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

**ADDENDUM**

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

(submitted by the evaluating Competent Authority)



REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS

Product type 19

DEET

REPULSIF ANTI-MOUSTIQUES ENFANTS Case Number MAC in R4BP: BC-AC021951-66

REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS Case Number MIC in R4BP : BC-QK052976-15

Evaluating Competent Authority: France

Updated : February 2021

**Table of Contents**

[1 CONCLUSION 4](#_Toc468895983)

[2 ASSESSMENT REPORT 7](#_Toc468895984)

[2.1 Summary of the product assessment 7](#_Toc468895985)

[2.1.1 Administrative information 7](#_Toc468895986)

[2.1.1.1 Identifier of the product 7](#_Toc468895987)

[2.1.1.2 Authorisation holder 7](#_Toc468895988)

[2.1.1.3 Manufacturer of the product 7](#_Toc468895989)

[2.1.1.4 Manufacturer of the active substance 7](#_Toc468895990)

[2.1.2 Product composition and formulation 8](#_Toc468895991)

[2.1.2.1 Identity of the active substance 8](#_Toc468895992)

[2.1.2.2 Identity of the active substance 8](#_Toc468895993)

[2.1.2.3 Candidate for substitution 8](#_Toc468895994)

[2.1.2.4 Qualitative and quantitative information on the composition of the biocidal product 9](#_Toc468895995)

[2.1.2.5 Information on the substance(s) of concern 9](#_Toc468895996)

[2.1.2.6 Type of formulation 9](#_Toc468895997)

[2.1.3 Hazard and precautionary statements 9](#_Toc468895998)

[2.1.4 Authorised use(s) 9](#_Toc468895999)

[2.1.4.1 Use description 9](#_Toc468896000)

[2.1.4.2 Use description 10](#_Toc468896001)

[2.1.4.3 Use description 11](#_Toc468896002)

[2.1.5 General directions for use 12](#_Toc468896003)

[2.1.5.1 Instructions for use 12](#_Toc468896004)

[2.1.5.2 Risk mitigation measures 13](#_Toc468896005)

[2.1.5.3 Particulars of likely direct or indirect effects, first aid instructions and emergency measures to protect the environment 13](#_Toc468896006)

[2.1.5.4 Instructions for safe disposal of the product and its packaging 13](#_Toc468896007)

[2.1.5.5 Conditions of storage and shelf-life of the product under normal conditions of storage 13](#_Toc468896008)

[2.1.6 Other information 14](#_Toc468896009)

[2.1.7 Packaging of the biocidal product 14](#_Toc468896010)

[2.1.8 Documentation 14](#_Toc468896011)

[2.1.8.1 Data submitted in relation to product application 14](#_Toc468896012)

[2.1.8.2 Access to documentation 14](#_Toc468896013)

[2.2 Assessment of the biocidal product 15](#_Toc468896014)

[2.2.1 Intended use(s) as applied for by the applicant 15](#_Toc468896015)

[2.2.2 Physical, chemical and technical properties 16](#_Toc468896016)

[2.2.3 Physical hazards and respective characteristics 22](#_Toc468896017)

[2.2.4 Methods for detection and identification 24](#_Toc468896018)

[2.2.5 Efficacy against target organisms 26](#_Toc468896019)

[2.2.5.1 Function and field of use 26](#_Toc468896020)

[2.2.5.2 Organisms to be controlled and products, organisms or objects to be protected 26](#_Toc468896021)

[2.2.5.3 Effects on target organisms, including unacceptable suffering 26](#_Toc468896022)

[2.2.5.4 Mode of action, including time delay 27](#_Toc468896023)

[2.2.5.5 Efficacy data 27](#_Toc468896024)

[2.2.5.6 Occurrence of resistance and resistance management 31](#_Toc468896025)

[2.2.5.7 Known limitations 31](#_Toc468896026)

[2.2.5.8 Evaluation of the label claims 31](#_Toc468896027)

[2.2.6 Risk assessment for human health 31](#_Toc468896028)

[2.2.6.1 Assessment of effects on Human Health 31](#_Toc468896029)

[2.2.6.2 Exposure assessment 32](#_Toc468896030)

[2.2.6.3 Risk characterisation for human health 42](#_Toc468896031)

[2.2.7 Risk assessment for animal health 47](#_Toc468896032)

[2.2.8 Risk assessment for the environment 47](#_Toc468896033)

[2.2.9 Measures to protect man, animals and the environment 47](#_Toc468896034)

[2.2.10 Assessment of a combination of biocidal products 47](#_Toc468896035)

[2.2.11 Comparative assessment 47](#_Toc468896036)

**Note to the reader**

This consolidated PAR for the major change of the product authorisation of REPULSIF CORPOREL ANTI-MOUSTIQUES is based on the consolidated PAR of the major change of the product REPULSIF ANTI-MOUSTIQUE ENFANTS which is itself based on the PAR of the initial authorisation of the product REPULSIF ANTI-MOUSTIQUES CORPOREL. All addenda have been included in this document.

In part 2.1 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* | - | 21/11/2014 | First authorisation REPULSIF ANTI-MOUSTIQUE CORPOREL (30% DEET) |
| NA-BBS | *FR* | BC-SJ019820-35 | 04/11/2015 | First authorisation REPULSIF ANTI-MOUSTIQUE ENFANTS (30 % DEET) |
| NA-MAC | *FR* | BC-AC021951-66 | 16/01/2017 | Major change assessment :   * Decrease of the active substance concentration: 10 % DEET * Addition of use: spraying on the clothes * Change of conditions of application |
| NA-BBS | *FR* | BC-LP053125-32 | 08/10/2019 | Same authorisation for the product REPULSIF CORPOREL ANT-MOUSTIQUES ENFANTS |
| NA-MAC | *FR* | BC-PV058594-98 | 19/05/2021 | Major change assessment :   * Change of classification for eye irritation. * Change of co-formulant. * Addition of trade names. * Modification of the application rate. * Addition of target organism, ticks, Ixodes ricinus. |

# CONCLUSION

**Major change application for REPULSIF ANTI-MOUSTIQUE ENFANTS – 2017:**

The major change consists in the reduction of active substance concentration in the product, from 30 % to 10 %, an addition of use (spraying on the clothes), a change of conditions of application and the addition of the target organism *Ixodes ricinus.*

**Conclusion on physico-chemical properties**

The product REPULSIF ANTI-MOUSTIQUES ENFANT (RAME) is a clear and colorless liquid with a characteristic odour. The pH of pure product is about 7.7 at 20°C and its relative density is 0.962. The dynamic viscosity of the product is < 6.62 mm²/s at 20°C and 40°C.

After accelerated storage procedure (14 days at 54 ± 2°C) product REPULSIF ANTI-MOUSTIQUES ENFANT and its commercial packaging (100 mL white spray in PET) were considered to be stable after an accelerated storage procedure 14 days at 54 ± 2°C.

The stability data submitted in post-authorisation, indicate the product REPULSIF ANTI-MOUSTIQUE ENFANTS is stable after 24 months storage at 25 °C in its commercial packaging (spray in PET).

RAME is not expected to be 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 “Shake before use”.

Concerning the biocidal product RAME, it was demonstrated that physical hazards can be extrapolated from studies performed with the initial formulation.

According to the results of the flash point (41.9°C), RAME is expected be classified as flammable liquid cat. 3, H226 according to CLP regulation (EC) 1272/2008.

RAME is not expected to present a significant hazard for explosive properties, self-reactivity, oxidising properties and auto-flammability.

