anopheles gambiae, Aedes albopictus and Culex pipiens).*

## An arm-in-cage study conducted with three human volunteers with the product REPULSIF ANTI-MOUSTIQUES CORPOREL (30 % m/m DEET) applied on fabric (coton) against four mosquito species *(Aedes aegypti, Anopheles gambiae, Aedes albopictus and Culex pipiens).*

* **Major change application for VAPO REPULSIF CORPOREL ANTI-MOUSTIQUE – 2020:**
* A laboratory study conducted with ten human volunteers with the product **VAPO REPULSIF CORPOREL ANTI-MOUSTIQUE** (30 % m/m DEET) applied on the skin againstone tick species (***Ixodes ricinus***).
* An arm-in-cage study conducted with ten human volunteers with the product **VAPO REPULSIF CORPOREL ANTI-MOUSTIQUE** (30 **%** m/m DEET) applied on the skin against three mosquitoes species *(****Aedes aegypti, Anopheles gambiae*** *and* ***Culex pipiens****).*

**Residues data:**

No specific residue data were submitted in context of this dossier. The product REPULSIF ANTI MOUSTIQUES CORPOREL 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**

Toxicity studies submitted were performed with REPULSIF ANTI MOUSTIQUES CORPOREL (see annex 5).

* **Major change application for VAPO REPULSIF CORPOREL ANTI-MOUSTIQUE– 2020:**
* New toxicological studies for eye irritation have been submitted: Barré T., 2019 ; Richeux. F, 2019.

**Ecotoxicology data**

One new study has been submitted for the product authorisation level:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **DOC-III B reference** | **Type of data** | **Date** | **Guideline** | **GPL** | **Reference** |
| 7.2.2. | Acute aquatic toxicity | Algae | 2013 | OECD 201(28/07/2011) | Yes | [Martin C., 2013, Algae *Pseudokirchneriella subcapitata*, 72h-growth inhibition test performed on the test item "SUBITO REPULSIF MOUSTIQUES ADULTE", according to the OECD 201 guideline, Limit test, FCBA, Report No.402/12/1048F/g-e. |

### Access to documentation

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

# Summary of the product assessment

## Identity related issues

The source of the active substance used in the biocidal product REPULSIF ANTI-MOUSTIQUES CORPOREL (RAMC) is one of the source used for annex I inclusion.

There is no substance of concern in the biocidal product.

The formulation of the biocidal product RAMC 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).

|  |  |
| --- | --- |
| **Classification - Directive 67/548/EEC** |  |
| Class of danger | Xn – HarmfulXi – Irritant |
| R phrases | R22: Harmful if swallowedR36/38: Irritating to eyes and skin.R52/53- Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment. |

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

### Classification of the biocidal product

|  |  |
| --- | --- |
| **Classification - Directive 99/45/EEC** |  |
| Class of danger | Xi - Irritant |
| R phrases | R10: Flammable R41: Risk of serious damage to eyes |
| S phrases (proposed by the RMS) | S2: Keep out of the reach of children.S26: In case of contact with eyes, rinse immediately with plenty of water and seek medical adviceS39: Wear eye/face protectionS46: If swallowed, seek medical advice immediately and show this container or label |

|  |  |
| --- | --- |
| **Classification - Regulation (EC) 1272/2008** |  |
| Hazard statement | Flam. Liq. 3 - H226 : Flammable liquid and vapourEye Dam. 1 - H318 : Causes serious eye damage |
| Precautionary statements (proposed by the RMS) |  P210 Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking.P233 Keep container tightly closed. |

**Major change application for VAPO REPULSIF CORPOREL ANTI-MOUSTIQUE – 2020:**

|  |  |
| --- | --- |
| **Classification - Regulation (EC) 1272/2008** |  |
| Hazard statement | Eye Irrit 2. 2 - H319 : Causes serious eye irritation |
| Precautionary statements (proposed by the RMS) | P233 Keep container tightly closed. |

### Labelling of the biocidal product

|  |
| --- |
| **Labelling - Directive 67/548/EEC** |
| Symbols: |  |
| Indications of danger: | Xi - Irritant |
| Risk phrases: | R10: Flammable.R41: Risk of serious damage to eyes  |
| Safety phrases: | S2: Keep out of the reach of children.S26: In case of contact with eyes, rinse immediately with plenty of water and seek medical adviceS39: Wear eye/face protectionS46: If swallowed, seek medical advice immediately and show this container or label |

|  |
| --- |
| **Labelling - Regulation (EC) 1272/2008** |
| Pictograms: |  |
| Signal words: | Flam. Liq. 3 ; Danger |
| Hazard statements: | Flam. Liq. 3 H226 : Flammable liquid and vapourEye Dam. 1; H318 : Causes serious eye damage |

**Major change application for VAPO REPULSIF CORPOREL ANTI-MOUSTIQUE – 2020:**

|  |
| --- |
| **Labelling - Directive 67/548/EEC** |
| Symbols: |  |
| Indications of danger: | Xi - Irritant |
| Risk phrases: | R41: Risk of serious damage to eyes  |
| Safety phrases: | S2: Keep out of the reach of children.S26: In case of contact with eyes, rinse immediately with plenty of water and seek medical adviceS39: Wear eye/face protectionS46: If swallowed, seek medical advice immediately and show this container or label |

|  |
| --- |
| **Labelling - Regulation (EC) 1272/2008** |
| Pictograms: |  |
| Signal words: |  |
| Hazard statements: | Eye Irrit. 2; H319 : Causes serious eye irritation |

### Packaging of the biocidal product

The product RAMC is packaged in a polypropylene flask with spray pump (PP/ polyoxymethylene) with three different volumes (80 mL, 100 mL and 150 mL).

## Physico/chemical properties and analytical methods

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

The source of the active substance used in the biocidal product REPULSIF ANTI-MOUSTIQUES CORPOREL (RAMC) is one of the 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 RAMC 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.

**Major change application for VAPO REPULSIF CORPOREL ANTI-MOUSTIQUE– 2020:** additional studies have been provided to support the new composition of the biocidal product.

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

The formulation of the biocidal product RAMC 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: REPULSIF ANTI-MOUSTIQUES CORPOREL, SUBITO/BEAST-OFF

Code number: RAMC

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

The product RAMC is packaged in a polypropylene flask with spray pump (PP/ polyoxymethylene) with three different volumes (80 mL, 100 mL and 150 mL).

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

Studies have been performed on biocidal product REPULSIF ANTI-MOUSTIQUES CORPOREL.

| **Subsection(Annex Point IIB. 3/TNsG)** | **Method** | **Purity/Specification** | **Results** | **Reference** |
| --- | --- | --- | --- | --- |
| **3.1 Appearance(IIB3.1/Pt. I-B3.1)** |  |  |  |  |
| **3.1.1 Physical state and nature****3.1.2 Colour****3.1.3 Odour** | Visual | 30% DEETBatch 965 | limpid liquid ColourlessNot performed | Study 402/12/1048F-eLegay 2012 |
| **3.2 Explosive properties(IIB3.2/Pt. I-B3.2)** | Statement and DSC | 30% DEETBatch 965 | During the DSC, only an endothermic peak was observed at 95.1°C. The test item shall not be classified as explosiveNot explosive | Defitrace report No.12-919062-001ASC report 12/04 |
| **3.3 Oxidising properties(IIB3.3/Pt. I-B3.3)** | Statement | - | Based on structural considerations, RAMC is not expected to have oxidising properties.Not oxidizing | ASC report 12/04 |
| **3.4 Flash-point and other indications of flammability or spontaneous ignition(IIB3.4/Pt. I-B3.4)** |
| Flammability | EC A.9 | 30% DEETBatch 965 | Flash point : 41.9°CClassified as R10 according to 99/45/ECClassified as flam liq 3; H226 according to CLP | Legay 2012 |
| Self ignition temperature of solids | Statement | - | Based on composition considerations, RAMC is expected to have auto-flammability point higher than 360 °C. | ASC report 12/04 |
| **3.5 Acidity/Alkalinity(IIB3.5/Pt. I-B3.5)** |  |  | Not required as pH of Biocidal product is > 4.0 and < 10.0 | - |
| **3.5 pH pure material** | CIPAC MT 75.3 | 30% DEETBatch 965 | pH of pure material: 8.1 at 20.6°C | Legay 2012 |
| **3.6 Bulk density (IIB3.6/Pt. I-B3.6)** | EC A.3 OECD 109 | 30% DEETBatch 965 | Liquid density : 0.950 | Legay 2012 |
| **3.7 Storage stability - (IIB3.7/Pt. I-B3.7)** | 3 years at ambient temperature (ongoing study) | 30% DEETBatch 965 | Ongoing study.Final study report is required in post registration  | Legay 2012 |
| 3 years at ambient temperatureCroplife monograph n°17Method for DEET determination: the one reported in part 2.3.2.3 | 30% DEETBatch 965 | Data received in January 2019 in the frame of the Mutual Recognition in Sequence :After 3 years at 20°C in PET flask :

|  |  |  |
| --- | --- | --- |
|  | T0 | 3y at 20°C |
| Appearance |  | As initial, no phase separation |
| Content of DEET  | 31.4% | 32.8%  |
|  | Variation | +4.5% |
| pH value | 8.1 | 7.9 |
| Volume delivered by spray | 0.12 mL/spray | 0.13 mL / spray |
| Weight change | - | -1.38% |

Biocide product was demonstrated stable after 3 year. However, as the initial authorisation was for a shelf life of 2 years and no minor change dossier was submitted, the shelf life is kept at 2 years. | Legay 2015 |
| **3.7 Storage stability - (IIB3.7/Pt. I-B3.7)** | CIPAC MT 46.3 14 days at 54 °C | 30% DEETBatch 965 | After 14 days at 54°C in glass bottle:

|  |  |  |
| --- | --- | --- |
|  | T0 | 14d 54°C |
| Appearance |  | As initial, no phase separation |
| Content of DEET  | 298 g/L | 302 g/L |
|  | Variation | +1% |
| pH value | 8.1 | 8.0 |

Biocidal product is stable 14 days at 54 °C in glass container. | Legay 2012 |
| **Effect of low temperature** | CIPAC MT 39.37 days at 0°C | 30% DEETBatch 965 | After 7 days at 0°C in plastic vial:A solid deposit (white particles) could be observed (0.15-0.20 mL) – after inverting once, no deposit was observed anymore. No phase partition or appearance change was observed.pH after storage = 8.0Biocidal 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”. | Legay 2012 |
| **Effects of light** |  |  | Not relevant as the product is not in contact with light acceptable |  |
| **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)** | EC A5OECD 115 | 30% DEETBatch 965 | 32.0 mN/mBiocidal product is surface active | Legay 2012 |
| **3.11 Viscosity(Pt. I-B3.10)** | OECD 114 | 30% DEETBatch 965 | < 5 mP a.s at 20.0°C | Legay 2012 |
| **3.12 Particle size distribution(Pt. I-B3.11)** | CIPAC MT 187 | 30% DEETBatch 965150 mL PET-bottles with PP/POM spray head | Particle size distribution of droplet when sprayed:1 % of particles < 9.4 µm10 % of particles < 34 µm50 % of particles < 66 µm90 % of particles < 104 µm | Biogenus study Mo4415 |
| **Other** |  |  | Volume delivered by pump is 0.12 mL/ spray | Legay 2013 |

* **Major change for VAPO REPULSIF CORPOREL ANTI-MOUSTIQUE CORPOREL – 2020**

**Results of the shelf life study provided for the old composition**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **3.7 Storage stability - (IIB3.7/Pt. I-B3.7)** | 3 years at ambient temperatureCroplife monograph n°17Method for DEET determination: the one reported in part 2.3.2.3 | 30% DEETBatch 965 |  As a minor change was submitted in June 2019, a shelf life of 3 years can be proposed. See results reported in the table above | Legay 2015 |