**Conclusion on efficacy**

The efficacy studies submitted demonstrate that the product REPULSIF ANTI-MOUSTIQUES ENFANTS is efficient as a mosquito repellent (genus *Culex spp., Aedes spp.* and *Anopheles spp.*) for 4 hours when applied on skin in temperate climate and for 3.5 hours when applied on skin in tropical climate at the application rate of 0.95 mg product / cm², and then for 3.5 hours when applied on fabric (cotton only), in tropical conditions at the application rate of 1.54 mg product / cm².

Post data authorization: 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.

**Conclusion on human health**

Due to the classification of the product (H318 - Eye Dam. 1.) and the risk of exposure of eyes during spray application, this product will not be authorized in accordance with Article 19 (1) of the BPR.

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

Regarding the intended use of the product REPULSIF ANTI-MOUSTIQUES ENFANTS, a contamination of food cannot be excluded.

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

**Conclusion on ecotoxicology and environment**

No change with the conclusions of the assessment on the reference product REPULSIF ANTI-MOUSTIQUE CORPOREL.

**Overall conclusion**

**In France, given the need to repel mosquitoes from human to prevent vector borne disease, the product REPULSIF ANTI MOUSTIQUE ENFANT will be authorized for use on humans against mosquitoesbased on article 19(5) with appropriated risk mitigation measures. It has to be applied on adults and on children above 3 years old, for the skin application twice a day, for the clothes application twice a day and for the combined application once a day. For children younger than 3 years old, skin application can be done twice a day and clothes application once a day. No combined application can be done for children under 3 years old.**

**Major Change application REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS – 2020 and change according to the EU discussion in the frame of mutual recognition in sequence regarding the product REPULSIF ANTI-MOUTSIQUES ENFANTS:**

The major change consists in the change of classification for eye irritation, modification of composition, addition of trade names and a modification of the application rate.

**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 should submit a minor change dossier to confirm the shelf life of 3 years including final results of the ongoing study.

**Conclusion on efficacy**

The efficacy studies submitted demonstrate that the product REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS is efficient as:

* a mosquito repellent:

for 6 hours when applied on skin in temperate conditions (genus *Culex spp., Aedes spp)* and tropical conditions (*Anopheles spp.)* at the application rate of 1.2 mg product / cm², and

for 7 hours when applied on fabric (cotton only), in temperate conditions (genus *Culex spp., Aedes spp)* and tropical conditions (*Anopheles spp.)* at the application rate of 1.8 mg product / cm².

* a tick repellent (*I. ricinus*) for 7 hours when applied on skin, in temperate conditions at the application rate of 1.2 mg product/cm².

The efficacy of the product REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS against ticks (*I.ricinus*) when applied on clothes has not been demonstrated.

**Human Health**

The data submitted by applicant are considered acceptable and lead to a modification of the classification of the product. Therefore, the product is now classified H319 instead of H318.

Several conditions related to the application of the product have changed as the application rate has been modified, those modifications have been reported in the SPC.

The risk evaluation leads to an unacceptable risk regarding the clothes application for the children and toddlers (1 to <6 years old) and for an application twice a day on adults and children above 6 years old.

Therefore the product REPULSIF CORPOREL ANTI MOUSTIQUE ENFANT is authorized for use on humans against mosquitoes:

* for the skin application: once a day for adults, children between 1 year and 12 years. The product must not be applied on the hands of children between one and 2 years.
* for the clothes application: once a day on adults and children above 6 years old.
* for the combined application: once a day for adults and children over 12 years.

***Risk assessment for 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 risk assessment has been revised considering the new application rates and leads to acceptable risks to the environmental compartments.

# ASSESSMENT REPORT

## Summary of the product assessment for the Major change application of REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS - 2020

### Administrative information

#### Identifier of the product

| **Trade name(s)** |  |
| --- | --- |
| REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS  Répulsif Spécial Enfants  Anti-Moustiques Enfants  Répulsif Anti-Moustiques Vêtements  Anti-Moustiques Vêtements  Répulsif Anti-Moustiques Peaux et Vêtements Répulsif Anti-Tiques Corporel  Répulsif Anti Tiques  Répulsif Anti-Moustiques et Anti-Tiques  Répulsif Anti-Moustiques  Répulsif Anti-Moustiques Familles  Répulsif Anti-Moustiques Adultes  Répulsif Anti-Moustiques Corporel et Textile |  |

#### Authorisation holder

|  |  |  |
| --- | --- | --- |
| **Name and address of the authorisation holder** | **Name** | SARL SPRING |
| **Address** | 4, rue Blaise Pascal  Z.I. du Bois de Leuze  13310 Saint-Martin-de-Crau  France |
| **Authorisation number** | FR-2015-0054 | |
| **R4BP asset reference number** | FR-00112847-0000 | |
| **Date of the authorisation** | 04/11/2015 | |
| **Expiry date of the authorisation** | 21/11/2024 | |

#### Manufacturer of the product

|  |  |
| --- | --- |
| **Name of manufacturer** | SARL SPRING |
| **Address of manufacturer** | 4, rue Blaise Pascal  Z.I. du Bois de Leuze  13310 Saint-Martin-de-Crau  France |
| **Location of manufacturing sites** | 4, rue Blaise Pascal  Z.I. du Bois de Leuze  13310 Saint-Martin-de-Crau  France |

#### Manufacturer of the active substance

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

### Product composition and formulation

#### Identity of the active substance

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

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

Yes

No

#### Identity of the active substance

|  |  |
| --- | --- |
| **Main constituent(s)** | |
| **ISO name** | DEET |
| **IUPAC or EC name** | N,N-diethyl-m-toluamide |
| **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 for substitution

No

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

| **Common name** | **IUPAC name** | **Function** | **CAS number** | **EC number** | **Content (%)** |
| --- | --- | --- | --- | --- | --- |
| DEET (technical) | Mixture containing minimum 97 % N,N-diethyl-*m*-toluamide | Active substance | 134-62-3 | 205-149-7 | 10.31 % m/m |

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

Please see the confidential annex for further details.

#### Type of formulation

|  |
| --- |
| AL : any other liquid (spray formulation) |

### Hazard and precautionary statements

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

| **Classification** | |
| --- | --- |
| Hazard category | Eye Irrit. 2 |
| Hazard statement | H319: Causes serious eye irritation |
|  | |
| **Labelling** | |
| Signal words | Danger |
| Hazard statements | H319: Causes serious eye irritation |
| Precautionary statements | P101: If medical advice is needed, have product container or label at hand.  P102: Keep out of reach of children  P103: Read label before use.  P305+P351+P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses if present and easy to do – continue rinsing.  P233: Keep container tightly closed.  P337+P313: If eye irritation persists: Get medical advice/ attention.  P264: Wash … thoroughly after handling. |
|  | |
| Note |  |

### Authorised use(s)

#### Use description

Table 1. Use # 1 – Spraying on the skin

|  |  |
| --- | --- |
| **Product Type** | PT19 – Repellents and attractants (pest control) |
| **Where relevant, an exact description of the authorised use** | The product RCAME is a ready-to-use lotion to be sprayed on the exposed area of human skin. |
| **Target organism(s) (including development stage)** | Culicidae (*Culex spp., Aedes spp., Anopheles spp.)* - Adults  Tick *(Ixodes ricinus) –* |
| **Field(s) of use** | Indoor and outdoor use |
| **Application method(s)** | Spraying |
| **Application rate(s) and frequency** | 1.2 mg product/cm² of skin, once a day for adults and children older than 1 year, equivalent to 5 sprays for an adult 600cm² forearm and 2 sprays per child forearm (2 – 6 years)  (5 sprays per adult forear  EU assessment:  Once a day for children older than 12 years and adults  Once a day for children between 1 year and 12 years  Temperate conditions:  Mosquitoes (*Aedes spp. and Culex spp)*: Protection time up to 6 hours  Ticks (*Ixodes ricinus*): Protection time up to 6 hours.  Tropical conditions:  Mosquitoes *(Anopheles spp):* Protection time up to 6 hours. |
| **Category(ies) of users** | General public (non-professional) |
| **Pack sizes and packaging material** | Spray bottles   * PET with PP/ polyoxymethylene spray: 80 mL, 100 mL, 150 mL |