**Results of the new studies provided to support the change of composition:**

| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **Reference** | **eCa assessment** |
| --- | --- | --- | --- | --- | --- |
| Physical state at 20 °C and 101.3 kPa | No guidelinerequired | Product VRCAMBatch number:2629Containing 30.5%w/w of DEET (N,Ndiethyl-metatoluamide) | Homogeneous colourless limpid liquid with a characteristic odour beforeand after the storage procedures (14 days at 54 ± 2°C in 80 mL whiteopaque PET spray and 7 days at 0 ± 2°C). | Halbwachs P., 2019Report no.19-919062-002,Défitraces | Acceptable  |
| Colour at 20 °C and 101.3 kPa | Visualobservation |
| Odour at 20 °C and 101.3 kPa | No guidelinerequiredOrganolepticobservation |
| Acidity / alkalinity | CIPAC MT 75.3(2000) | Product VRCAMBatch number:2629Containing 30.5%w/w of DEET (N,Ndiethyl-metatoluamide) | The pH of the pure test item VRCAM was 6.80 (after 2 min) at 18.8°Cbefore storage and 5.75 (after 2 min) at 20.2°C after 14 days at 54 ± 2°Cin its commercial packaging (80 mL white opaque PET spray).As the pH values determined during the tests were higher than 4 orlower than 10, the acidity of the product VRCAM was not determined | Halbwachs P., 2019Report no.19-919062-002,Défitraces | Acceptable  |
| Relative density / bulk density | Calculation | Product VRCAMContaining 30%w/w of DEET (N,Ndiethyl-metatoluamide) | Relative density of the individual components of the products are ranging from 0.996 to 1.03 .No data is available regarding the density of the minor component 3. However, due to its very low content, it is not expected to impact the density of the product VRCAM (a reference value of 1.00 will be taken for the calculation). The calculated density of the product VRCAM is **1.009** (0.3093\*0.996 + 0.35\*1.03 + 0.0005\*1 + 0.3402\*1).  |  | All components have a similar relative density, meaning that the relative density is expected to be around 1. The calculation is acceptable.  |
| Storage stability test – **accelerated storage** | CIPAC MT 46.3method (storagestability)(2000)ValidatedanalyticalmethodCIPAC MT 75.3Internatl method | Product VRCAMBatch number:2629Containing 30.5%w/w of DEET (N,Ndiethyl-metatoluamide)Packaging:80 mL whiteopaque PET spray | The test item VRCAM was considered to be stable after an acceleratedstorage procedure for 14 days at 54 ± 2°C in its commercial packaging(80 mL white opaque PET spray). | Halbwachs P., 2019Report no.19-919062-002,Défitraces | Acceptable. The new composition is stable 14 days at 54°C in PET packaging with PP trigger. Extrapolation to PP material (material for the bottle and trigger) is acceptable as the product is an aqueous formulation. |
| Storage stability test – **long term storage at ambient temperature** | TechnicalMonographNo.17, 2ndedition, CropLife | Product VRCAMBatch number:2629Containing 30.5%w/w of DEET (N,Ndiethyl-metatoluamide)Packaging:80 mL whiteopaque PET spray | The long term storage stability study (36 months at 20 ± 2°C) of the testitem VRCAM in its commercial packagings (white opaque PET spray (80mL)) is on-going. The results concerning the appearance of the productand of its commercial packagings, the N,N-diethyl-meta-toluamide(DEET) content, the pH of the pure product, the spray pattern, thepulverisation volume and the satisfactory operation of the spray will beprovided when available | Halbwachs P., 2019Study plan no.19-919062-003, Défitraces | A long term study is ongoing. The previous composition was found stable up to 3 years at ambient temperature. Only a shelf life of 2 years can only been extrapolated from the results of the accelerated storage. If the applicant claims a shelf life of 3 years, a minor change dossier including results of the storage stability study with the new formulation should be provided |
| Storage stability test – **low temperature stability test for liquids** | CIPAC MT 39.3method (2000) | Product RCAMEBatch number:2630Containing 10.0%w/w of DEET (N,Ndiethyl-metatoluamide) | The products RCAME and VRCAM have similar composition. Please refer to the read across in confidential annex. The low temperature storage stability of the product VCRAM is expected to be similar to the low temperature storage stability of the tested productRCAME. At the start of the test, the test item RCAME was a homogeneouscolourless limpid liquid. The appearance of the test item was considered to be stable after a low temperature stability for 7 days at 0 ± 2°C, no change was observed inthe test item aspect | Halbwachs P., 2019Report no.19-919062-005,Défitraces | The bridging is acceptable for this endpoint (see confidential PAR). The product RCAME is stable following 7 days at 0°C. Results can be extrapolated to VRCAM. |
| Effects on content of the active substance and technical characteristics of the biocidal product - **light** |  |  | Not required as the commercial packagings (white PET sprays) of theproduct VRCAM are opaque. |  | Acceptable. No mitigation measure was proposed for the first authorisation. The active ingredient is also not sensitive to light according to the assessment report. |
| Effects on content of the active substance and technical characteristics of the biocidal product – **temperature and humidity** |  |  | The product VRCAM is considered to be stable after 14 days at 54 ± 2°Cand after 7 days at 0 ± 2°C. It contains water as co-formulant, thereforestudy for humidity effects is not required.Furthermore, the individual commercial packagings are hermeticallysealed, the packaging are leak-tight |  | Acceptable.  |
| Effects on content of the active substance and technical characteristics of the biocidal product - **reactivity towards container material** |  |  | See the storage stability test – long term storage at ambienttemperature |  | Report of the study should be provided once available to confirm the shelf life of the product. |
| Wettability |  |  | Not required as the product is a ready-to-use liquid |  | Not applicable. |
| Suspensibility, spontaneity and dispersion stability |  |  | Not required as the product is a ready-to-use liquid |  | Not applicable. |
| Wet sieve analysis and dry sieve test |  |  | Not required as the product is a ready-to-use liquid |  | Not applicable. |
| Emulsifiability, re-emulsifiability and emulsion stability |  |  | Not required as the product is a ready-to-use liquid |  | Not applicable. |
| Disintegration time |  |  | Not required as the product is a ready-to-use liquid |  | Not applicable. |
| Particle size distribution, content of dust/fines, attrition, friability | CIPAC MT 187(2003)ISO 13320-2009(laser diffraction) | Product VRCAMBatch number:2629Containing 30.5%w/w of DEET (N,Ndiethyl-metatoluamide)Packaging:80 mL whiteopaque PET spray | The spray droplet size distribution of the test item VRCAM in itscommercial packaging (80 mL white opaque PET spray with PP trigger) was determinedby laser diffraction.The percentage of the respirable volume fraction less than 10 µm iszero.Mean on the three sprays:Dv(0.1) = 42.481 µm (particle size not exceeded by 10% in volume of the particles)Dv(0.5) = 74.417 µm (particle size not exceeded by 50% in volume of the particles) Dv(0.9) = 135.186 µm (particle size not exceeded by 90% in volume of the particles)D[3;2] = 67.457 µm (mean diameter in surface/volume)D[4;3] = 85.846 µm (mean diameter in volume) | Halbwachs P., 2019Report no.19-919062-009,Défitraces | Acceptable. |
| Persistent foaming |  |  | Not required as the product is a ready-to-use liquid |  | Not applicable. |
| Flowability/Pourability/Dustability |  |  | Not required as the product is a ready-to-use liquid |  | Not applicable. |
| Burning rate — smoke generators |  |  | Not required as the product is a ready-to-use liquid |  | Not applicable. |
| Burning completeness — smoke generators |  |  | Not required as the product is a ready-to-use liquid |  | Not applicable. |
| Composition of smoke — smoke generators |  |  | Not required as the product is a ready-to-use liquid |  | Not applicable. |
| Spraying pattern — aerosols | No guidelinerequired | Product VRCAMBatch number:2629Containing 30.5%w/w of DEET (N,Ndiethyl-metatoluamide)Packaging:80 mL whiteopaque PET spray | The mean volume of a pulverisation was considered to be stable after theaccelerated storage procedure (14 days at 54 ± 2°C). The mean volumesof a pulverisation of the test item before and after accelerated storageprocedure were respectively 0.132 mL and 0.123 mL.The pump and the trigger of the sprays were checked and no blockingwas observed.The mean spray diameter of a pulverisation was 17 cm at initial time and16 cm after the accelerated storage procedure (14 days at 54 ± 2°C). Theshape of the spray on the wetted patch was circular. | Halbwachs P., 2019Report no.19-919062-002,Défitraces | Acceptable.  |
| Physical compatibility |  |  | Not applicable. VRCAM is a ready-to-use product and is not intended tobe used in conjunction with any other products or active substances. |  | Not applicable. |
| Chemical compatibility |  |  | Not applicable. VRCAM is a ready-to-use product and is not intended tobe used in conjunction with any other products or active substances. |  | Not applicable. |
| Degree of dissolution and dilution stability |  |  | Not required as the product is a ready-to-use liquid. |  | Not applicable. |
| Surface tension | EU Method A.5(2008)OECD TestGuideline115(1995)(ring method) | Product VRCAMBatch number:2629Containing 30.5%w/w of DEET (N,Ndiethyl-metatoluamide) | The mean surface tension of the pure test item at 20.2°C was 36.5mN/m. The test item was considered as surface-active in the experimentalconditions used. | Halbwachs P., 2019Report no.19-919062-001,Défitraces | Acceptable. The formulation is surface active. |
| Viscosity | OECD TestGuideline 114(2012)ISO 3219(1993)(rotationalviscometer) | Product VRCAMBatch number:2629Containing 30.5%w/w of DEET (N,Ndiethyl-metatoluamide) | 15.4 mPa.s at 20.0 ± 0.2°C (same results from 10 to 38 RPM, decreasing and increasing gradient)6.34 mPa.s at 40.0 ± 0.2°C (similar results from 10 to 80 RPM, decreasing and increasing gradient)The test item was considered to have newtonian properties in theexperimental conditions used | Halbwachs P., 2019Report no.19-919062-001,Défitraces | Acceptable. The viscosity in independent from the shear rate and is considered as a Newtonian liquid. |

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| **Conclusion on the physical, chemical and technical properties of the product** |
| The product VRCAM is a homogeneous colourless limpid liquid with a characteristic odour. The mean pH of the pure product is about 6.8 (after 2 min) at 18.8°Cand its mean relative density is expected to be 1.009. The product VRCAM has a mean surface tension of 36.5 mN/m at a temperature of 20.2°C (surfaceactive material). Its mean dynamic viscosity is 15.4 mPa.s at 20.0 ± 0.2°C and 6.34 mPa.s at 40.0 ± 0.2°C (newtonian properties). The percentage of the respirable volume fraction less than 10 µm using its packaging (white opaque PET spray with PP trigger) is zero. As the product is an aqueous formulation, compatibility with PP (also proposed as material for the bottle and trigger) is acceptable.The test item VRCAM in its commercial packaging (80 mL white opaque PET spray) was considered to be stable after an accelerated storage procedure for 14 days at 54 ± 2°C. The appearance of the product and of its commercial packagings, the N,N-diethyl-meta-toluamide (DEET) content, the pH of the pure product, the spray pattern, the pulverisation volume and the satisfactory operation of the spray were considered to be stable after the accelerated storage procedure for 14 days at 54 ± 2°C.The long term storage stability study (36 months at 20 ± 2°C) of the test item VRCAM in its commercial packagings is on going. The results concerning the appearance of the product and of its commercial packagings, the N,N-diethyl-meta-toluamide (DEET) content, the pH of the pure product, the spray pattern, the pulverisation volume and the satisfactory operation of the spray are required in post registration.  A shelf-life of 36 months is claimed. The new formulation is considered stable 14 days at 54°C. A new shelf life study 3 years at ambient temperature is ongoing. Only a shelf life of 2 years can only been extrapolated from the results of the accelerated storage. If the applicant claims a shelf life of 3 years, a minor change dossier including results of the storage stability study with the new formulation should be providedMoreover, the appearance of the test item is expected to be stable after a low temperature stability for 7 days at 0 ± 2°C. |

| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **Reference** | **eCa assessment** |
| --- | --- | --- | --- | --- | --- |
| Explosives | Justification | Product VRCAMContaining 30% w/wof DEET (N,Ndiethyl-metatoluamide) | The product VRCAM contains 30.93% w/w of N,N-diethyl-m-toluamide (DEET) (technical) which has no explosive properties according to the Assessment Report of this active substance, Product-type 19, March2010. Moreover, the mixture contains more than 30% w/w water, an inert component, and 35% w/w of a component which does not contain chemical groups indicating explosive properties and moreover has no explosive properties according to its safety data sheet. The other components (maximum 0.05% w/w of the formulation) are not considered to present a significant hazard for explosive properties due to their low contents.Therefore, the product VRCAM is not expected to present a significant hazard for explosive properties and test is not required. | / | The active substance and the formulants are not classified as explosive. Based on the composition and the nature of the product (aqueous solution), the product is not classified.  |
| Flammable gases |  |  | Not required as the product is a ready-to-use liquid |  | Not applicable  |
| Flammable aerosols |  |  | Not required as the product is a ready-to-use liquid and is not conditioned in aerosols. |  | Not applicable |
| Oxidising gases |  |  | Not required as the product is a ready-to-use liquid |  | Not applicable |
| Gases under pressure |  |  | Not required as the product is a ready-to-use liquid |  | Not applicable |
| Flammable solids |  |  | Not required as the product is a ready-to-use liquid |  | Not applicable |
| Flammables liquids | EC A9 (closed cup method) | Product VRCAMContaining 30% w/wof DEET (N,Ndiethyl-metatoluamide), batch 3098, manufacturing date: 22/09/2020 | The product VRCAM contains 30.93% w/w of N,N-diethyl-m-toluamide (DEET) (technical) which is not a self-reactive substance according to the Assessment Report of this active substance, Product-type 19, March 2010. Moreover, the mixture contains more than 30% w/w water, an inert component, and 35% w/w of a component which does not contain chemical groups indicating self-reactive properties. The other components (maximum 0.05% w/w of the formulation) are not considered to present a significant hazard for self-reactive properties due to their low contents. Therefore, the product VRCAM is not expected to present a significant hazard for self-reactive properties and test is not requiredA study was also provided to support the absence of classification:No flash point was observed up to 140°C. At 140.0°C, the test item boiled and overflowed just before the presentation of the flame. Then the test was stopped. | Statement and Study report, Padilla P., 2020 Report No.20-919062-001  | eCA agrees with applicant that the product is not expected to be classified. The study also confirms that the new composition is not anymore classified flammable H226.  |
| Pyrophoric liquids | Justification | Product VRCAMContaining 30% w/wof DEET (N,Ndiethyl-metatoluamide) | The product VRCAM does not contain any components classified as pyrophoric. Moreover, experience in manufacture and handling shows that the product VRCAM does not ignite spontaneously on coming intocontact with air at normal temperature. Therefore the product VRCAM is not expected to be pyrophoric liquidand test is not required |  | Acceptable. |
| Pyrophoric solids |  |  | Not required as the product is a ready-to-use liquid |  | Not applicable |
| Self-heating substances and mixtures | Justification | Product VRCAMContaining 30% w/wof DEET (N,Ndiethyl-metatoluamide) | Test is not required as experience in manufacture and handling shows that the product VRCAM does not ignite spontaneously on coming into contact with air at normal temperature. The product is not expected to be a self-heating mixtures and test is not required. Moreover, the product is not expected to present a significant hazard for auto-flammability (please refer to the point “Auto-ignition temperatures of products (liquids)” below) |  |  Not applicable to products with a melting point below 160°C. |
| Substances and mixtures which in contact with water emit flammable gases | Justification | Product VRCAMContaining 30% w/wof DEET (N,Ndiethyl-metatoluamide) | Test is not required as the product VRCAM already contains more than 30% w/w of water. Moreover, the others components are not classified as substances which in contact with water emit flammable gases |  | Acceptable.  |
| Oxidising liquids | Justification | Product VRCAMContaining 30% w/wof DEET (N,Ndiethyl-metatoluamide) | The product VRCAM contains 30.93% w/w of N,N-diethyl-m-toluamide (DEET) (technical) which has no oxidising properties according to the Assessment Report of this active substance, Product-type 19, March2010. Moreover, the mixture contains more than 30% w/w water, an inert component, and 35% w/w of a component with no structural alert (the substance contains oxygen and these elements are chemically bonded only to carbon or hydrogen). Moreover this component has no oxidising properties according to its safety data sheet. The other components (maximum 0.05% w/w of the formulation) are not considered to present a significant hazard for oxidising properties due to their low contents. Therefore, the product VRCAM is not expected to present a significant hazard for oxidising properties and test is not required |  | Acceptable according to the composition. No components are classified nor contain chemical groups related to such hazard. |
| Oxidising solids |  |  | Not required as the product is a ready-to-use liquid |  | Not applicable |
| Organic peroxides |  |  | Not required as its components are not expected to form or contain organic peroxides. |  | Not applicable |
| Corrosive to metals | Justification | Product VRCAMContaining 30% w/wof DEET (N,Ndiethyl-metatoluamide) | The product VRCAM is halogen-free, does not contain any bases, acids and complexing agents and its pH is nearly neutral (pH = 6.8 according to study No.19-919062-002). The product VRCAM is not expected to be corrosive to metals and test is not required. |  | A test should be provided at the renewal of the product in order to comply with the BPR. |
| Auto-ignition temperatures of products (liquids and gases) | Justification | Product VRCAMContaining 30% w/wof DEET (N,Ndiethyl-metatoluamide) | The product VRCAM contains 30.93% w/w of N,N-diethyl-m-toluamide (DEET) (technical) which is not auto-flammable according to the Assessment Report of this active substance, Product-type 19, March 2010.Moreover, the mixture contains more than 30% w/w water, an inert component, and 35% w/w of a component which has an auto-ignition temperature of 332°C according to its safety data sheet. The other components (maximum 0.05% w/w of the formulation) arenot considered to present a significant hazard for auto-flammability due to their low contents. Therefore, the product VRCAM is not expected to present a significant hazard for auto-flammability and test is not required |  | According to the composition, the product is an aqueous formulation with a high proportion of water and of an inert ingredient. The product is not expected be auto flammable in the conditions of use.  |
| Relative self-ignition temperature for solids |  |  | Not required as the product is a ready-to-use liquid |  | Not applicable |
| Dust explosion hazard |  |  |  |  | Not applicable |