##### Use-specific instructions for use

|  |
| --- |
| * In case of sunscreen product use, wait at least 20 minutes before applying the repellent, after the sunscreen product. |

##### Use-specific risk mitigation measures

|  |
| --- |
| * Do not exceed one applications per day. * Do not use on children under 1 year-old. * Only apply on uncovered skin. * Wash hands before handling food. * Do not treat hands of children. * Do not spray directly on face but spray on hands and apply to face. * Do not apply on eyelids and eyes |

##### 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

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| --- |
| - |

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

|  |
| --- |
| - |

#### Use description

Table 2. Use # 2 – Spraying on the clothes

|  |  |
| --- | --- |
| **Product Type** | PT19 – Repellents and attractants (pest control) |
| **Where relevant, an exact description of the authorised use** | The product RCAME is a ready-to-use lotion to be sprayed on clothes. |
| **Target organism(s) (including development stage)** | Culicidae (*Culex spp., Aedes spp., Anopheles spp.)*  Adults |
| **Field(s) of use** | Indoor and outdoor use |
| **Application method(s)** | Spraying |
| **Application rate(s) and frequency** | 1.80 mg product/cm² of clothes, equivalent to 7 sprays for an adult 600 cm² covered forearm.  Once a day for adults and children older than 6 years old.  Temperate conditions:  Mosquitoes (*Aedes spp. and Culex spp)*: Protection time up to 7 hours  Ticks (*Ixodes ricinus*): Protection time up to 7 hours.  Tropical conditions:  Mosquitoes *(Anopheles spp):* Protection time up to 7 hours |
| **Category(ies) of users** | General public (non-professional) |
| **Pack sizes and packaging material** | Spray bottles : PET with PP/ polyoxymethylene spray: 80 mL, 100 mL, 150 mL |

##### Use-specific instructions for use

|  |
| --- |
| * Only applied on cotton clothes. |

##### Use-specific risk mitigation measures

|  |
| --- |
| * Do not apply on clothes of children younger than 6 years * Do not exceed one application per day for adults and children of 6 years old or more |

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

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

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

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#### Use description

Table 3. Use # 3 – Combined spraying on the skin and on the clothes

|  |  |
| --- | --- |
| **Product Type** | PT19 – Repellents and attractants (pest control) |
| **Where relevant, an exact description of the authorised use** | The product RCAME is a ready-to-use lotion to be sprayed and spread on the exposed area of human skin, and to be sprayed on clothes. |
| **Target organism(s) (including development stage)** | Culicidae (*Culex spp., Aedes spp., Anopheles spp.)*  Adults |
| **Field(s) of use** | Indoor and outdoor use |
| **Application method(s)** | Combined spraying on the skin and on the clothes |
| **Application rate(s) and frequency** | 1.2 mg product/cm² of skin, equivalent to 3 sprays for a child (12 years) 390 cm² forearm, once a day.  1.8 mg product/cm² of clothes, equivalent to 5 sprays for a child (12 years) 390 cm² forearm, once a day.  Temperate conditions:  Mosquitoes (*Aedes spp. and Culex spp)*: Protection time up to 6 hours  Tropical conditions:  Mosquitoes *(Anopheles spp):* Protection time up to 6 hours |
| **Category(ies) of users** | General public (non-professional) |
| **Pack sizes and packaging material** | Spray bottles : PET with PP/ polyoxymethylene spray: 80 mL, 100 mL, 150 mL |

##### Use-specific instructions for use

|  |
| --- |
| * Apply only on cotton clothes. * In case of sunscreen product use, wait at least 20 minutes before applying the repellent, after the sunscreen product. |

##### Use-specific risk mitigation measures

|  |
| --- |
| * Do not exceed one application on skin combined to one application on clothes per day for adults and children of 12 years old and older. * Do not combine the use on skin and clothes for children younger than 12 years. * Wash hands before handling food.   **For skin application:**   * Only apply on uncovered skin. * Do not spray directly on face but spray on hands and apply to face. * Do not apply on eyelids and eyes * Do not treat hands of children. |

##### 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

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| --- |
| - |

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

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| - |

### General directions for use

#### Instructions for use

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| --- |
| * Comply with the instructions of use * Respect the recommended application doses. * The users should report straightforward to the registration holder any alarming signals which could be assumed to be resistance development. * Protection time can be lowered by sweating, water wash off, rubbing, high temperature (>30°C), wind velocity, etc. * Shaken before use. * Use in well-ventilated areas. * When applying a sunscreen, wait at least 20 minutes after application of the sunscreen to apply the product. |

#### Risk mitigation measures

|  |
| --- |
| * Keep out of the reach of children. * Do not use the product before bathing or showering. * Do not apply to damaged skin (wounds, sunburn, skin disease ...). * 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. * For children until 12 years: the repellent must be applied by adults. |

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

|  |
| --- |
| * The active substance contained in the product (DEET) is liable to induce nerve hyperexcitability especially in susceptible persons (epileptic) or in the case of co-exposure with a convulsant product. * Ingestion: Risk of dizziness and loss of consciousness. Ingestion may lead to acute intoxication. Immediately contact poison control center. Do not induce vomiting without medical advice. * Eyes contact: Remove the contact lenses. Wash eyes under a stream of lukewarm water for about 10 minutes, eyes open, not forgetting to wash under the eyelids. If the eyes remain red two hours after washing, consult a doctor. * Skin contact: if redness or persistent pain after application, consult a physician. |

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

|  |
| --- |
| * Dispose of contents / container at appropriate collection point. * Do not transfer the product. Do not mix with other wastes. * Containers containing residues of the product must be treated in accordance with national regulations. * Do not discharge into environment or sewers. * In case of accidental spillage, collect the product with a liquid-absorbing material (eg sand, diatomaceous earth) and dispose of as hazardous waste. |

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

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| --- |
| * Do not store more than 2 weeks at 54 °C. * The product can be stored up to 2 years at ambient temperature |

### Other information

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| --- |
| - |

### Packaging of the biocidal product

*Please refer to the product assessment report related to REPULSIF ANTI-MOUSTIQUES CORPOREL product authorisation (FR-2014-0088) under Regulation (UE) n° 528/2012.*

### Documentation

#### Data submitted in relation to product application

Complete physico-chemical data package on the product have been submitted*.*

New efficacy data on the product have been submitted:

* An arm-in-cage study conducted with three human volunteers (3 replicates) with the product Répulsif anti-moustiques corporel SUBITO – 10% DEET (10% w/w DEET) applied on skin with four mosquito species *(Aedes aegypti, Anopheles gambiae, Aedes albopictus and Culex pipiens).*
* An arm-in-cage study conducted with three human volunteers (3 replicates) with the product Répulsif anti-moustiques corporel SUBITO – 10% DEET (10% w/w DEET) applied on fabric (cotton) with four mosquito species *(Aedes aegypti, Anopheles gambiae, Aedes albopictus and Culex pipiens).*
* An arm-in-cage study conducted with three human volunteers (3 replicates) with the product Répulsif anti-moustiques corporel SUBITO – 10% DEET (10% w/w DEET) applied on skin with four mosquito species *(Aedes aegypti, Anopheles gambiae, Aedes albopictus and Culex pipiens).*

No new toxicology and ecotoxicology data have been submitted.

*Please refer to the product assessment report related to REPULSIF ANTI-MOUSTIQUES CORPOREL product authorisation (FR-2014-0088) under Regulation (UE) n° 528/2012.*

**Major change application for REPULSIF CORPOREL ANTI MOUSTIQUES ENFANTS – 2020:**

New physico chemical studies and analytical methods have been submitted with the new composition.

New efficacy data on the product have been submitted:

* An arm-in-cage study conducted with ten human volunteers with the product REPULSIF CORPOREL ANTI MOUSTIQUES ENFANTS – 10% DEET (10% w/w DEET) applied on skin with three mosquito species *(Aedes aegypti, Anopheles gambiae, and Culex pipiens).*
* An arm-in-cage study conducted with ten human volunteers with the product REPULSIF CORPOREL ANTI MOUSTIQUES ENFANTS – 10% DEET (10% w/w DEET) applied on fabric (cotton) with three mosquito species *(Aedes aegypti, Anopheles gambiae, and Culex pipiens).*
* An arm-in-cage study conducted with ten human volunteers with the product REPULSIF CORPOREL ANTI MOUSTIQUES ENFANTS – 10% DEET (10% w/w DEET) applied on skin with one tick species *(Ixodes ricinus).*

New toxicological data have been submitted in the frame of the major change : Barré T., 2019, Richeux F., 2019.

#### Access to documentation

*Please refer to the product assessment report related to REPULSIF ANTI-MOUSTIQUES CORPOREL product authorisation (FR-2014-0088) under Regulation (UE) n° 528/2012.*

## Assessment of the biocidal product

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

Table 1. Intended use #1 – Spraying on skin

|  |  |
| --- | --- |
| **Product Type(s)** | PT19 – Repellents and attractants (pest control) |
| **Where relevant, an exact description of the authorised use** | RCAME is a ready-to-use lotion to sprayed and spread on the surface of exposed human skin. |
| **Target organism (including development stage)** | Culicidae, e.g. mosquitoes, Aedes mosquitoes, Anopheles mosquitoes  Adults  Ticks: *(Ixodes ricinus)*  *Adults and nymphs* |
| **Field of use** | Indoor and outdoor use |
| **Application method(s)** | Spraying  The product is sprayed on the palms of the hands and spread on exposed skin surfaces (face, neck, 1/2 arms, hands and 1/2 legs) |
| **Application rate(s) and frequency** | 1.2 mg product/cm² of skin, equivalent to 5 sprays for an adult 600 cm² forearm, or 2 sprays for a child (2-6 years) 286 cm² forearm  up to 2 times a day for adults and children 1 year and older. - 0  Complete protection time in a temperate and tropical environment: 6 hours |
| **Category(ies) of user(s)** | General public (non-professional) |
| **Pack sizes and packaging material** | The product RCAME is packaged in polypropylene bottles from 80 mL to 150 mL, with a polypropylene / polyoxymethylene pump. |

Table 2. Use #2 – Spraying on clothes

|  |  |
| --- | --- |
| **Product Type(s)** | PT19 – Repellents and attractants (pest control) |
| **Where relevant, an exact description of the authorised use** | RCAME is a ready-to-use lotion to spray on clothes. |
| **Target organism (including development stage)** | Culicidae, e.g. mosquitoes, Aedes mosquitoes, Anopheles mosquitoes  Adults |
| **Field of use** | Indoor and outdoor use |
| **Application method(s)** | Spraying on clothes |
| **Application rate(s) and frequency** | 1,80 mg product/cm² clothes, equivalent to 7 sprays for an adult 600 cm² covered forearm, or 3 sprays for a child (2-6 years) 286 cm² covered forearm. Up to 2 times a day for adults and children 3 years and older and once a day for children 1 to 2 years old. - 0  Complete protection time: 7heures in temperate and tropical climate |
| **Category(ies) of user(s)** | General public (non-professional) |
| **Pack sizes and packaging material** | The product RCAME is packaged in polypropylene bottles from 80 mL to 150 mL, with a polypropylene / polyoxymethylene pump. |

Table 3. Use #3 – Combined spray on skin and clothes

|  |  |
| --- | --- |
| **Product Type(s)** | PT19 – Repellents and attractants (pest control) |
| **Where relevant, an exact description of the authorised use** | RCAME is a ready-to-use lotion that can be sprayed and spread on the surface of exposed human skin and on clothing. |
| **Target organism (including development stage)** | Culicidae, e.g. mosquitoes, Aedes mosquitoes, Anopheles mosquitoes  Adults  Ticks (*Ixodes ricinus*) – Adults and nymphs |
| **Field of use** | Indoor and outdoor use |
| **Application method(s)** | Spraying  The product is sprayed on the palms of the hands and spread over exposed skin surfaces (face, neck, 1/2 arms, hands and 1/2 legs).  The product is sprayed on clothes. |
| **Application rate(s) and frequency** | 1.20 mg product / cm² of skin, equivalent to 3 sprays for a child (12 years) 390 cm² forearm, once a day.  1. 80 mg product / cm² of clothing, equivalent to 5 sprays for a child (12 years) 390 cm² forearm, once a day.  Full protection time: 6hours. |
| **Category(ies) of user(s)** | General public (non-professional) |
| **Pack sizes and packaging material** | The product RCAME is packaged in polypropylene bottles from 80 mL to 150 mL, with a polypropylene / polyoxymethylene pump. |