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| **Conclusion on the physical hazards and respective characteristics of the product** |
| The product VRCAM is not expected to be flammable and to present a significant hazard for explosive properties, flammable, self-reactivity, pyrophoric properties, oxidising properties and auto-flammability. The product VRCAM is not expected to be corrosive to metals and does not emit flammable gases in contact with water.  |

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

Reference: S. LEGAY 2012; Physico-chemical tests on ready to use anti mosquito solution “Repulsif anti-moustiques corporel, Subito/ breat off”; study n°402/12/1048F-e.

The method to determine the content of DEET in the biocidal product RAMC by HPLC-UV (210 nm) using external standard calibration is validated according to document SANCO 3030/99.

Validation data

|  |  |  |
| --- | --- | --- |
| Linearity  | Recovery rate and Repeatability | Specificity |
| Range 80-120% of nominal value n=5x3 r²=0.992 | 12 fortified placebo injected one time by 2 different operators (12 values)Mean of recovery = 99.27RSD= 1.351% | Chromatograms data (Dilution solvent and placebo) demonstrate that method is specific |

The provided method is acceptable for the product RAMC.

* **Major change for VAPO REPULSIF CORPOREL ANTI-MOUSTIQUE CORPOREL – 2020**

A new study has provided with the new formulation.



Following SANCO/3030/99 rev.5 from 22/03/2019, an analytical method for the determination of N,Ndiethyl-meta-toluamide (DEET) content in the product VRCAM was validated during this study by definition of the specificity, the linearity, the accuracy, the precision and the reproducibility of the method.

**Principle of the method**: A quantity of 1.0 g of the test item was weighed (to the nearest 0.01 mg) into a 100-mL volumetric flask and the volume was made up with acetonitrile. The solution was homogenised then diluted 55.6 times (0.45 mL into 25 mL) with acetonitrile. N,N-diethyl-meta-toluamide (DEET) is analysed after extraction from the formulation and quantified by liquid chromatography using a reverse phase column and a UV detector (retention times: about 8.5 min for DEET 1 and 8.8 min for DEET 2)



**Test item:** VRCAM batch 2629 and FORMULATION BLANK OF VRCAM batch not reported (ID 19-164-1)

**Specificity**
Specificity was studied by analysis of the solvent blank (acetonitrile), the matrix without the active substance (blank formulation), the N,N-diethyl-meta-toluamide (DEET) reference item (DEET standard), and the test item (VRCAM). The specificity was assessed by checking for any interference in HPLC-UV at the retention time of the peaks of DEET (about 8.5 min for DEET 1 and 8.8 min for DEET 2). No peak appears in the solvent blank and in the formulation blank near the peaks of N,N-diethyl-metatoluamide (DEET). In the reference item and in the test item, the peaks at the retention times around 8.489 min and 8.825 min represent respectively DEET 1 and DEET 2. No additional peak appears in the reference item and in the test item near the peaks of N,N-diethyl-metatoluamide (DEET). Therefore, the analytical method showed a good specificity for analysis of N,N-diethyl-meta-toluamide (DEET) in formulation VRCAM.

**Linearity**
To define the linearity of the detector answer of N,N-diethyl-meta-toluamide (DEET), five concentrations
taken between 50% and 150% w/w of nominal content in the product (from 26.85 mg/L to 83.78 mg/L in measuring solutions) of DEET reference item were analysed
(two determinations for each concentration). The response of the detector during the analysis of N,N-diethyl-meta-toluamide (DEET) was linear within the range of 26.85 mg/L to 83.78 mg/L (y = 2.52 \* 10-1 \* x + 2.71 \* 10-1 (y = sum of the DEET peaks area, x = DEET amount (in mg/L), r = 1.0000). The correlation coefficient r was > 0.99 showing a good linearity.

**Accuracy**
Accuracy was checked by analyses of two reconstituted samples (blank formulation spiked with known
amounts of N,N-diethyl-meta-toluamide (DEET) reference item). The accuracy results of DEET were in conformity with the Guidelines requirements for formulations containing higher than 10% of an active substance. Indeed, the recovery results should be in the range 97% - 103% and they were experimentally equal to 99.8% and 100.3%. Mean recovery rate = 100.1% (n = 2).

**Precision**
The precision was determined by analysing twice five test item solutions. The content of N,N-diethyl-metatoluamide (DEET) for each analysis was calculated with the average value of the response factor of the
two calibration solutions bracketing the test item. Then, the average value of the content, the standard
deviation and the Relative Standard Deviation (R.S.D.) were calculated. The concentration of DEET in the test item was equal to 30.8% w/w or 308 g/kg. In the case of DEET, the precision was acceptable as the R.S.D. was lower than the result of the modified Horwitz equation: 1.02% < 1.60% (C = 0.308) with Horwitz ratio (Horrat) equal to 0.64.

**Reproducibility**
The reproducibility was determined by analysing preparations (twice n = 5) carried out at two different
days by two different analysts. The content of DEET for each analysis was calculated then the average
value of the content, the standard deviation and the Relative Standard Deviation (R.S.D.) were calculated.
See precision for the results of first series. For the second series, the concentration of DEET in the test item was equal to 30.2% w/w or 302 g/kg. And the precision was acceptable as the R.S.D. was lower than the result of the modified Horwitz equation: 1.33% < 1.60% (C = 0.302) with Horwitz ratio (Horrat) equal to 0.83. The mean average content of DEET for the two reproducibility tests was equal to 30.5% w/w. The mean Relative Standard Deviation of DEET for the two reproducibility tests was equal to 1.18%.

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| **Validation results** |
| Specificity | Retention times for DEET peaks match between DEET reference item and test item, confirming the identity of the analyte. Chromatograms were provided for calibration standard, blank formulation, test item, solvent blank. No interference was observed in solvent bank, DEET reference item, blank formulation and test item at the retention times of DEET. Therefore, the analytical method showed a good specificity for analysis of DEET in formulation VRCAM |
| **Linearity** | Calibration range: 26.85 – 83.78 mg/L of DEET in measuring solution (n = 5, eq to 50 – 150% w/w of nominal active substance in the product):y = 2.52 \* 10-1 \* x + 2.71 \* 10-1 (y = sum of the DEET peaks area, x = DEET amount(in mg/L))r = 1.0000 |
| **Accuracy** | Blank formulation was fortified with DEET standard at approx. 30% w/wSample 1= 100.3% (two replicates)Sample 2 = 99.8% (two replicates)Mean recovery rate = 100.1%  |
| **Precision** | Mean average content = 30.8 w/w (n = 5)RSD = 1.02% < modified Horwitz 1.60%Horwitz ratio (Horrat) = 0.64 |
| **Reproducibility**  | 1st series (see precision)2nd series:Mean average content = 30.2 w/w (n = 5)RSD = 1.33% < modified Horwitz 1.60%Horwitz ratio (Horrat) = 0.83Mean average content = 30.5% w/wMean RSD = 1.18% |

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| **Conclusion on the methods for detection and identification of the products** |
| The N,N-diethyl-meta-toluamide (DEET) content in the product VRCAM is determined using Liquid Chromatography with UV detection. Quantification is performed using external standard calibration.This analytical method for the determination of N,N-diethyl-meta-toluamide (DEET) content in the productVRCAM was validated by definition of the specificity, the linearity, the accuracy, the precision and thereproducibility of the method and Guidelines requirements were fulfilled.  |

* + - 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 REPULSIF ANTI-MOUSTIQUES CORPOREL 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

REPULSIF ANTI-MOUSTIQUES CORPOREL 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 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. 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 2 weeks at 54°C.

Results of the two years storage stability study should be provided in post registration. Compatibility of biocidal product will be assessed with shelf life study.

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

* **Major change application for VAPO REPULSIF CORPOREL ANTI- MOUSTIQUE – 2020**

Results of a 3 years storage stability study was provided for the previous composition during the mutual recognition in sequence process. As the biocidal product is a water based formulation, PP can be extrapolated from PET packaging. Compatibility of biocide product with its packaging was therefore demonstrated.

It should be noticed that the new formulation is considered stable 14 days at 54°C. A new shelf life study 3 years at ambient temperature is ongoing. Only a shelf life of 2 years can only been extrapolated from the results of the accelerated storage with the new composition. If the applicant claims a shelf life of 3 years, a minor change dossier including results of the storage stability study with the new formulation should be submitted.

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

The product must be shaken before use

Do not store more than 2 weeks at 54°C

***Required information linked to assessment of physico-chemical properties***

Long term storage stability in commercial packaging study including data on volume delivered by pump after 2 years is required in post registration.

* **Major change application for VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE– 2020**

No data required.

## Effectiveness against target organisms

### Function

Main Group 03: Pest Control

Product Type 19: Repellents and attractants

VAPO REPULSIF ANTI-MOUSTIQUES CORPOREL 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, arms, hands and legs).

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

* **First authorization – 2014 (REPULSIF ANTI-MOUSTIQUES CORPOREL)**

According to the uses claimed by the applicant, REPULSIF ANTI-MOUSTIQUES CORPOREL is intended to be used to repel arthropods. The target organisms to be controlled are mosquitoes.The organisms to be protected are humans.

The application rates recommended by the applicant are the following:

The number of spraying recommended is ranged from 4 to 6 sprays per forearm (average 600 cm²). The recommended application rates are 1.1 mg / cm² on skin and 1.67 mg / cm² on fabric.

It has to be noted that the tested arthropods are not all present in France and in the overseas territories but RMS consider than they are representative of their genus:

*- Aedes aegypti (Stegomya aegypti):* this species occurs in overseas territories of France (Reunion, Mayotte, Guadeloupe, Martinique islands and in Guyane). This species is a vector of Dengue and Chikungunya 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.

*- 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.

* **Major change application for VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE – 2020**

VAPO CORPOREL REPULSIF ANTI-MOUSTIQUE is the same product than REPULSIF ANTI-MOUSTIQUES CORPOREL**.**

In the frame of the major change application for the product **VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE** (30 % w/w DEET), a modification of the composition of the product with the replacement of a solvent by an other one has been submitted by the applicant.

For application on skin, an aditionnal use against ticks (*Ixodes ricinus*) and a reduction of the application rate to 0.5 mg/cm² have been also claimed by the applicant.

The application rate recommended by the applicant is the following: 0.5 mg / cm² on skin against mosquitoes (*Aedes spp*., *Culex spp*. And *Anopheles spp*.) and ticks (*Ixodes ricinus*).

Note that application on textiles is not claimed in the frame of this major change application for the product VAPO CORPOREL REPULSIF ANTI-MOUSTIQUE.

### Effects on target organisms and efficacy

* **First authorization – 2014 (REPULSIF ANTI-MOUSTIQUES CORPOREL)**

## *Preamble:*

## According to the TNsG on PT18/19, the repellence effectiveness is based on the protection time, that is, the time between repellent application and the time of 2 or more bites on the treated arm, or the first confirmed bite (a bite followed by another within 30 minutes). But in the studies presented by the applicant, the exposure interval is one hour instead of 30 minutes so it does not allow confirming the second biting within 30 minutes. Furthermore, the criteria “10 landings in 30 sec or 2 bites during 3 minutes exposure" probably overestimates the time of efficacy since the WHO guideline consider the protection as the time between application and the first mosquito landing and/or probing

 The applicant submitted following studies:

For the use against mosquitoes:

## An arm-in-cage study conducted with 3 human volunteers per test organism with the product REPULSIF ANTI-MOUSTIQUES CORPOREL applied on the skin against four mosquito species *(Aedes aegypti, Anopheles gambiae, Aedes albopictus and Culex pipiens).*

The duration of efficacy of the product REPULSIF ANTI-MOUSTIQUES CORPOREL was tested under laboratory conditions against 4 mosquito species: *Aedes aegypti, Anopheles gambiae, Aedes albopictus* and *Culex pipiens*.

The product was sprayed on the forearm and spread, from the wrist to the elbow, for an average surface area of 600 cm².

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 in 30 seconds or 5 bites), the treated forearm was inserted into the cage for 3 minutes (exposure time).

The same procedure was repeated every hour until 9 hours or inefficacy. The time of protection is up to 8 hours for the 4 tested species at the application rate of 1.67 mg / cm² product (0.5 mg / cm² DEET). Even if this application rate demonstrated the efficacy of the product, this application rate is not claimed by the applicant and will not be taken into account regarding this product.

* An arm-in-cage study conducted with 3 human volunteers per test organism with the product REPULSIF ANTI-MOUSTIQUES CORPOREL applied on the skin against 4 mosquito species *(Aedes aegypti, Anopheles gambiae, Aedes albopictus and Culex pipiens)*

The duration of efficacy of the product REPULSIF ANTI-MOUSTIQUES CORPOREL was tested under laboratory conditions against 4 mosquito species: *Aedes aegypti, Anopheles gambiae, Aedes albopictus* and *Culex pipiens*.

The product was sprayed on the forearm and spread, from the wrist to the elbow, for an average surface area of 600 cm².

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 in 30 seconds or 5 bites), the treated forearm was inserted into the cage for 3 minutes (exposure time).

The same procedure was repeated every hour until 9 hours or inefficacy. The time of protection is up to 4 hours for the 4 tested species at the application rate of 1.1 mg / cm² product (0.33 mg / cm² DEET).

* An arm-in-cage study conducted with 3 human volunteers per test organism with the product REPULSIF ANTI-MOUSTIQUES CORPOREL applied on fabric (cotton) against 4 mosquito species (*Aedes aegypti*, *Anopheles gambiae*, *Aedes albopictus* and *Culex pipiens*).

The duration of efficacy of the product REPULSIF ANTI-MOUSTIQUES CORPOREL was tested under laboratory conditions against 4 mosquito species: *Aedes aegypti, Anopheles gambiae, Aedes albopictus* and *Culex pipiens*.

The product was sprayed on a cotton fabric used to cover the forearm, from the wrist to the elbow.

The trial began 30 minutes after the product had been applied. The control forearm, with untreated fabric, was inserted into the cage, and after validation of this control (10 landings in 30 seconds or 5 bites), the treated forearm was inserted into the cage for 3 minutes (exposure time).

The same procedure was repeated every hour until 9 hours or inefficacy. The time of protection is up to 8 hours for the 4 tested species at the application rate of 1.67 mg / cm² product on cotton fabric (0.5 mg / cm² DEET).

All efficacy studies are presented in annex 8.

Based on the efficacy laboratory data, the time of protection of the product REPULSIF ANTI-MOUSTIQUES CORPOREL is:

* up to 8 hours for the 4 mosquito species *Aedes aegypti, Anopheles gambiae, Aedes albopictus* and *Culex pipiens,* when used at a dose of 1.67 mg / cm² on skin and cotton fabric,,
* up to 4 hours on the same species, when used at a dose of 1.1 mg/cm² on skin*.*

Furthermore, no field studies have been submitted in support of this authorisation. As under field conditions, many fact*o*rs can influence and even decrease the protection time 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 an 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 REPULSIF ANTI-MOUSTIQUES CORPOREL.

* **Major change application for VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE – 2020**

For application on skin, considering the addition of the use against ticks (*Ixodes ricinus),* the modification of the composition with the solvent’s replacement by an other one and the reduction of the application rate claimed.

The applicant has submitted 2 new studies performed with the product **VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE** (30 % w/w DEET) to support these major changes.

These studies demonstrate that the product **VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE** is effective to repel:

* mosquitoes (*Culex spp., Aedes spp*.) during 8.2 hours in temperate conditions and mosquitoes (*Anopheles spp)* during 7.2 hours in tropical conditions when applied on skin at an application rate of 0.5 mg/cm².
* ticks (*Ixodes ricinus*) during 7 hours when applied on skin at an application rate of 0.5 mg / cm² in temperate conditions.

This study is summarized in Section 6.7 of the IUCLID file and the main points are summarized in the table below.

|  |
| --- |
| **Experimental data on the efficacy of the biocidal products against target organism(s)** |
| **Function** | **Field ofuse** | **Testsubstance** | **Test organism(s)** | **Test method** | **Test system / concentrations applied /exposure time** | **Test results: effects** | **Reference** |
| Repellent | Outdoor | VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE (30 % w/w DEET)Batch: 2629 | *Culex pipiens* *Aedes aegypti* *Anopheles gambiae*Female 5 to 7 days old adults. 200 ± 10 mosquitoes per replicate.  | Based on WHO/HTM/NTD/ WHOPES/2009.4; Guideline for efficacy testing of mosquito repellents for human skin - § 2.2 Laboratory test. Arm-in-cage study. 10 volunteers Product applied on one forearm of each volunteer, the other untreated one being used as a control.  | Dose of product 0.5 mg/cm² of skin (i.e. 0.3 g/600 cm² forearm).The trial began 1 minute 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 in 30 s or 5 bites), the treated forearm was inserted into the cage for 5 minutes (exposure time).The same procedure was repeated every hour until the first landing, then every 30 minutes until inefficacy Climatic conditions: *Culex pipien and Aedes aegypti*:temperature 25 ±2 °C; relative humidity 65 % ± 5 %*Anopheles gambiae*:Temperature 32°C ±2 °C; relative humidity 90 % ± 5 % | After application of the product at 0.5 mg/cm² of skin, the duration of protection was: - 8.1 hours for *C. pipiens* - 8.2 hours for *A. aegypti* - 7.2 hours for *A. gambiae*. Based on the less sensitive species, the protection duration of the product is 7 hours when the product is applied on skin.  | B. Serrano (2019)Report 2513a-VRCAM/10196.7\_01R.I = 1 |
| Repellent | Outdoor | VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE (30 % w/w DEET)Batch: 2629 | *Ixodes ricinus* (sheep tick): 60 nymphs | 6 ticks \* 10 volunteersTemperature and relative humidity continuously recorded, and ambient conditions maintained during the period of testing at an average temperature of 22.4°C ± 0.5°C, relative humidity 44.9 % ± 2.9% in the test room (temperate conditions). | Laboratory test.Simulated-use test: run test.10 volunteers (5 men and 5 women). Dose of product: 0.5 mg/cm2 of skin Product applied on one forearm of each volunteer, leaving the lowest 3 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 5 minutes.The test lasted for 8 hours post application, with 6 ticks tested per hour (3 ticks every 30 minutes) and per volunteer. 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 5 minutes were further used on the treated arm. | The product VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE shows an efficacy period of 7 hours. | Dautel, H.(2019) STA\_IR\_0119\_01S6.7\_02R.I = 2 |

**Conclusion on the efficacy of the product**

In conclusion, in accordance with the submitted tests and the requirements of the efficacy guidance (Vol II, Parts B+C), the product VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE is effective when applied on skin at a rate of 0.5 mg / cm² to repel:

* Mosquitoes (*Culex spp., Aedes spp*) up to 8 hours in temperate conditions and up to 7 hours for mosquitoes (*Anopheles spp.)* in tropical conditions
* Ticks (*Ixodes ricinus*) up to 7 hours in temperate conditions.

To ensure a satisfactory level of efficacy and avoid the development of resistance, the recommendations proposed in the SPC have to be implemented and 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.

### 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*.[[6]](#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*.[[7]](#footnote-8) developed a new biological model based on mosquito neurons isolated from adults *Anopheles gambiae* heads and revealed that AgNav channeland 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.*[[8]](#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.[[9]](#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[[10]](#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

* **First authorization - 2014**

French competent authorities (FR CA) assessed data presented in the dossier demonstrate that the product product REPULSIF ANTI-MOUSTIQUES CORPOREL provides a protection time up to 3.9 hours when used on skin at the application rate of 1.1 mg / cm² and up to 7.9 hours at the application rate of 1.67 mg / cm² when used on fabric (cotton) against fours species of mosquitoes (*Aedes aegypti, Anopheles gambiae, Aedes albopictus* and *Culex pipiens)*

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): 1.1 mg/cm² of skin and 1.67 mg/cm² of fabric

* **Major change application for VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE – 2020**

French competent authorities (FR CA) assessed data presented in the dossier demonstrate that the product product VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE provides a protection time against mosquitoes (*Culex spp. and Aedes spp.*) up to 8 hours in temperate conditions, mosquitoes (*Anopheles spp*.) up to 7 hours in tropical conditions, and ticks (*Ixodes ricinus*) up to 7 hours in temperate conditions, when used on skin at the application rate of 0.5 mg / cm². To ensure a satisfactory level of efficacy and avoid the development of resistance, the recommendations proposed in the SPC have to be implemented.

##  Description of the intended use(s)

* **First authorization – 2014 (REPULSIF ANTI-MOUSTIQUES CORPOREL)**

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 ControlPT19: Repellents and attractants | Repellent against mosquitoes*Aedes aegypti, Anopheles gambiae, Aedes albopictus and Culex pipiens* | 1.67 mg/cm2 on fabric (cotton), protection time up to 8 hours1.1 mg/cm² on skin, protection time up to 4 hours |

**Method of application**

The product REPULSIF ANTI-MOUSTIQUES CORPOREL is an insect repellent lotion containing 30 % DEET as active substance and intended to be applied on human skin and on fabric (cotton) to repel mosquitoes.

The product is sprayed on the exposed area of the skin (i.e. face, neck, arms, hands and legs) or sprayed on clothes.

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

* **Major change application for VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE – 2020**

In the frame of the major change application, 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 ControlPT19: Repellents and attractants | Repellent against mosquitoes (*Culex spp., Aedes spp. and Anopheles spp*) | 0.5 mg/cm² on skin, - Protection time up 8 hours in temperate conditions (*Culex spp., Aedes spp*.) -protection time up 7 hours in tropical conditions (*Anopheles spp.*) |
| Main Group 03; Pest ControlPT19: Repellents and attractants | Repellent against ticks (*Ixodes ricinus*) | 0.5 mg/cm² on skin protection time up to 7 hours in temperate conditions |

**Method of application**

The product VAPO CORPOREL REPULSIF ANTI-MOUSTIQUEis an insect repellent lotion containing 30 % DEET as active substance and intended to be applied on human skin to repel mosquitoes and ticks.

The product is sprayed on the exposed area of the skin (i.e. face, neck, arms, hands and legs) or sprayed on clothes.

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

## 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, R22Xi, R36/38No specific concentration limit  | Acute Tox. 4 H302Eye Irrit. 2 H319Skin Irrit. 2 H315No 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*”, RAMC does not contain any substance of concern.

* **Major Change application for VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE – 2020**

According to the definition of a substance of concern laid down in the Guidance on the BPR Volume III Human Health – Part B and C Risk Assessment, no co-formulant of the formulation of the product RCAME, has been identified as SOC.

#### Toxicology of the biocidal product

The toxicology of the biocidal product was examined appropriately according to standard requirements.

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

* **Major change application for VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE – 2020**

**Note to the reader:**

VCRAM is a same of REPULSIF CORPOREL ANTI-MOUSTIQUES.

The major change corresponds to a modification of the composition with replacement of a co-formulant by another (please see confidential part) and a modification of the classification.

The change of composition can have an impact on eye irritation and has no impact on the other hazard properties (please see confidential PAR).

Only eye irritation studies were provided and are detailed below.

##### Percutaneous absorption

No study is available for percutaneous absorption of RAMC. A dermal absorption value of 20% was determined in the DEET assessment report based on a human study using a 15% (w/w) solution in ethanol or the undiluted technical grade material. The content in DEET in RAMC being higher than in the human study (30% vs 15%), this value is considered as worst-case and will be used for the risk characterisation of RAMC.

* **Major Change application for VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE – 2020 :**

The change has no impact on the dermal absorption.

##### Acute toxicity

In an acute oral toxicity study (OECD 423), no mortality occurred up to 2000 mg/kg bw (daily examination during 14 days). Clinical signs were noted during the first minutes of the test: decrease in spontaneous activity (4/6), and piloerection (3/6). No clinical signs related to the administration of the test item were observed between 1 and 24 hours post dose. The body weight evolution of the animals remained normal throughout the study. The macroscopical examination of the animals at the end of the study did not reveal treatment related changes.

No mortality was observed in the dermal acute toxicity study (LD50 > 2000 mg/kg bw). Neither cutaneous reactions nor systemic clinical signs related to the administration of RAMC were observed. The body weight evolution of the animals remained normal throughout the study. The macroscopical examination of the animals at the end of the study did not reveal treatment-related changes.

Based on the results, no classification is required for RAMC.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Route | SpeciesStrainSexNo/group | Dose levelsDuration of exposure | Value LD50/LC50 | Remarks |
| Oral | RatSprague Dawley (SPF Caw)6 female/group | Single dose at 2000 mg/kg bwPost exposure period: 14 days | LD50>2000 mg/kg bwClinical signs noted during the first minutes of the test: decrease in spontaneous activity (4/6), and piloerection (3/6)No effect on body weightNo macroscopical changes |  |
| Dermal | RatSprague Dawley 5/sex/group | Single dose of 2000 mg/kg bw, applied to 10% body surface for 24 hours | LD50>2000 mg/kg bwNo clinical signsNo cutaneous reactionsNo effect on body weightNo macroscopical changes |  |

No acute inhalation toxicity study was generated for RAMC. The product RAMC does not contain ingredient classified for health effects resulting from an acute exposure by inhalation. Therefore, according to the classification rules in Directive 1999/45/EC, no classification regarding acute inhalation toxicity is warranted for the product RAMC.

##### Irritation and corrosivity

* Irritation and corrosivity

No cutaneous reactions (erythema, eschar and edema) were observed in the skin irritation study, whatever the examination times (i.e. 1, 24, 48 and 72 hours after the patch removal). Therefore, no classification is required for RAMC regarding skin irritation.