### Physical, chemical and technical properties

| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **Reference** |
| --- | --- | --- | --- | --- |
| Physical state at 20 °C and 101.3 kPa | Visual observation | Product RAME  Batch number: 866  Containing 10.0% w/w of DEET | Liquid  Clear and colorless at initial time and cloudy with a light deposit after 14 days at 54 ± 2°C | Raphalen E., 2015  Report no. 402/15/1027F/abcdefgijk-e, FCBA |
| Colour at 20 °C and 101.3 kPa |
| Odour at 20 °C and 101.3 kPa | No guideline required | Product RAME | The product RAME has a characteristic odour. | SDS of RAME, 2015 |
| Acidity / alkalinity | CIPAC MT 75 | Product RAME  Batch number: 866  Containing 10.0% w/w of DEET | The pH of the pure test item RAME was respectively 7.7 and 7.5 at 20 ± 0.5°C, before and after 14 days at 54 ± 2°C. | Raphalen E., 2015  Report no. 402/15/1027F/abcdefgijk-e, FCBA |
| Relative density / bulk density | OECD Guideline No.109 (2012) (immersed body method) | Product RAME  Batch number: 866  Containing 10.0% w/w of DEET | The mean relative density of the test item RAME was D (20°C / 4°C) = 0.962 ± 0.001. | Raphalen E., 2015  Report no. 402/15/1027F/abcdefgijk-e, FCBA |
| Storage stability test – **accelerated storage** | CIPAC MT 46.3 method (storage stability)  Method for DEET: Raphalen E. 2015 (validated in in part 2.2.4) | Product RAME  Batch number: 866  Containing 10.0% w/w of DEET | After 14 days at 54°C in glass bottle\* and PET commercial bottle:   |  |  |  | | --- | --- | --- | |  | T0 | 14d 54°C | | Content of DEET | 10.29 % | 10.25% | |  | Variation | -0.3% | | pH (pure) 20°C | 7.7 | 7.5 | | Viscosity  mm²/s | <6.62 | <6.62 |   After 14 days at 54°C in PET commercial bottle:   |  |  |  | | --- | --- | --- | |  | T0 | 14d 54°C | | Appearance | colorless liquid no phase separation | As initial, no phase separation | | Weight test item | 115g | 114g | | Volume delivered by spray | 0.12 mL | 0.12mL |   Biocidal product is stable 14 days at 54 °C in glass bottle and compatibility of biocide product with PET bottle is demonstrated. | Raphalen E., 2015  Report no. 402/15/1027F/abcdefgijk-e, FCBA |
| Storage stability test – **long term storage at ambient temperature** | Technical Monograph No.17, 2nd edition, CropLife | Product RAME  Batch number: 866  Containing 10.0% w/w of DEET | After 6 and 12 month at ambient temperature in PET commercial bottle:   |  |  |  |  | | --- | --- | --- | --- | |  | T0\* | 6M RT | 12m RT | | Appearance | colorless transparent liquid no phase separation | | | | Weight test item variation |  | -0.7% | -1.31% | | Appearance of packaging |  | No potential sign of corrosion or degradation | | | Content of DEET | 10.29% | 10.25%  (-0.4%) | 10.59 %  (+2.9%) | | Volume delivered by spray | 0.12 m/ | 0.127mL |  |   *\* Determined in accelerated storage study above*  Biocidal product is stable 12 month at ambient temperature in PET bottle.  Final stability study will have to be submitted in post registration. | Legay S., 2015  Study plan no. 15/1027F/h, FCBA  Legay S., 2016  Certificate of analysis no. COA-  402/15/1027F/1/h/T6M-e  Certificate of analysis no. COA-  402/15/1027F/1/h/T12M-e |
|  |  | 10% DEET | Before and after 2 years at 20±2 °C in 100 mL PET flask:   |  |  |  | | --- | --- | --- | |  | T0 | 24 months 20 °C | | Appearance | Liquid  Limpide and colorless  No deposit  No phase partition | Liquid  Limpide and colorless  No deposit  No phase partition | | Content of DEET\* | 10.4% w/w | 10.44% w/w (+0.4%) | | Appearance of the commercial packaging | No sign of degradation | No sign of degradation (-2.7% weight change) | | pH value (pure) | 7.7 (20.2°C) | 7.4 (20.5°C) | | Volume delivered by spraying | 0.122 mL/spraying | 0.122 mL/spraying (with the same sprayer) |   The test item is considered stable in commercial packaging after 24 months storage at room temperature.  \**Content of DEET was determined as the mean of two measures with a validated HPLC/UV analytical method according to SANCO 3030/99/rev 4.* | Legay 2018 |
| Storage stability test – **low temperature stability test for liquids** | CIPAC MT 39.3 method (2000) | old composition of RAME (registered under the name of RAMC)  Batch number: 965  Containing 30.0% w/w of DEET  Read across to RAME acceptable | 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 = 8.0  Biocidal product is not considered stable after 7 days at 0°C.  The test item has to be manually shaken before use.  The label on the packaging of the test item should mention “Shaken before use”. | Legay S., 2013  Report no. 402/12/1048F-e, FCBA |
| Effects on content of the active substance and technical characteristics of the biocidal product - **light** |  |  | Not required as DEET is not light sensitive |  |
| Effects on content of the active substance and technical characteristics of the biocidal product – **temperature and humidity** |  |  | See the storage stability test |  |
| Effects on content of the active substance and technical characteristics of the biocidal product - **reactivity towards container material** |  |  | See the storage stability test |  |
| Wettability |  |  | Data not required as the product is a ready to use spray |  |
| Suspensibility, spontaneity and dispersion stability |  |  | Data not required as the product is a ready to use spray |  |
| Wet sieve analysis and dry sieve test |  |  | Data not required as the product is a ready to use spray |  |
| Emulsifiability, re-emulsifiability and emulsion stability |  |  | Data not required as the product is a ready to use spray |  |
| Disintegration time |  |  | Data not required as the product is a ready to use spray |  |
| Particle size distribution, content of dust/fines, attrition, friability |  |  |  |  |
| Persistent foaming |  |  | Data not required as the product is a ready to use spray |  |
| Flowability/Pourability/Dustability |  |  | Data not required as the product is a ready to use spray |  |
| Burning rate — smoke generators |  |  | Data not required as the product is a ready to use spray |  |
| Burning completeness — smoke generators |  |  | Data not required as the product is a ready to use spray |  |
| Composition of smoke — smoke generators |  |  | Data not required as the product is a ready to use spray |  |
| Spraying pattern — ~~aerosols~~ spray | No guideline required | Product RAME  Batch number: 866  Containing 10.0% w/w of DEET | There was no blocking of the spray of the test item RAME before and after 14 days of storage at 54 ± 2°C.  The volume delivered per spraying was 0.12 mL and did not change after 14 days of storage at 54 ± 2°C.  A mass median aerodynamic diameter (MMAD) of 66 μm was measured and only 1% of particles was < 9.4 μm. | Raphalen E., 2015  Report no. 402/15/1027F/abcdefgijk-e, FCBA |
| Physical compatibility |  |  | Not applicable. RAME is a ready-to-use product and is not intended to be used in conjunction with any other products or active substances. |  |
| Chemical compatibility |  |  | Not applicable. RAME is a ready-to-use product and is not intended to be used in conjunction with any other products or active substances. |  |
| Degree of dissolution and dilution stability |  |  | Data not required as the product is a ready to use spray |  |
| Surface tension | EC A5  OECD 115 | 30% DEET  Batch 965 | Pure biocidal product: 32.0 mN/m  Biocidal product is surface active | Legay 2012 |
| Viscosity | OECD Test Guideline 114  ISO Standard 2431 (flow cup method) | Product RAME  Batch number: 866  Containing 10.0% w/w of DEET | < 6.62 mm²/s at 20.0 ± 0.5°C and 40.0 ± 0.5°C | Raphalen E., 2015  Report no. 402/15/1027F/abcdefgijk-e, FCBA |

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| **Conclusion on the physical, chemical and technical properties of the product** |
| The product REPULSIF ANTI-MOUSTIQUES ENFANT is a clear and colorless liquid with a characteristic odour. The pH of pure product is about 7.7 at 20°C and its relative density is 0.962. The dynamic viscosity of the product is < 6.62 mm²/s at 20°C and 40°C.  After accelerated storage procedure (14 days at 54 ± 2°C) product REPULSIF ANTI-MOUSTIQUES ENFANT and its commercial packaging (100 mL white spray in PET) were considered to be stable after an accelerated storage procedure 14 days at 54 ± 2°C.  A long term storage procedure (2 years at ambient temperature) is currently on going. After long term storage procedure (12 month at 20+/-5°C) in commercial packaging (100mL PET) product was stable on active substance content and spray delivery. Final result after 24 months of storage, related to the physical stability of the test item REPULSIF ANTI-MOUSTIQUES ENFANT and the commercial packaging (100 mL white spray in PET), analytical quantification of the active substance, pH value of the pure test item, satisfactory operation of the sprayer and the spray volume will be provided when available.  RAME is not expected to be 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 “Shake before use”.  Post-authorisation data – 2018:  There is no effect of high temperature on the stability of the formulation, since after 14 days at 54 °C or 24 months at room temperature, neither the active ingredient content nor the technical properties were significantly changed. The stability data indicate a shelf life of at least 2 years at 25 °C when stored in its commercial packaging (spray in PET). |

* **Major Change application REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS – 2020:**