Due to irreversible lesions on the rabbit’s cornea, RAMC is classified Xi, R41 Risk of serious damage to eyes.

|  |  |  |  |
| --- | --- | --- | --- |
| SpeciesStrainNo/group | Average score 24, 48, 72h | Reversibility? | Result |
| erythema | oedema |
| RabbitAlbino New Zealand3 females | 0.00 | 0.00 | No (no cutaneous reactions) | Not irritating to the skin |

|  |  |  |  |
| --- | --- | --- | --- |
| SpeciesStrainNo/group | Average score | Reversibility? | Result |
| cornea | iris | Conjunctiva |
| Redness | Chemosis |
| RabbitAlbino New Zealand3 males | 1.32.02.0 | 0.31.01.0 | 1.72.32.0 | 1.31.32.0 | No. Moderate corneal opacity, noted 24 hours after the test item instillation remaining on the last day of the test (day 21: same intensity) in one animal  | R41Cat.1, H318. |

* . **Major change application for VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE – 2020**

For eye irritation, two studies have been done on the product VRCAM.

| **Summary table of in vitro studies on serious eye damage and eye irritation**  |
| --- |
| **Method,Guideline,****GLP status, Reliability** | **Test substance, Doses** | **Relevant information about the study** | **Results** | **Remarks** *(e.g. major deviations)* | **Reference** |
| OECD 438Isolated chicken eyeGLPReliability: 1 | VRCAM, 30 µL undiluted product  | enucleated chicken eyes: 3exposure during 10 seconds following by rinsingpositive and negative controls | Maximal mean score of corneal opacity: 2.0 corresponding to ICE class IIIMean score of fluorescein retention: 3.0 corresponding to ICE class IVMaximal mean corneal swelling: 13% (240 min) corresponding to ICE class II1\*IV, 1\*III, 1\*II No prediction can be made | No deviations | Barré T., 2019 |

|  |
| --- |
| **Summary table of animal studies on serious eye damage and eye irritation** |
| **Method,Guideline,** **GLP status, Reliability** | **Species,Strain,Sex,No/group** | **Test substance,Dose levels, Duration of exposure** | **Results***Average score (24, 48, 72h)/**observations and time point of onset, reversibility* | **Remarks** *(e.g. major deviations)* | **Reference**  |
| OECD 405 Eye irritationGLPReliability: 1 | New Zealand rabbitsMales3 | VRCAM as supplied* 1. mL
 | Average score (24, 48, 72h:Conjunctivae : -chemosis: 0.0/0.0/0.0 -redness: 1.3/0.3/0.3Iris :0.0 /0.0/0.0Cornea : 2.0/1.0/1.7Reactions totally reversible.* H319
 | No deviations | Richeux F., 2019 |

|  |
| --- |
| **Conclusion used in Risk Assessment – Eye irritation**  |
| Value/conclusion | Eye irritating of category 2H319 cause serious eye irritation |
| Justification for the value/conclusion | Three animals have a positive response for corneal opacity (mean score >1) |
| Classification of the product according to CLP and DSD | Eye irritating of category 2H319 cause serious eye irritation |

##### Sensitisation

A Magnusson and Kligman sensitisation test was submitted. No cutaneous reaction attributable to allergy was recorded in animals from the treated group after the challenge phase, on the treated areas with the test item at 100% and 50%. Therefore, RAMC is not classified as skin sensitiser.

|  |  |  |  |
| --- | --- | --- | --- |
| SpeciesStrainSex | Method | Number of animals sensitized/total number of animals | Result |
| Guinea pigsAlbino Dunkin-HartleyFemales | GPMT assay | Controls: 0/5 femalesTest group: 0/10 females | Not sensitising |

##### Other studies

No other study was performed on the biocidal product, since none of the non-active substances is a substance of concern and as RAMC will not be applied directly to feeding stuffs. In addition, intake of RAMC by animals producing food (eggs, milk, meat) is not expected based on the intended uses.

Therefore, no additional data are considered necessary

### Human exposure assessment

RAMC is an insect repellent containing 30% DEET as active substance and intended to be applied on human skin or on clothes to repel mosquitoes. Since the product is formulated as a ready-for-use product, no dilution or other preparation is necessary.

Applicant required authorisation for consumer adults and children aged 6 years and over.

|  |  |  |
| --- | --- | --- |
| **MG/PT** | **Field of uses envisaged** | **Likely concentrations at which a.s. will be used** |
| Main Group 03; Pest ControlPT19: Repellents and attractants | Professional uses |
| No | Not relevant |
| Non-professional uses |
| Repellent for use by consumers (non-professional users/adults and children older than 6 years, dermal application) against mosquitoes' attacks | 30% (w/w)  |

Method of application:

RAMC is intended to be applied by spraying on human skin or clothes to repel mosquitoes.

The product is formulated as a ready-to-use product, no dilution or other preparation is necessary.

RAMC is packaged in 80 mL, 100 mL or 150 mL bottles for use by consumers.

During one spray, 120 µL of product with a density of 0.95 were released.

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

**Inhalation exposure:**

RAMC will be applied by spraying. In this context an exposure by inhalation could be considered. However, the aerosol droplets generated by RAMC were assessed in a study. A mass median aerodynamic diameter (MMAD) of 66 μm was measured and only 1% of particles was < 9.4 μm.

RAMC is not expected to generate particles which are deposited in tracheobronchial and alveolar regions therefore the respirable fraction could be considered as negligible.

Although this dose 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.).

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:**

For the primary exposure, as mentionned above, the non respirable fraction of the inhalable dose will be considered as swallowed.

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

Hand-to-mouth transfer scenario concerns mainly the infant between 3 months and 3 years.

However, adults and children aged 6 years and over may be incidentally 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:**

This route is the main route of exposure as the product is directly applied on the skin.

The exposures of a person applying RAMC on him or herself and of a person who applies the product on another person are considered.

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

RAMC is an insect repellent containing 30% DEET as active substance and is intended to be used by adult and child aged 6 years and over consumers (non-professional exposure). Therefore the assessment of professional exposure is not relevant.

##### Exposure of non-professional users

For the inhalation exposure, as quoted above, considering the aerosol droplet diameter, the amount of substance could not be respirable but swallowed.

In a worst case, it was considered that all the amount of substance is swallowed without taking into account 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, is used.

| **Tier** | **Oral exposure by inhalation exposure** |
| --- | --- |
| Without PPE | Systemic dose  |
|  | mg a.s. / kg bw /day |
| **Task – time frame:** | **Scenario : exposure during application – one application**  |
| Adult woman | *5.38x10-4* |
| Adult man | *4.43x10-4* |
| 3-9 years | *8.05x10-4* |
| 9 -14 years | *6.41x10-4* |

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

The exposure by dermal route to RAMC can be calculated according to the following equation:



where:

ID Internal dose (mg/kg b.w./day)

ARp Average dose of product applied on skin (mg/cm²)

CDEET Average concentration of substance in product (%)

BS Body surface exposed to the product (cm²)

DA Dermal absorption (%)

N Number of product application per day (/day)

BW Body weight (kg)

This equation can be applied to male and female adults and to children.

ARp, CDEET, Dermal absorption and N remain the same, body parameters (such as body surface exposed to the product and body weight) vary according to gender and to age range.

The body parameters are issued from RIVM. The data for range 9-14 years cover a child of 11 years, and the data for range 3-9 years cover a child of 6 years.

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 + ¾ arms + hands + ½ legs.** When RAMC is applied on clothes, the following body segments which correspond to dressed parts: **trunk + ¼ arms + ½ legs** . No protection factor is taken into account

Summary of parameters for RAMC application

**Table: Parameters for the calculation of consumer exposure to RAMC**

|  |  |  |
| --- | --- | --- |
| Parameter | Value | Source |
| Average dose of product applied on skin (mg/cm²) | 1.1  | Applicant data  |
| Average concentration of substance in product | 30% w/w | Applicant data |
| Body surface exposed to the product (cm²) | See Table below | RIVM General Fact Sheet |
| Dermal absorption (%) | 20 | DEET Assessment Report |
| Number of product applications per day (/day) | 1 | Applicant data |
| Body weight (%) | See Table below | RIVM General Fact Sheet |

Table: results of exposure by dermal route after application of **RAMC** at 1.1 mg/cm2 (application on skin)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|   | **BS****Body surface areacm2 (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 per kgmg/kg** |
| Man | 7215 | 74 | 7936.5 | 30% | 2381.0 | 20% | 476.2 | 6.4 |
| Woman | 6451 | 61 | 7096.1 | 30% | 2128.8 | 20% | 425.8 | 7.0 |
| Child3-9 years | 3040 | 16.3 | 3344.0 | 30% | 1003.2 | 20% | 200.6 | 12.3 |
| Child9-14 years | 5361 | 39.3 | 5897.1 | 30% | 1769.1 | 20% | 353.8 | 9.0 |

Table: results of exposure by dermal route after application of **RAMC** at 1.67 mg/cm2 (application on clothes)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|   | **Body surface areacm2 (trunk + 1/4 arm + 1/2 legs) BS** | **Body weight(kg)** **BW** | **Mass of applied product(mg)** | **Active substance concentration (%)**CDEET | **Mass of applied active substance(mg)** | **Dermal absorption (%)** | **Mass of absorbed active substance(mg)** | **Active substance per kgmg/kg** **ID**  |
| Man | 10643 | 74 | 17774.6 | 30 | 5332.4 | 20  | 1066.5 | 14.4 |
| Woman | 9190 | 61 | 15346.6 | 30 | 4604.0 | 20  | 920.8 | 15.1 |
| Child3-9 years | 3547 | 16.3 | 5923.1 | 30 | 1776.9 | 20  | 355.4 | 21.8 |
| Child9-14 years | 6763 | 39.3 | 11294.0 | 30 | 3388.2 | 20  | 677.6 | 17.2 |

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.

* **Major change application for VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE – 2020**

VAPO CORPOREL REPULSIF ANTI-MOUSTIQUE is the same product than REPULSIF ANTI-MOUSTIQUES CORPOREL**.**

For application on skin, an additionnal use against ticks (*Ixodes ricinus*) and a reduction of the application rate to 0.5 mg/cm² have been also claimed by the applicant.

The same population (adults and children older 6 years) and number of application per day are claimed.

The exposure assessment is performed according to the Recommendation no. 11, 2018 of the BPC Ad hoc Working Group on Human Exposure (not available during the initial assessment).

This assessment covers the French approach.

Scenario [1]: Primary exposure – **application to the skin against mosquitoes/ticks**: Dermal exposure assessment for adults and children.

| **Description of Scenario [1]** |
| --- |
| Adults and children older 6 years can be exposed directly when spraying the product to the skin.It is considered that the exposure of the person spraying the product is covered by the exposure to the product he applies on his skin.The exposure by dermal route to VRCAM can be calculated according to the following equation:where:ID Internal dose (mg/kg b.w./day)ARp Average dose of product applied on skin (mg/cm²)CDEET Average concentration of active 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)The product is not intended to be applied on the total body surface but on the following body segments corresponding to uncovered parts. According to Recommendation no. 11, 2018[[11]](#footnote-12), the uncovered body surface area is approximately equal to 55% of the total body surface (head, neck, hands, lower arms, lower legs, feet and 70% of upper arms and thighs), assuming that during the whole season (mid-term exposure within a year) a short-sleeved shirt (i.e. T-shirt) and shorts are worn).For this use, only one application per day has been considered in the exposure assessment as claimed by the applicant. |
|  | Parameters1 | Value | Reference |
| Tier 1 | Dermal absorption | 20% | CAR |
| % of active substance in biocidal product | 30 % | Applicant’s data |
| Number of product application/day  | 1 | Applicant’s data |
| **Body weight (kg)** | Recommendation no. 14, 2017[[12]](#footnote-13) |
| Adult | 60 |  |
| Child (6 to <12 years old) | 23.9 |
| **Body surface exposed (cm²)** | Recommendation no. 11, 2018 Recommendation no. 14, 2017**Body surface** considering exposure to head, neck, hands (palms and backs), arms (lower arms and 70% of upper arms), lower legs, 70% of thighs and feet. |
| Adult | 9588.2 |
| Child (6 to <12 years old) | 5096.3 |  |

Calculations for Scenario [1]

**For one application**

| **Summary table: systemic exposure from non-professional uses** |
| --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake** | **Estimated dermal uptake****mg/kg/d** | **Estimated oral uptake** | **Estimated total uptake****mg/kg/d** |
| Scenario [1] adult | Tier 1 | NR | 4.79 | NR | 4.79 |
| Scenario [1] child 6-12 years | Tier 1 | NR | 6.40 | NR | 6.40 |

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

**Hand to mouth transfer**

Adults and children aged 6 years and over may be incidentally exposed orally to RAMC via hand-to-mouth behaviour. Even if the product contains a bittering agent, a reverse scenario calculation was included.

The hand surface area to put in the mouth to reach the AEL short-term has been determined by a reverse scenario.

The following parameters were taken into account in the calculations:

* Quantity of RAMC applied to the skin: 1.1 mg/cm2;
* Concentration of DEET in RAMC: 30%;
* Hand surface area; this value depends on the type of population (RIVM).
* Body weight; this value depends on the type of population (RIVM).

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|   |   | Body weight  | Hand surface area | Dose of AS to eat to reach the AEL short-term | Dose of product to eat to reach the AEL short-term | Skin surface area to put in the mouth to reach the AEL | % hand surface area to put in the mouth to reach the AEL |
| Age group | Mean | kg | cm² | mg | mg | cm² | % |
| 3-6 months | 4.5 months | 6.21 | 88 | 4.7 | 15.5 | 14.1 | 16% |
| 6-12 months | 7.5 months | 7.62 | 103 | 5.7 | 19.1 | 17.3 | 17% |
| 12-18 months | 13.5 months | 9.47 | 124 | 7.1 | 23.7 | 21.5 | 17% |
| 1.5-3 years | 1.5 years | 9.85 | 124 | 7.4 | 24.6 | 22.4 | 18% |
| 3-9 years | 4.5 years | 16.3 | 195 | 12.2 | 40.8 | 37.0 | 19% |
| 9-14 years | 12.5 years | 39,3 | 373 | 29,5 | 98,3 | 89,3 | 24% |
| Adult - man |  | 74 | 468 | 55,5 | 185,0 | 168,2 | 36% |
| Adult - woman |  | 61 | 412 | 45,8 | 152,5 | 138,6 | 34% |

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 34% (woman) or 36% (man) 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 19% (child 6-9 years old) or 24% (child 9-14 years old) of the surface of one hand.

**Chewing treated clothes (infants/children)**

Infants may be secondary exposed when chewing their parents’ treated clothes. A reverse scenario was used to determine the cloth surface area that a child or infant should chew to attain the acute AEL, based on the following parameters:

* Application rate: 1.67 mg/cm²
* % DEET in product: 30%
* Oral absorption factor: 100%
* Dislodgeable fraction from cloth: 100% (worst-case)
* Body weight: 3 kg (infant) or 15 kg (child)
* Reference dose: AEL acute = 0.75 mg/kg bw/day

The cloth surface area to be chewed is calculated as follows:

Cloth surface area = (AEL acute x body weight)/(Application rate x %DEET)

Cloth surface area (infant) = (0.75 mg/kg bw/day x 3 kg)/(1.67 mg/cm² x 30%) = 4.5 cm²

Cloth surface area (child) = (0.75 mg/kg bw/day x 15 kg)/(1.67 mg/cm² x 30%) = 22.5 cm²

* **Major change application for VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE – 2020**

The indirect exposure assessment performed during the initial assessment covers the major change since the dose is decreased from 1.1 mg/cm2 to 0.5 mg/cm2.