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| --- | --- | --- | --- | --- | --- |
| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **Reference** | **Assessment** |
| Relative density / bulk density | OECD Guideline No.109 (2012) (immersed body method) | Calculation | As the product RCAME contains a high proportion of water and only 2 other main components with similar relative density (0.996-1.03), its density was calculated using the densities of its components.  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 RCAME (a reference value of 1.00 will be taken for the calculation).  The calculated density of the product RCAME is **1.010** (0.1031\*0.996 + 0.35\*1.03 + 0.0005\*1 + 0.5464\*1). | / | Acceptable. As components have a similar relative density, the product is expected to have a relative density close to 1 and the calculation is acceptable. |
| Storage stability test – accelerated storage | CIPAC MT 46.3 method (storage stability)  Validated analytical method  CIPAC MT 75.3  Internal method | Product RCAME Batch number: 2630 Containing 10.0% w/w of DEET (N,N diethyl-meta toluamide) Packaging: 80 mL white opaque PET spray | The test item RCAME was considered to be stable after an accelerated storage procedure for 14 days at 54 ± 2°C in its commercial packaging (80 mL white opaque PET spray). | Halbwachs P., 2019 Report no.19-919062-006, Défitraces | Acceptable. The product is stable 14 days at 54°C in commercial PET packaging. Extrapolation to PP material is acceptable as the product is an aqueous formulation. |
| Storage stability test – **long term storage at ambient temperature** | Technical Monograph No.17, 2nd edition, CropLife | Product RCAME Batch number: 2630 Containing 10.0% w/w of DEET (N,N diethyl-meta toluamide) Packaging: 80 mL white opaque PET spray | The long term storage stability study (36 months at 20 ± 2°C) of the test item RCAME in its commercial packagings (white opaque PET spray (80 mL)) 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 will be provided when available. | Halbwachs P., 2019 Study plan no.19-919062- 007, Défitraces | The long term study 3 years is ongoing.  The applicant claims a shelf life of 3 years. However, only a shelf life of 2 years can be granted from results of the accelerated storage stability study. The applicant should submit a minor change dossier to confirm the shelf life of 3 years. |
| Storage stability test – **low temperature stability test for liquids** | CIPAC MT 39.3 method (2000) | Product RCAME Batch number: 2630 Containing 10.0% w/w of DEET (N,N diethyl-meta toluamide) | At the start of the test and after 7 days at 0°C, the test item was a homogeneous colourless 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 in the test item aspect. | Halbwachs P., 2019 Report no.19-919062-005, Défitraces | Acceptable. The product is stable 7 days at 0°C. |
| Particle size distribution, content of dust/fines, attrition, friability | CIPAC MT 187 (2003) ISO 13320-2009 (laser diffraction) | Product RCAME Batch number: 2630 Containing 10.0% w/w of DEET (N,N diethyl-meta toluamide) Packaging: 80 mL white opaque PET spray | The spray droplet size distribution of the test item RCAME in its commercial packaging (80 mL white opaque PET spray with PP trigger) was determined by laser diffraction. The percentage of the respirable volume fraction less than 10 µm is 0.686%.  Mean on the three sprays: Dv(0.1) = 37.491 µm (particle size not exceeded by 10% in volume of the particles) Dv(0.5) = 68.264 µm (particle size not exceeded by 50% in volume of the particles) Dv(0.9) = 127.553 µm (particle size not exceeded by 90% in volume of the particles)  D[3;2] = 58.023 µm (mean diameter in surface/volume)  D[4;3] = 82.348 µm (mean diameter in volume) | Halbwachs P., 2019 Report no.19-919062-010, Défitraces | Acceptable |
| Surface tension | EU Method A.5 (ring method) | Product VRCAM Batch number: 2629 Containing 30.5% w/w of DEET (N,N diethyl-meta toluamide) | The products RCAME and VRCAM have very close compositions. Please refer to the read across in confidential annex. The surface tension of the product RCAME is expected to be similar to the surface tension of the tested product VRCAM. The product RCAME is expected to have a mean surface tension of 36.5 mN/m at a temperature of 20.2°C and is considered as surface active in the experimental conditions used. | Halbwachs P., 2019 Report no.19-919062-001, Défitraces | Please refer to the bridging in confidential annex. Results are considered acceptable for RCAME and the product is considered as surface active. |
| Viscosity | OECD Test Guideline 114 (2012) ISO 3219 (1993) (rotational viscometer) | Product RCAME Batch number: 2630 Containing 10.0% w/w of DEET (N,N diethyl-meta toluamide) | Mean = 7.14 mPa.s at 20.0 ± 0.2°C (similar value from 10 to 80 RPM, increasing of decreasing gradient) mean = 3.41 mPa.s at 40.0 ± 0.2°C (similar value from 20 to 160 RPM, increasing of decreasing gradient) The test item was considered to have newtonian properties in the experimental conditions used. | Halbwachs P., 2019 Report no.19-919062-005, Défitraces | Acceptable. The product is considered as a Newtonian fluid as viscosity in independent from the shear rate. |

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| **Conclusion on the physical, chemical and technical properties of the product** |
| The product RCAME is a homogeneous colourless limpid liquid with a characteristic odour. The mean pH of the pure product is about 6.2 (after 2 min) at 19.4°C and its mean relative density is expected to be 1.010. The product RCAME is expected to have a mean surface tension of 36.5 mN/m at a temperature of 20.2°C (surface-active material).  Its mean dynamic viscosity is 7.14 mPa.s at 20.0 ± 0.2°C and 3.41 mPa.s at 40.0 ± 0.2°C (newtonian properties). The percentage of the respirable volume fraction less than 10 µm using the commercial packaging (white opaque PET spray) is 0.686%  The test item RCAME 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. As the product is an aqueous formulation, extrapolation to PP material also used for the commercial spray is acceptable. 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 RCAME 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 will be provided when available. A shelf-life of 36 months is claimed by the applicant. However only a shelf life of 2 years can be granted from the results of the accelerated storage study. The applicant should submit a minor change dossier to confirm the shelf life of 3 years.  Moreover, the appearance of the test item was considered to be stable after a low temperature stability for 7 days at 0 ± 2°C |

### Physical hazards and respective characteristics

| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **Reference** |
| --- | --- | --- | --- | --- |
| Explosives | Statement and DSC | old composition of RAME (registered under the name of RAMC)  30% DEET  Batch 965 | During the DSC, only an endothermic peak was observed at 95.1°C. The test item shall not be classified as explosive  Not explosive | Defitrace report No.12-919062-001  ASC report 12/04 |
| Flammable gases |  |  | Not required as the product is a ready-to-use emulsion. |  |
| Flammable aerosols |  |  | Not required as the product is a ready-to-use emulsion. |  |
| Oxidising gases |  |  | Not required as the product is a ready-to-use emulsion. |  |
| Gases under pressure |  |  | Not required as the product is a ready-to-use emulsion. |  |
| Flammable liquids | EC A.9  NF EN ISO 2719 | old composition of RAME (registered under the name of RAMC)  30% DEET  Batch 965 | Flash point : 41.9°C  Classified as flam liq 3; 226  Read across to RAME is acceptable | Legay 2012 |
| Flammable solids |  |  | Not required as the product is a ready-to-use emulsion. |  |
| Self-reactive substances and mixtures | D.S.C. | old composition of RAME (registered under the name of RAMC)  Batch number: 965  Containing 30.0% w/w of DEET | The product RAMC is unlikely to be self-reactive and the test on self-reactive properties according to UN Test series A to H described in Part II of the UN-MTC  Read across to RAME is acceptable | GREVIN P., 2012  Report no. 12-919062-001, Défitraces |
| Pyrophoric liquids |  |  | The product RAME is not a pyrophoric liquid. Test is not required as experience in manufacture and handling shows that the product does not ignite spontaneously on coming into contact with air at normal temperature. |  |
| Pyrophoric solids |  |  | Not required as the product is a ready-to-use emulsion. |  |
| Self-heating substances and mixtures |  |  | Not required as the product is a ready-to-use emulsion. |  |
| Substances and mixtures which in contact with water emit flammable gases |  |  | The product RAME does not emit flammable gases when in contact with water. Test is not required as RAME contains about 60% w/w water and forms a stable mixture. |  |
| Oxidising liquids | Statement | - | Based on structural considerations, RAMC is not expected to have oxidising properties.  Not oxidizing  Read across to RAME is acceptable | ASC report 12/04 |
| Oxidising solids |  |  | Not required as the product is a ready-to-use emulsion. |  |
| Organic peroxides |  |  | Not required as the product does not  contain organic peroxides. |  |
| Corrosive to metals |  |  | The product RAME is not expected to be corrosive to metals. Test is not required as no ingredient is classified as corrosive to metals. |  |
| Auto-ignition temperatures of products (liquids and gases) | Statement | - | Based on composition considerations, RAMC is expected to have auto-flammability point higher than 360 °C.  Read across to RAME is acceptable | ASC report 12/04 |
| Relative self-ignition temperature for solids |  |  | Not required as the product is a ready-to-use emulsion. |  |
| Dust explosion hazard |  |  | Not required as the product is a ready-to-use emulsion. |  |

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| **Conclusion on the physical hazards and respective characteristics of the product** |
| Concerning the biocidal product RAME, it was demonstrated that physical hazards can be extrapolated from studies performed with the initial formulation.  According to the results of the flash point (41.9°C), RAME is expected be classified as flammable liquid cat. 3, H226 according to CLP regulation (EC) 1272/2008.  RAME is not expected to present a significant hazard for explosive properties, self-reactivity, oxidising properties and auto-flammability. |

* **Major Change application REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS – 2020:**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **Reference** | **Assessment** |
| Flammable liquids | Justification | Product RCAME Containing 10% w/w of DEET (N,N diethyl-meta toluamide) | The product RCAME contains 10.31% w/w of N,N-diethyl-m-toluamide (DEET) (technical) which is not a flammable liquid (flash point = 144°C) according to the Assessment Report of this active substance, Product-type 19, March 2010. Moreover, the mixture contains more than 85% w/w of compound which are not classified as flammable. The other components (maximum 0.05% w/w of the formulation) are not considered to present a significant hazard for flammability due to their low contents. Therefore, the product RCAME is not expected to present a significant hazard for flammability and test is not required  A read across with VRCAM is also proposed:  Test item: VRCAM, batch 3098  No flash point was observed up to 140.0°C (corrected value). 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  Défitraces | eCA agrees that the product is not expected to be anymore classified H226. The applicant has also proposed a read across with VRCAM. This product was not flammable due to a flash point >140°C. Please refer to confidential PAR for details on the composition of VRCAM. |

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| **Conclusion on the physical hazards and respective characteristics of the product** |
| Concerning the biocidal product RAME, it was demonstrated that physical hazards can be extrapolated from studies performed with the initial formulation. RAME is not expected to present a significant hazard for explosive properties, flammability, self-reactivity, oxidising properties and auto-flammability. |

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### Methods for detection and identification

Extract from *product assessment report related to REPULSIF ANTI-MOUSTIQUES CORPOREL product authorisation (FR-2014-0088) under Regulation (UE) n° 528/2012.*

Reference: Raphalen E. 2015; Physico-chemical properties, technical characteristics and chemical analyses of the biocidal product RAME before and after an accelerated storage procedure for 14 days at 54 ± 2°C, in compliance with CIPAC MT 46.3 method (Handbook J, 2000)

report n° 402/15/1027F/abcdefgijk-e

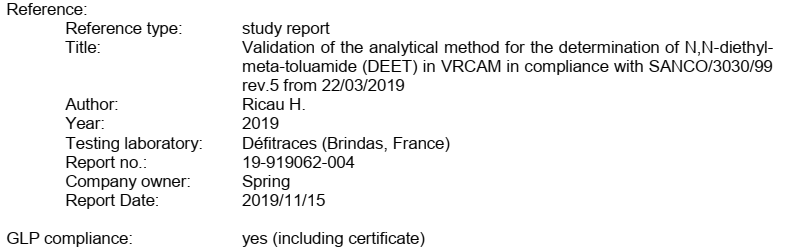
The method to determine the content of DEET in the biocidal product REPULSIF ANTI-MOUSTIQUES ENFANT by HPLC-UV (210 nm) using external standard calibration is validated according to document SANCO 3030/99.

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| **Validation results** | |
| **Specificity** | No interference at the selected wavelength (210 nm) contributes more than 3% to the total peak area measured for the active substance DEET. |
| **Linearity** | Calibration range: 24 – 36 mg/L of DEET (n = 5, 80 – 120% range):  y = 4.355648 \* 104 \* x – 7.117582 \* 103 (y = area, x = DEET amount in mg/L),  r = 0.99995 |
| **Accuracy** | Mean recovery rate = 101.2% (n = 6) |
| **Precision** | RSD = 0.48% (n = 6) |

The provided method is acceptable for the product REPULSIF ANTI-MOUSTIQUES ENFANT.

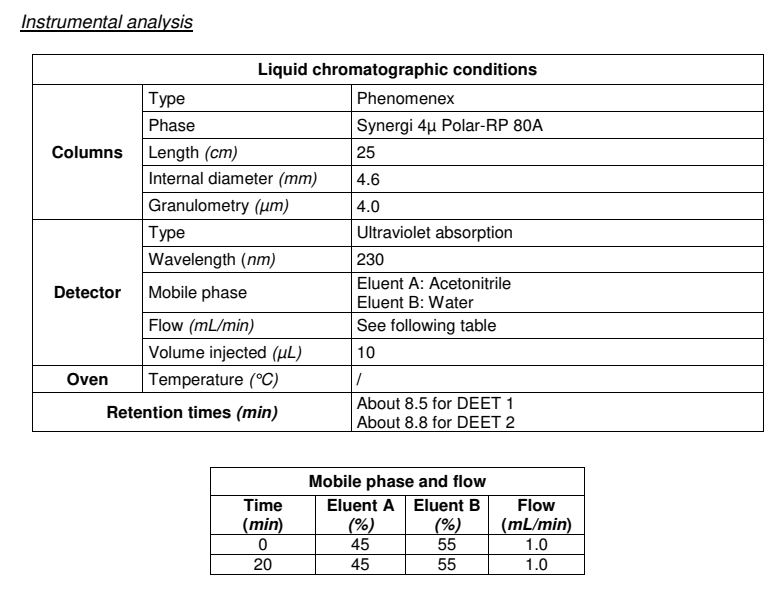
* **Major Change application REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS – 2020:**

A validation for a similar product VRCAM has been provided. Bridging is reported in confidential annex and found suitable.



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 test item (from 26.85 mg/L to 83.78 mg/L in measuring solution) 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%.

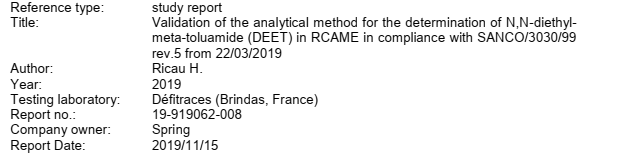
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| **Validation results** | |
| Specificity | Retention times for DEET peaks match between DEET reference item and test item, confirming the identity of the analyte. Chromatograms were provided for calibration standard, blank formulation, test item, 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, 50 – 150% w/w of nominal content in test item): 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/w  Sample 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) = 0.83  Mean average content = 30.5% w/w Mean RSD = 1.18% |

**Additional statement from the applicant:**

The analytical method for the determination of N,N-diethyl-meta-toluamide (DEET) content in the similar product VRCAM was validated by definition of the specificity, the linearity, the accuracy, the precision and the reproducibility of the method and Guidelines requirements were fulfilled (study No. 19-919062-004). The linearity was validated within the range of 26.85 mg/L to 83.78 mg/L, which correspond to 15% w/w to 45% w/w equivalent of DEET in the test item. In order to be covered by the validated linearity interval, the quantity of product weighed for the determination of N,N-diethyl-meta-toluamide (DEET) content is adjusted by dilution according to the active substance content in the product (the dilution factor is three times higher for the product VRCAM)

Furthermore, the analytical method for the determination of N,N-diethyl-meta-toluamide (DEET) content in the product RCAME was validated by definition of the specificity, the precision and the reproducibility of the method and Guidelines requirements were fulfilled (study No. 19-919062-008). See results below.