#### Indirect exposure via residues in food

No specific residue data were submitted in the context of this dossier. The product REPULSIF ANTI MOUSTIQUES CORPOREL 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.

A worst case exposure calculation for the product REPULSIF ANTI MOUSTIQUES CORPOREL was realized based on proposed and acceptable conditions of use following primary exposure assesment (i.e. only adults).



**Comment** : this calculation include a dilution factor of “3” following a washing hand preconised as a restriction of use to be realized after application and before eating foods. This default value was collected from the ConsExpo model[[13]](#footnote-14). 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 slightly 100% for adults. 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.

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, the Agency believes that the normal use of DEET does not present a health concern to the general population. EPA completed this review and issued its re-registration decision (called a RED) in 1998.[[14]](#footnote-15)

U.S. EPA label requirements state that[[15]](#footnote-16) :

* 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 REPULSIF ANTI MOUSTIQUES CORPOREL and EPA label requirements, the following restrictions of use are proposed:

* Do not applied near food
* 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

No combined exposure is assessed.

The exposure by inhalation route during spraying could be considered as negligible compared to exposure by dermal route post application.

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: Risk characterisation results for **RAMC** – Application on skin

|  |  |  |  |
| --- | --- | --- | --- |
|   | **Systemic exposure****active substance per kgmg/kg** | **AEL (mg/kg/d)** | **% AEL (%)** |
| Man | 6.4 | 8.2 | 78 |
| Woman | 7.0 | 8.2 | 85 |
| Child3-9 years | 12.3 | 8.2 | 150 |
| Child9-14 years | 9.0 | 8.2 | 110 |

Table: Risk characterisation results for **RAMC** – Application on clothes

|  |  |  |  |
| --- | --- | --- | --- |
|   | **Systemic exposure****active substance per kgmg/kg** | **AEL (mg/kg/d)** | **% AEL (%)** |
| Man | 14.4 | 8.2 | 176 |
| Woman | 15.1 | 8.2 | 184 |
| Child3-9 years | 21.8 | 8.2 | 266 |
| Child9-14 years | 17.2 | 8.2 | 210 |

An acceptable risk is identified for adults (men and women) when RAMC is applied on skin directly. However, the risk is unacceptable when RAMC is applied on clothes, considering a worst-case penetration factor from cloth of 100%.

In addition, the results demonstrate that the risk is unacceptable for children since the estimated systemic exposure for children aged 6 years or over is above the proposed systemic AEL of 8.2 mg/kg b.w./day.

Moreover, a reverse scenario has demonstrated that an adult can apply RAMC only once a day. Therefore, an adult will not be able to apply RAMC on another adult.

Overall, an acceptable risk is demonstrated for adult consumers only, when RAMC is applied on the bare skin only, once a day, at the application rate of 1.1 mg/cm².

* **Major change application for VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE – 2020**

**Systemic assessment**

| **Task/****Scenario** | **Tier** | **Systemic NOAEL****mg/kg bw/d** | **AEL****mg/kg bw/d** | **Estimated uptake****mg/kg bw/d** | **Estimated uptake/ AEL** **(%)** | **Systemic risk** **Acceptable****(yes/no)** |
| --- | --- | --- | --- | --- | --- | --- |
| **Scenario [1] application on skin** |
| Adult | 1 | 1000 | 8.2 | 4,79 | 58.5% | Yes |
| Child (6 to 12 years old) | 1 | 1000 | 8.2 | 6,40 | 78% | Yes |

The risk is acceptable for adults and children older 6 years.

**Local effects assessment**

Due to the classification of the product H319 - Eye irritating of category 2, RMM are needed to avoid exposure of eyes:

* Do not spray directly on face but spray on hands and apply to face
* Do not apply on eyelids and eyes
* For children between 6 and 12 years old, the repellent should be applied by adults.

#### Risk for indirect exposure

**Hand-to-mouth transfer**

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.

**Chewing treated clothes (infants/children)**

Infants may be secondary exposed when chewing their parents’ treated clothes. A reverse scenario was used to determine the cloth surface area that a child or infant should chew to attain the acute AEL, based on the following parameters:

* Application rate: 1.67 mg/cm²
* % DEET in product: 30%
* Oral absorption factor: 100%
* Dislodgeable fraction from cloth: 100% (worst-case)
* Body weight: 3 kg (infant) or 15 kg (child)
* Reference dose: AEL acute = 0.75 mg/kg bw/day

The cloth surface area to be chewed is calculated as follows:

Cloth surface area = (AEL acute x body weight)/(Application rate x %DEET)

Cloth surface area (infant) = (0.75 mg/kg bw/day x 3 kg)/(1.67 mg/cm² x 30%) = 4.5 cm²

Cloth surface area (child) = (0.75 mg/kg bw/day x 15 kg)/(1.67 mg/cm² x 30%) = 22.5 cm²

Although the transfer coefficient of DEET from cloth to mouth is a worst-case value, this surface is considered as very small especially for infants. However, this exposure scenario could be considered as accidental since parents are supposed to not allow their young children to chew the treated clothes. In addition, the presence of a bittering agent in the formulation will prevent the chewing of treated clothes by infants/children.

* **Major change application for VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE – 2020**

The major change has no impact on the conclusion of risk for indirect exposure.

#### Risk for indirect exposure

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 for consumers via residues in food

This assessment is based on acceptable primary conditions of use from the applicant and resulted acceptable first exposure (i.e. adults).

When the palm of hands are washed after application (proposed as precautionary statement on the labels), acute exposure to residues in food resulting from the intended uses for REPULSIF ANTI MOUSTIQUES CORPOREL is unlikely to cause a significant risk to the categories of users supported (adults)). Regarding consumer health protection, there are no objections against the intended uses.

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 REPULSIF ANTI MOUSTIQUES CORPOREL is unlikely to cause a significant dietary risk to the adults.

#### Conclusion of risks assessment for human health

An acceptable risk is identified for adult consumers only, when RAMC is applied on the bare skin only, once a day, at the application rate of 1.1 mg/cm².

When the palm of hands are washed after application, acute exposure to residues in food resulting from the intended uses for REPULSIF ANTI MOUSTIQUES CORPOREL is unlikely to cause a significant risk to the categories of users supported (adults).

* **Major Change application for VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE – 2020**

Change in the classification of the product VCRAM, with a lower eye irritation classification is concluded.

The change has no impact on the conclusions of the previous systemic risk assessment.

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

* Only use by adults
* Do not exceed one application per day
* Only applied 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
* 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

* **Major change application for VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE – 2020**

VAPO CORPOREL REPULSIF ANTI-MOUSTIQUE is the same product than REPULSIF ANTI-MOUSTIQUES CORPOREL**.**

In the frame of the major change application for the product **VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE** (30 % w/w DEET), a modification of the composition of the product with the replacement of a solvent by an other one has been submitted by the applicant. As these solvents are not classified for the environment, there is no impact on the initial environmental risk assessment.

For application on skin, an aditionnal use against ticks (*Ixodes ricinus*) and a reduction of the application rate to 0.5 mg/cm² have been also claimed by the applicant. This reduction of application rate has no impact on the initial environmental risk assessment.

### 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 – 96hEbC50 – 72h | 43117 | 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 RÉPULSIF ANTI-MOUSTIQUES CORPOREL 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, exposed to the biocidal product RÉPULSIF ANTI-MOUSTIQUES CORPOREL. 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).

A bittering agent is used in the biocidal product. 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 RÉPULSIF ANTI-MOUSTIQUES CORPOREL, 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.

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

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

##### Aquatic organisms

The product RÉPULSIF ANTI-MOUSTIQUES CORPOREL is not toxic to algae (ErC50 >100 mg/L).

Table 2.8.3.1‑1: algae test with RÉPULSIF ANTI-MOUSTIQUES CORPOREL SUBITO

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Test item** | **Species** | **Guideline** | **Endpoints** | **Toxicity (mg product/L)** | **Reference** |
| ***Algae*** |
| **SUBITO RÉPULSIF ANTI-MOUSTIQUES ADULTE SUBITO**  | *Pseudokirchneriella subcapitata* | OECD 201Static conditions | ErC50 – 72hEbC50 – 72h | >1001>1001 | III-B 7.2.2.2 |

1 based on nominal concentration and checked by analytical analysis

A new study with the product SUBITO RÉPULSIF ANTI-MOUSTIQUES ADULTE which is strictly identical to REPULSIF ANTI-MOUSTIQUES CORPOREL was submitted by the applicant. A summary is presented in the table below:

|  |  |
| --- | --- |
| **Title** | **Growth inhibition test on *Pseudokirchneriella subcapitata* with RÉPULSIF ANTI-MOUSTIQUES CORPOREL SUBITO / BEAST-OFF** |
| Author, date, N° reference | Martin C., 2013, Algae *Pseudokirchneriella subcapitata*, 72h-growth inhibition test performed on the test item "SUBITO REPULSIF MOUSTIQUES ADULTE", according to the OECD 201 guideline, Limit test, FCBA, Report No.402/12/1048F/g-e. |
| GLP | Yes |
| Deviation | No |
| Validity/ Acceptability | * In the controls, cell density increased by an average factor of > 16 within three days (161).
* The mean coefficient of variation for section-by-section specific growth rates in the control cultures did not exceed 35% (15.3%).
* The coefficient of variation of average specific growth rates during the whole test period in replicate control cultures did not exceed 7% (0.85%)
* the pH did not change by more than 1.5 units (0.3).
 |
| Method | Guideline | OECD Guideline No.201, 2006; Annex 5 corrected 28/07/2011. |
|  | Organisms | *Pseudokirchneriella subcapitata* |
|  | Test item | Trade name: SUBITO REPULSIF MOUSTIQUES ADULTE (Batch number 965)Chemical name: N,N-diethyl-m-toluamide (DEET)CAS No 134-62-3 |
|  | Treatments | - 6 replicates of the exposed algae to 100 mg SUBITO REPULSIF MOUSTIQUES ADULTE /L (limit test due to result of preliminary test), - 6 replicates of the control. |
|  | Exposure | 250 mL Erlenmeyer flasks, containing 100 mL of test solution placed in incubator where algal cells were kept in suspension by continuous shaking, under continuous light for 72 hours |
| Results | Analysis | The algae concentrations have been measured during the test at 24, 48 and 72 hours with a particle counter or under a microscope with a Malassez counting cell (in order to distinguish test substance particles from *Pseudokirchneriella subcapitata* alga cells).In order to verify the initial concentrations and maintenance of the exposure concentrations during the ecotoxicological testing, chemical analyses of test item in algae medium solutions have been performed according to the following protocol:* at the beginning of the test (T = 0h) for the Control (*i.e.* algae medium), and for the six replicates of the test concentration (100 mg/L);
* at the end of the test (T = 72h), for the Control and for the six replicates of the test concentration (100 mg/L).

A total of 14 analyses have been carried out. |
|  | Lethal effects | Not detected. No inhibition of growth rate was observed after 72 hours of exposure. The inhibition of average specific growth rate was -1.21%, indicating thus an increase compared to the control. The inhibition of yield was -6.40%, indicating also an increase compared to the control. |
|  | Sub-lethal effects | The EC50 for growth rate reduction (ErC50: 0-72h) and the EC50 for yield inhibition (EyC50: 0-72h) were beyond the range tested, *i.e.* exceeded 100 mg test item/L. |
| Conclusion | Endpoints | **ErC50 and** EyC50: **> 100 mg SUBITO REPULSIF MOUSTIQUES ADULTE /L (>30 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

Refer to section 2.8.2.1.3

#### 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

Refer to section 2.8.2.4

### Environmental exposure assessment

#### Assessment of exposure to the environment

The product RÉPULSIF ANTI-MOUSTIQUES CORPOREL is an insect repellent lotion containing 30% DEET as active substance and intended to be applied by spraying on human skin or clothes to repel mosquitoes. It is to be used by adults and children. The product is spread on the exposed area of the skin (*i.e*. face, neck, three-quarter arms, hands and half-legs) to protect people. Otherwise, the product can be sprayed on clothes. The recommended dose rate is one daily application only of **1.1 mg product.cm-2** of skin and/or **1.67** **mg product.cm-2** of fabric. Nevertheless, for applications on textile, it was decided to consider that 25% of the total quantity of the product applied per day was for clothes, as it was stated in the CAR of the active substance inclusion.

The first route of entry in the environment is assumed to be indirect, DEET reaching the water compartment *via* STP effluents, when people take a shower after DEET application or wash the DEET treated clothes. 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. This route of entry to 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-17) 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-18)) with some modifications in order to be conservative enough.

#### Environmental emission calculations and PEC derivations

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

Different scenarios are presented to cover the application schemes of RÉPULSIF ANTI-MOUSTIQUES CORPOREL:

* Skin: An application on skin only, at the dose rate of 1.1 mg product.cm-2 of skin considering a treated body surface of 7 215 cm2 according to the human exposure section, corresponding to 7.94 g product per application.
* Clothes: An application on clothes only considering that the quantity applied on clothes represents 25% of the total quantity applied by one person, corresponding to 2.65 g product per application (= 7.94 x (25/75)). No adsorption by fabric is taken into account in order to extrapolate the calculation to all kind of materials (Fwater=1).
* Skin and clothes: A simultaneous application on skin and clothes considering both application types cumulated

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

According to the ESD for PT01, Elocalwater (kg.d-1), *i.e.* theinflow 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 skin Fraction released to wastewater during skin cleaning (adapted CAR value for DEET applied on skin only = 0.865)

Fwater clothes Fraction released to wastewater during clothes washing (adapted CAR value for DEET applied on clothes only = 0.95)

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

Qforminh clothes Consumption per inhabitant per day (g.day-1; Nappl\*2.65 g product)

Qforminh skin and clothes Consumption per inhabitant per day (g.day-1; Qforminh skin + Qforminh clothes

Cformweight Concentration of the active substance in the product (specific value for RÉPULSIF ANTI-MOUSTIQUES CORPOREL = 300 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 RÉPULSIF ANTI-MOUSTIQUES CORPOREL = 1 day-1)

Qformappl skin Consumption per application (specific value for RÉPULSIF ANTI-MOUSTIQUES CORPOREL = 1.1 mg product.cm-2 for skin)

BS Body surface treated (7215 cm2)

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 RÉPULSIF ANTI-MOUSTIQUES CORPOREL. 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 0.865 released to wastewater (Fwater) is considered for the exposure assessment of RÉPULSIF ANTI-MOUSTIQUES CORPOREL. The evaporation reported in the CAR (5%) and the dermal absorption rate specific to RÉPULSIF ANTI-MOUSTIQUES CORPOREL (9%) are subtracted from the amount of DEET applied on skin only. In fact, when the product RÉPULSIF ANTI-MOUSTIQUES CORPOREL 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 RÉPULSIF ANTI-MOUSTIQUES CORPOREL used on skin. It should be noted that considering the lower dermal absorption value of 9% used in the CAR (specific to the active substance DEET regardless to the product properties) compared to the specific value for RÉPULSIF ANTI-MOUSTIQUES CORPOREL (20%; see toxicology section) represents a worst case approach for the environmental exposure assessment. Concerning the applications on clothes only, no dermal adsorption is considered and only the evaporation allows lowering the fraction of emission which is therefore stated at 0.95.

The applicant supplied a document justifying the use of a market share (Fpenetr) specific to RÉPULSIF ANTI-MOUSTIQUES CORPOREL 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 (Boomsma and Parathasarathy, 1990) 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 RÉPULSIF ANTI-MOUSTIQUES CORPOREL (Qformappl × Cformweight × BS x 10-6= 7.94 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. Nevertheless, the value for RÉPULSIF ANTI-MOUSTIQUES CORPOREL covers also the 75th percentile values (1.5 g or 1.66 g of DEET per skin application for male adult or children respectively). The total quantity of DEET for applications on skin and clothes used for the assessment of RÉPULSIF ANTI-MOUSTIQUES CORPOREL also covers the quantity used in the CAR (1.2 g).

Then,

 **Elocalwater skin= 2.13 kg DEET.d-1**

 **Elocalwater clothes= 0.78 kg DEET.d-1**

 **Elocalwater skin and clothes= 2.91 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 skin = 1.07mg DEET.L-1**

 **Clocalinf clothes = 0.39 mg DEET.L-1**

 **Clocalinf skin and clothes = 1.46 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 2.8.4.2‑1: 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 2.8.4.2‑2: Input and output values for calculation of concentrations in STP and surface water

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Local emission of active substance to waste water during episode:** | **Skin** | **Clothes** | **Skin and clothes** | **Unit** | **Reference** |
| **INPUTS** |  |  |  |  |  |  |
| Elocalwater | Emission rate to wastewater | 2.13 | 0.78 | 2.91 | [kg.d-1] | - |
| Clocalinf | Concentration in sewage water to default STP | 1.07 | 0.39 | 1.46 | [mg.L-1] | TGD Eq. 32 |
| Fstp water | Fraction emitted to water by STP |  | 12.6 |  | [%] | Table 2.8.4.2‑1 |
| Koc | Partition coefficient organic carbon-water |  | 43.3 |  | [L.kg-1] | - |
| Kpsusp | Solids-water partitioning coefficient |  | 4.33 |  | [L.kg-1] | TGD Eq. 23 |
| **OUPUTS** |  |  |  |  |  |  |
| **PECSTP** | PEC in the treated wastewater | 0.13 | 4.92E-02 | 0.18 | [mg.L-1] | TGD Eq. 33 |
| **PEClocalwater** | PEC in water during emission episode | 1.34E-02 | 4.92E-03 | 1.84E-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 2.8.4.2‑3. Degradation of the substance in soil is considered based on its ready biodegradability (DT50 soil: 30 days at 12°C); dissipation by leaching and volatilisation is also taken into account based on the TGD equations.

Table 2.8.4.2‑3: Input values and output values for the calculation of soil concentrations

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Local emission of active substance to soil during episode:** | **Skin** | **Clothes** | **Skin and clothes** | **Unit** | **Reference** |
| **INPUTS** |
| Elocalwater | Emission rate to wastewater | 2.13 | 0.78 | 2.91 | [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. 56TGD 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 |
| **OUTPUT** |
| **Csludge** | Concentration in dry sewage sludge | 12.23 | 4.48 | 16.71 | [mg.kg-1dwt] | TGD Eq. 36 |
| **PEC local soil** | PEC in soil after 10 years of application - Twa over 30 d | 1.27E-02 | 4.64E-03 | 1.73E-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. Modeling 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-19)). 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 2.8.4.2‑4: 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 Table 2.8.4.2‑5 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 2.8.4.2‑5: 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 RÉPULSIF ANTI-MOUSTIQUES CORPOREL 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 RÉPULSIF ANTI-MOUSTIQUES CORPOREL 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-20),[[20]](#footnote-21), 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 RÉPULSIF ANTI-MOUSTIQUES CORPOREL 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 = 0.865. 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 RÉPULSIF ANTI-MOUSTIQUES CORPOREL 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 RÉPULSIF ANTI-MOUSTIQUES CORPOREL = 300 g.kg-1)

Nappl Number of applications (specific value for RÉPULSIF ANTI-MOUSTIQUES CORPOREL = 1 day-1)

Qformappl Consumption per application (specific value for RÉPULSIF ANTI-MOUSTIQUES CORPOREL = 1.1 mg product.cm-2)

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

Fwater Fraction of the product emitted to the swimming water (0.865)

**Then,**

**Elocalwater = 0.17 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\*106 / Vbathing area**

**Then,**

**Clocalwater = 2.38E-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):

$$Clocalwater\\_annual =\frac{Elocal water}{Vwaterbody×k} \left[1- \frac{\left[1-e^{\left(-Temission × k\right)}\right]}{Temission × k}\right]$$

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 = 3.08E-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 = 5.46E-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 2.8.4.3‑1: 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) - Skin application** |
| STP | 0.13 | [mg.L-1] |
| Surface water | 1.34E-02 | [mg.L-1] |
| **Indirect emissions (via the STP – ESD PT01) - Clothes application** |
| STP | 4.92E-02 | [mg.L-1] |
| Surface water | 4.92E-03 | [mg.L-1] |
| **Indirect emissions (via the STP – ESD PT01) - Clothes and skin application** |
| STP | 0.18 | [mg.L-1] |
| Surface water | 1.84E-02 | [mg.L-1] |
| **Direct emissions (Swimming scenario) - Skin application** |
| Surface water – ClocalwaterShort term assessment in the bathing area | 2.38E-03 | [mg.L-1] |
| Surface water – Clocalwater\_annualLong term assessment in the lake | 3.08E-03 | [mg.L-1] |
| Surface water – Total ClocalwaterCumulative assessment | 5.46E-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 2.8.4.3‑2: Summary of PEC values for DEET for the terrestrial compartment only for indirect emissions (via the STP)

|  |  |  |
| --- | --- | --- |
|  | **PEC** | **Unit** |
| **Indirect emissions (via the STP)-Skin application** |
| Soil | 1.27E-02 | [mg.kg-1wwt] |
| Groundwater Focus PEARL 4.4.4 | < 0.1 | [µg.L-1] |
| **Indirect emissions (via the STP)-Clothes application** |
| Soil | 4.64E-03 | [mg.kg-1wwt] |
| Groundwater Focus PEARL 4.4.4 | < 0.1 | [µg.L-1] |
| **Indirect emissions (via the STP)-Skin and clothes application** |
| Soil | 1.73E-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 RÉPULSIF ANTI-MOUSTIQUES CORPOREL 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)

Table 2.8.5.1‑1: Risk characterization in the aquatic compartment

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **PEC** | **PNEC** | **Unit** | **PEC/PNEC** |
| **Indirect emissions (via the STP – ESD PT01) - Skin application** |
| STP | 0.13 | 10 | [mg.L-1] | 1.34E-02 |
| Surface water | 1.34E-02 | 4.3E-02 | [mg.L-1] | 0.31 |
| **Indirect emissions (via the STP – ESD PT01) - Clothes application** |
| STP | 4.92E-02 | 10 | [mg.L-1] | 4.92E-03 |
| Surface water | 4.92E-03 | 4.3E-02 | [mg.L-1] | 0.11 |
| **Indirect emissions (via the STP – ESD PT01) - Clothes and skin application** |
| STP | 0.18 | 10 | [mg.L-1] | 1.84E-02 |
| Surface water | 1.84E-02 | 4.3E-02 | [mg.L-1] | 0.43 |
| **Direct emissions (Swimming scenario) - Skin application** |
| STP | NR | 10 | [mg.L-1] |  |
| Surface water – ClocalwaterShort term assessment in the bathing area | 2.38E-03 | 4.3E-02 | [mg.L-1] | 5.53E-02 |
| Surface water – Clocalwater\_annual Long term assessment in the lake | 3.08E-03 | [mg.L-1] | 7.17E-02 |
| Surface water – Total Clocalwater Cumulative assessment | 5.46E-03 | [mg.L-1] | 0.13 |

NR: Not relevant

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, after 1 daily skin and/or clothes applications of RÉPULSIF ANTI-MOUSTIQUES CORPOREL.

##### 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 2.8.5.1‑2: Risk characterization in the terrestrial compartment only for indirect emissions (via the STP)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **PEC** | **PNEC** | **Unit** | **PEC/PNEC** |
| **Indirect emissions (via the STP) - Skin application** |
| Soil | 1.27E-02 | 3.79E-02 | [mg.kg-1wwt] | 0.33 |
| Groundwater Focus PEARL 4.4.4 | <0.1 | 0.1 | [µg.L-1] | <0.1 µg/LThreshold value in groundwater |
| **Indirect emissions (via the STP) - Clothes application** |
| Soil | 4.64E-03 | 3.79E-02 | [mg.kg-1wwt] | 0.12 |
| Groundwater Focus PEARL 4.4.4 | <0.1 | 0.1 | [µg.L-1] | <0.1 µg/LThreshold value in groundwater |
| **Indirect emissions (via the STP) - Skin and clothes application** |
| Soil | 1.73E-02 | 3.79E-02 | [mg.kg-1wwt] | 0.43 |
| Groundwater – Tier IIFocus PEARL 4.4.4 | <0.1 | 0.1 | [µg.L-1] | < 0.1 µg/LThreshold value in groundwater |

The PEC/PNEC ratio for soil compartiment is below the trigger value of 1 for skin and/or clothes repellent applications. Then, risks for terrestrial organisms are acceptable after only one daily skin application of RÉPULSIF ANTI-MOUSTIQUES CORPOREL .

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 (DEET CAR[[21]](#footnote-22), 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

* **Major change application for VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE – 2020**

VAPO CORPOREL REPULSIF ANTI-MOUSTIQUE is the same product than REPULSIF ANTI-MOUSTIQUES CORPOREL**.**

In the frame of the major change application for the product **VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE** (30 % w/w DEET), a modification of the composition of the product with the replacement of a solvent by an other one has been submitted by the applicant. As these solvents are not classified for the environment, there is no impact on the previous conclusions.

For application on skin, an aditionnal use against ticks (*Ixodes ricinus*) and a reduction of the application rate to 0.5 mg/cm² have been also claimed by the applicant. This reduction of application rate has no impact on the the previous conclusions.

Considering indirect emissions through the STP, and according to the applicant intended uses for RÉPULSIF ANTI-MOUSTIQUES CORPOREL, risks for surface water (including water and STP), soil and groundwater are acceptable.

Considering direct emissions through recreational bathing activities and according to the applicant intended uses for RÉPULSIF ANTI-MOUSTIQUES CORPOREL, the risk for surface water is acceptable.

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

**Therefore, it can be concluded** on acceptable environmental risks for the biocidal product RÉPULSIF ANTI-MOUSTIQUES CORPOREL applied on skin and/or clothes.

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 1 application of the product per day.

## Measures to protect man, animals and the environment

*See Summary of product characteristics.*

# Appendices

Annex 2: List of studies reviewed



|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Data submitted in January 2019 | yes | no | Yes | no |
| B3.7 | B3.7 | S. Lehay 2015 | 2015 | Storage stability during 3 years at ambient temperature on ready-to-use anti mosquito solution « repulsif anti moustiques corporel, subito / beast-off »H. Detrimont, 2015FCBA, report n° 402/12/1048F/f-e | Spring |  | x | x |  |



* **Major change application for VAPO CORPOREL REPULSIF ANTI- MOUSTIQUE – 2020**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Data submitted in January 2019 for the product VAPO REPULSIF CORPOREL ANTI-MOUSTIQUES  | yes | no | Yes | no |
| S3.1, S3.2, S3.4.1, S3.5 | 19-919062-002 | Halbwachs P. | 2019 | Physico-chemical tests and chemical analyses before and after an accelerated storage procedure at 54 ± 2°C for 14 days on the product VRCAM in compliance with CIPAC MT 46.3 CIPAC Handbook J (2000) | Spring |  | x | x |  |
| S3.4.1 | 19-919062-003 | Halbwachs P. | 2019 | Physico-chemical tests and chemical stability before, during and after a storage procedure for 36 months at 20 °C ± 2 °C on the product VRCAM In compliance with Technical Monograph No. 17, 2nd edition CropLife International | Spring |  | x | x |  |
| S3.4.1 | 19-919062-005 | Halbwachs P. | 2019 | Physico-chemical tests on the product RCAME | Spring |  | x | x |  |
| S3.5 | 19-919062-009 | Halbwachs P. | 2019 | Spray droplet size distribution by laser diffraction on the product VRCAM In compliance with the CIPAC Handbook K – MT 187 method (2003) and ISO 13320:2009 | Spring |  | x | x |  |
| S3.8, S3.9 | 19-919062-001 | Halbwachs P. | 2019 | Physico-chemical tests on the product VRCAM | Spring |  | x | x |  |
| S4.6 | 20-919062-001 | Padilla P. | 2020 | Flash point test on the product VRCAM | Spring |  | x | x |  |
| S5.1 | 19-919062-004 | Halbwachs P. | 2019 | Validation of the analytical method for the determination of N,N-diethyl-meta-toluamide (DEET) in VRCAM in compliance with SANCO/3030/99 rev.5 from 22/03/2019 | Spring |  | x | x |  |
| B6-7 | B6.7-01 | H. Dautel, 2019 | 2019 | Evaluation of the repellent efficacy of a product against the European Sheep Tick *Ixodes ricinus* on human volunteers H. Dautel, 2019IS Insect Services GmbHreport n° STA\_IR\_0218 | GmbH |  | x | x |  |





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 acuteADI Not applicableARfD Not applicable | 0.75 mg/kg/d | 8 week study (dogs, oral)[[22]](#footnote-23) | 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) | XnR22 R36/38 |
| with regard to toxicological data(according to the criteria in Reg. 1272/2008) | Acute Tox. 4 H302: Harmful if swallowedEye Irrit. 2 H319: Causes serious eye irritationSkin Irrit. 2 H315: Causes skin irritation. |

Annex 5 : Toxicology – biocidal product

<RAMC>

|  |
| --- |
| General information |
| Formulation Type | AL |
| Active substance(s) (incl. content) | 30% DEET |
| Category | PT 19 |

| Acute toxicity, irritancy and skin sensitisation of the preparation (Annex IIIB, point 6.1, 6.2, 6.3) |
| --- |
| Rat LD50 oral (OECD 423) | LD50>2000 mg/kg  |  |  |  |
| Rat LD50 dermal (OECD 402) | LD50>2000 mg/kg  |  |  |  |
| Rat LC50 inhalation (OECD 403) | No study submitted |  |  |  |
| Skin irritation (OECD 404) | Non irritant  |  |  |  |
| Eye irritation (OECD 405) | Severely irritant  |  |  |  |
| Skin sensitisation (OECD 406; GPMT) | Not sensitizing  |  |  |  |

| Additional toxicological information (e.g. Annex IIIB, point 6.5, 6.7) |
| --- |
| Short-term toxicity studies | None |  |  |  |
| Toxicological data on active substance(s)(not tested with the preparation) | None |  |  |  |
|  |  |  |  |  |
| Toxicological data on non-active substance(s)(not tested with the preparation) | None |  |  |  |
|  |  |  |  |  |
| Further toxicological information | None |

|  |
| --- |
| Classification and labelling proposed for the preparation with regard to toxicological properties (Annex IIIB, point 9) |
| Directive 1999/45/EC | Xi, R41 |
| Regulation 1272/2008/EC | Eye Dam. 1; H318 “Causes serious eye damage”. |

Annex 6 : Safety for professional operators

<RAMC>

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

<RAMC>

| General information |
| --- |
| Formulation Type | AL |
| Active substance(s) (incl. content) | 30% DEET |
| Category |  |
| 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 + amount applied on skin |
| Secondary exposure, acute | Oral exposure by hand-to-mouth transfer |
| Secondary exposure, chronic | Not relevant |

Conclusion:

The risk is considered as acceptable for adults when RAMC is applied on the bare skin only, once a day, at the application rate of 1.1 mg/cm², but as unacceptable for children to the biocidal product containing 30% DEET as active substance.

**Exposure and risk characterization after application of the product at 1.1 mg/cm2**

Application on skin

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **application rate** | 1.1 | mg/cm² |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |
|   | **Body surface areacm² (head + 3/4 arm + hands + 1/2 legs)** | **Body weight(kg)** | **Mass of applicated product(mg)** | **Active substance concentration (%)** | **Mass of applicated active substance(mg)** | **Dermal absorption (%)** | **Mass of absorbed active substance(mg)** | **Active substance per kgmg/kg** | **AEL MT cutmg/kg/d)** | **expo/AEL (%)** | **Number of acceptable applications per day**  |
| man | 7215 | 74 | 7936.5 | 30% | 2381.0 | 20.00% | 476.2 | 6.4 | 8.2 | 78% | 1.27 |
| woman | 6451 | 61 | 7096.1 | 30% | 2128.8 | 20.00% | 425.8 | 7.0 | 8.2 | 85% | 1.17 |
| 3-6 months | 1572 | 6.21 | 1729.2 | 30% | 518.8 | 20.00% | 103.8 | 16.7 | 8.2 | 204% | 0.49 |
| 6-12 months | 1777 | 7.62 | 1954.7 | 30% | 586.4 | 20.00% | 117.3 | 15.4 | 8.2 | 188% | 0.53 |
| 12-18 months  | 2034 | 9.47 | 2237.4 | 30% | 671.2 | 20.00% | 134.2 | 14.2 | 8.2 | 173% | 0.58 |
| 1.5-3 years | 2094 | 9.85 | 2303.4 | 30% | 691.0 | 20.00% | 138.2 | 14.0 | 8.2 | 171% | 0.58 |
| 3-9 years(4.5) | 3040 | 16.3 | 3344.0 | 30% | 1003.2 | 20.00% | 200.6 | 12.3 | 8.2 | 150% | 0.67 |
| 9-14 years | 5361 | 39.3 | 5897.1 | 30% | 1769.1 | 20.00% | 353.8 | 9.0 | 8.2 | 110% | 0.91 |

Application on clothes

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **application rate** | 1,67 | mg/cm² |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
|   | **Body surface areacm² (trunk + 1/4 arm + 1/2 legs)** | **Body weight(kg)** | **Mass of applicated product(mg)** | **Active substance concentration (%)** | **Mass of applicated active substance(mg)** | **Dermal absorption (%)** | **Cloth** | **Mass of absorbed active substance(mg)** | **Active substance per kgmg/kg** | **AEL MT cutmg/kg/d)** | **expo/AEL (%)** | **Number of acceptable applications per day**  |
| man | 10643 | 74 | 17774.6 | 30% | 5332.4 | 20.00% | 100.00% | 1066.5 | 14.4 | 8.2 | 176% | 0.57 |
| woman | 9190 | 61 | 15346.6 | 30% | 4604.0 | 20.00% | 100.00% | 920.8 | 15.1 | 8.2 | 184% | 0.54 |
| 3-6 months | 1646.095 | 6.21 | 2749.0 | 30% | 824.7 | 20.00% | 100.00% | 164.9 | 26.6 | 8.2 | 324% | 0.31 |
| 6-12 months | 1924.33 | 7.62 | 3213.6 | 30% | 964.1 | 20.00% | 100.00% | 192.8 | 25.3 | 8.2 | 309% | 0.32 |
| 12-18 months  | 2304.645 | 9.47 | 3848.8 | 30% | 1154.6 | 20.00% | 100.00% | 230.9 | 24.4 | 8.2 | 297% | 0.34 |
| 1.5-3 years | 2389.2 | 9.85 | 3990.0 | 30% | 1197.0 | 20.00% | 100.00% | 239.4 | 24.3 | 8.2 | 296% | 0.34 |
| 3-9 years(4.5) | 3546.7725 | 16.3 | 5923.1 | 30% | 1776.9 | 20.00% | 100.00% | 355.4 | 21.8 | 8.2 | 266% | 0.38 |
| 9-14 years | 6762.875 | 39.3 | 11294.0 | 30% | 3388.2 | 20.00% | 100.00% | 677.6 | 17.2 | 8.2 | 210% | 0.48 |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|   |   | Body weight  | Hand surface area | Dose of AS to eat to reach the AEL short-term | Dose of product to eat to reach the AEL short-term | Skin surface area to put in the mouth to reach the AEL | % hand surface area to put in the mouth to reach the AEL |
| Age group |  Mean | kg | cm² | mg | mg | cm² | % |
| 3-6 months | 4.5 months | 6.21 | 88 | 4.7 | 15.5 | 14.1 | 16% |
| 6-12 months | 7.5 months | 7.62 | 103 | 5.7 | 19.1 | 17.3 | 17% |
| 12-18 months | 13.5 months | 9.47 | 124 | 7.1 | 23.7 | 21.5 | 17% |
| 1.5-3 years | 1.5 years | 9.85 | 124 | 7.4 | 24.6 | 22.4 | 18% |
| 3-9 years | 4.5 years | 16.3 | 195 | 12.2 | 40.8 | 37.0 | 19% |
| 9-14 years | 12.5 years | 39,3 | 373 | 29,5 | 98,3 | 89,3 | 24% |
| Adult - man |   | 74 | 468 | 55,5 | 185,0 | 168,2 | 36% |
| Adult - woman |   | 61 | 412 | 45,8 | 152,5 | 138,6 | 34% |

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 |
| --- | --- | --- | --- | --- | --- | --- |
| RAMC (less than one year old),DEET 300 g/l | *Culex pipiens**Aedes albopictus**Aedes aegypti**Anopheles gambiae*For each test organism, 200 ± 10 females (5 to 7 days old) for each replicate.  | The average duration of efficacy was 8 hours for the 4 species of mosquitoes.Laboratory test. Arm-in-cage study.3 volunteers (2 men and 1 woman).3 replicates per volunteerProduct applied on one forearm of each volunteer, the other untreated one being used as a control. Dose of product 1 g / 600 cm² (± 3%), *i.e.* 3 sprays, a forearm corresponding 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 9 hours or inefficacy. Landings and bites were counted during each exposure time. | 200 ± 10 insects in each cage. 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 65 ± 10%, with a light intensity of 700 lux. | The study demonstrates in laboratory condition, the reppelent efficacy of the product RAMC (liquid, DEET 300 g/l) at the application rate of 1 g / 600 cm² (equivalent to 1.67 mg product/ cm²; 0.5 mg DEET /cm²) against the four mosquitoes tested.The duration of protection was:* 8 hours for *Culex pipiens*
* 8.1 hours for *Aedes albopictus*
* 7.9 hours for *Aedes aegypti*
* 8.1 hours for *Anopheles gambiae*

Based on the less sensitive species, the protection duration of the product is 8 hours when the product is applied on skin in laboratory conditions.Note that this application rate has not been claimed by the applicant and has not been taken into account | Serrano B. (2012)B5.10/01 | 2 |
| RAMC (less than one year old),DEET 300 g/L | *Culex pipiens**Aedes albopictus**Aedes aegypti**Anopheles gambiae*For each test organism, 200 ± 10 females (5 to 7 days old) for each replicate. | The average duration of efficacy was 4 hours for the 4 species of mosquitoes.Laboratory test. Arm-in-cage study.3 volunteers (2 men and 1 woman).3 replicates per volunteerProduct applied on one forearm of each volunteer, the other untreated one being used as a control. Dose of product 0.66 g / 600 cm² (± 3%), *i.e.* 3 sprays, a forearm corresponding 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 9 hours or inefficacy. Landings and bites were counted during each exposure time. | 200 ± 10 insects in each cage. 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 65 ± 10%, with a light intensity of 700 lux. | The study demonstrates in laboratory condition, the reppelent efficacy of the product RAMC (liquid, DEET 300 g/l) at the application rate of 0.66 g / 600 cm² (equivalent to 1.1 mg product/ cm²; 0.33 mg DEET /cm²) against the four mosquitoes tested.The duration of protection was:* 4.1 hours for *Culex pipiens*
* 3.9 hours for *Aedes albopictus*
* 3.9 hours for *Aedes aegypti*
* 4.1 hours for *Anopheles gambiae*

Based on the less sensitive species, the protection duration of the product is 4 hours when the product is applied on skin in laboratory conditions. | Serrano B. (2013)B5.10/02 | 2 |
| RAMC (less than one year old),DEET 300 g/L | *Culex pipiens**Aedes albopictus**Aedes aegypti**Anopheles gambiae*For each test organism, 200 ± 10 females (5 to 7 days old) for each replicate. | The average duration of efficacy was 4 hours for the 4 species of mosquitoes.Laboratory test. Arm-in-cage study.3 volunteers (2 men and 1 woman).3 replicates per volunteerProduct applied on one forearm of each volunteer, the other untreated one being used as a control. Dose of product 1 g / 600 cm² (± 3%), *i.e.* 3 sprays, a forearm corresponding to an average area of 600 cm². The trial began 30 minutes after the product had been applied. The product was sprayed on cotton fabric that was used to cover one forearm volunteer.The control forearm was covered with an untreated cotton and was inserted in the cage, and after validation of this control, the treated foream was inserted into the cage for 3 minutes (exposure time). The same procedure was repeated every hour until 9 hours or inefficacy. Landings and bites were counted during each. | 200 ± 10 insects in each cage. 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 65 ± 10%, with a light intensity of 700 lux. | The study demonstrates in laboratory condition, the reppelent efficacy of the product RAMC (liquid, DEET 300 g/l) at the application rate of 1 g / 600 cm² (equivalent to 1.67 mg product/ cm²; 0.5 mg DEET /cm²) against the four mosquitoes tested.The duration of protection was:* 7.9 hours for *Culex pipiens*
* 8.0 hours for *Aedes albopictus*
* 8.2 hours for *Aedes aegypti*
* 8.1 hours for *Anopheles gambiae*

Based on the less sensitive species, the protection duration of the product is 8 hours when the product is applied on fabric (cotton) in laboratory conditions. | Serrano B. (2013)B5.10/03 | 2 |

1. Please delete as appropriate. [↑](#footnote-ref-2)
2. For micro-organisms based products: indication on the need for the biocidal product to carry the biohazard sign specified in Annex II to Directive 2000/54/EC (Biological Agents at Work). [↑](#footnote-ref-3)
3. Copy this section as many times as necessary (one table per use, together with any instructions for use, risk mitigation measures and other directions for use that are use-specific. It has to be noted that in accordance with Document CA-May14-Doc.5.6 – Final, the SPC of a biocidal product presents the authorised uses as a number of pre-defined uses to which the product label shall have full correspondence. [↑](#footnote-ref-4)
4. Describe the necessary instructions for use like for example: period of time needed for the biocidal effect; the interval to be observed between applications of the biocidal product or between application and the next use of the product treated, or the next access by humans or animals to the area where the biocidal product has been used, including particulars concerning decontamination means and measures and duration of necessary ventilation of treated areas; particulars for adequate cleaning of equipment; particulars concerning precautionary measures during transport; precautions to be taken to avoid the development of resistance. [↑](#footnote-ref-5)
5. Describe the necessary instructions for use like for example: period of time needed for the biocidal effect; the interval to be observed between applications of the biocidal product or between application and the next use of the product treated, or the next access by humans or animals to the area where the biocidal product has been used, including particulars concerning decontamination means and measures and duration of necessary ventilation of treated areas; particulars for adequate cleaning of equipment; particulars concerning precautionary measures during transport; precautions to be taken to avoid the development of resistance. [↑](#footnote-ref-6)
6. V.Corbel, M. Stankiewicz, C. Pennetier, D. Fournier, J. Stojan, E. Girard, M. Dimitrov, J. Molgó, J-M. Hougard, B. Lapied, *Evidence for inhibition of cholinesterases in insect and mammalian nervous systems by the insect repellent deet*, *BMC Biology* 2009, **7**:47. [↑](#footnote-ref-7)
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