**Additional validation data submitted for RCAME**



Following SANCO/3030/99 rev.5 from 22/03/2019, an analytical method for the determination of N,Ndiethyl-meta-toluamide (DEET) in VRCAM was validated during the study No. 19-919062-004 by definition of the specificity, the linearity, the accuracy the precision and the reproducibility of the method. A complementary validation of the analytical method of N,N-diethyl-meta-toluamide (DEET) in RCAME was performed during the study No. 19-919062-008 by definition of the specificity, the precision and the reproducibility of the method

**Test item:** RCAME, batch 2630 and formulation blank of RCAME ID 19-163-1

**Principle of the method**

**Study 19-919062-008 (RCAME)**

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 18.2 times (1.10 mL into 20 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). Instrumental analysis conditions are the same as in the previous report 19-919062-004.

Specificity (RCAME)

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 (RCAME). 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 8.502 min and 8.838 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 RCAME

Linearity (results for VRCAM)

To define the linearity of the detector answer of N,N-diethyl-meta-toluamide (DEET), five concentrations taken between 50% and 150% (from 26.85 mg/L to 83.78 mg/L) 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 = peak area (DEET), x = DEET amount (in mg/L), r = 1.0000).  
The correlation coefficient r was > 0.99 showing a good linearity.

Accuracy (results for VRCAM)

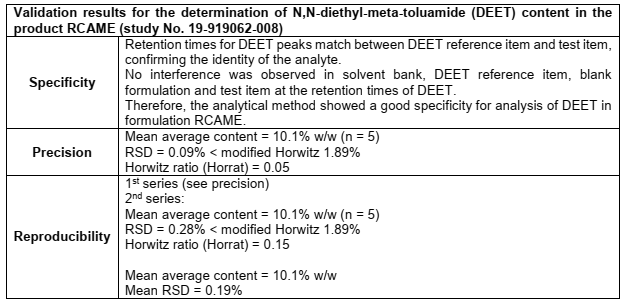
Accuracy was checked by analyses of two reconstituted samples (blank formulation spiked with known amounts (~30% w/w) of N,N-diethyl-meta-toluamide (DEET) reference item).  
The accuracy results of DEET were in conformity with the Guidelines requirements for formulations containing higher than 10% of 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).

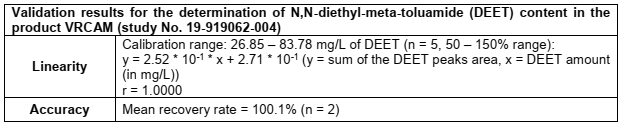
Precision (RCAME)

The precision was determined by analysing twice five test item solutions. The content of 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 10.1% w/w or 101 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: 0.09% < 1.89% (C = 0.101) with Horwitz ratio (Horrat) equal to 0.05.

Reproducibility (RCAME)

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 10.1% w/w or 101 g/kg. And the precision was acceptable as the R.S.D. was lower than the result of the modified Horwitz equation: 0.28% < 1.89% (C = 0.101) with Horwitz ratio (Horrat) equal to 0.15. The mean average content of DEET for the two reproducibility tests was equal to 10.1% w/w. The mean Relative Standard Deviation of DEET for the two reproducibility tests was equal to 0.19%





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| **Conclusion on the methods for detection and identification of the products** |
| The N,N-diethyl-meta-toluamide (DEET) contents 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 product VRCAM was validated by definition of the specificity, the linearity, the accuracy, the precision and the reproducibility of the method and Guidelines requirements were fulfilled. Additional data on specificity and precisions were provided for RCAME and found acceptable. As products VRCAM and RCAME are similar (see bridging in confidential annex), eCA considers that the method is fully validated for the product RCAME. |

**Active substance analysis**

*Active substance residues in soil, air, water, animal and human body fluids and tissues*

Taking to account the conclusion of Assessment Report N,N-diethyl-m-toluamide (DEET) Product-type 19, March 2010:

- analytical methods for DEET residues in soil and water are available,

- analytical method for DEET residues in body fluids (plasma) is available. However, no data is required as DEET is not classified as toxic or highly toxic. Considering the use pattern of the biocidal product RCAME and the properties of DEET, the contamination of air compartment during application is not significant and no method of analysis in air is required. Please refer to Letter of Access from Vertellus Performance Materials Inc

Soil (principle of method and LOQ) DEET:

LC-MS/MS with 1 transition (LOQ: 0.01 mg/kg).

Air (principle of method and LOQ):

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

Water (principle of method and LOQ):

A LC-MS/MS method taken from the open literature is proposed with a stated MRL (Method Reporting Limit) of 0.1 ng/L. However, further validation data is needed to verify the usefulness of the method for the natural water compartment.

Body fluids and tissues (principle of method and LOQ):

DEET in blood plasma: HPLC-UV (LOQ = 49.4μg/L) No confirmatory method provided. No further data required as DEET is not classified as toxic or highly toxic

*Active substance residues in food and feeding stuff*

Taking to account the conclusion of Assessment Report N,N-diethyl-m-toluamide (DEET) Product-type 19, March 2010:

- analytical methods for DEET residues in food/feed of plant and animal origin are not required as the use pattern of DEET will not results in any contact with food or feeding stuffs.

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes):  
Not required as the use pattern of DEET will not results in any contact with food or feeding stuffs

Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes):

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

### Efficacy against target organisms

#### Function and field of use

Main Group 03: Pest Control

Product Type 19: Repellents and attractants

REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANT is presented as a ready-for-use lotion to be applied on human skin, and also textiles (cotton). 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), or directly sprayed on textile.

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

* **First authorization - 2014**

The product REPULSIF ANTI-MOUSTIQUES ENFANT (30 % w/w DEET) 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).*

* **Major change - 2017**

In the frame of a major change dossier, the applicant requires an authorization for a new use (spraying on clothes) and at new application rates and at a different concentration of the product (10 % w/w DEET, instead of 30 % w/w DEET).

The new application rates recommended by the applicant are the following:

The ready-for-use spray bottle dispenses a spray dose of 0.19 mg per spray. The number of spraying recommended is 5 sprays per adult forearm, 1 spray per child forearm, 8 sprays on adult forearm fabric (cotton) and 2 sprays on child foream fabric (coton). The recommended application rates are 0.95 mg / cm² on skin and 1.54 mg / cm² on fabric.

It has to be noted that the tested mosquitoes are not all present in France or in the overseas territories but FR CA considers 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*.*

*- 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.

*- 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.

* **Major change application for REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANT – 2020**

REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANT is the same product than REPULSIF ANTI-MOUSTIQUES ENFANT.

In the frame of the major change application for the product **REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANT** (10 % w/w DEET), a modification of the composition with replacement of a solvent by an other one has been submitted by the applicant. An aditionnal use against ticks (*Ixodes ricinus*) and an increase of the application rate to 1.2 mg/cm² when applied on skin and 1.8 mg product/cm² when applied on textile, have been claimed by the applicant.

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

*Please refer to the product assessment report related to REPULSIF ANTI-MOUSTIQUES CORPOREL product authorisation (FR-2014-0088) under Regulation (UE) n° 528/2012.*

#### Mode of action, including time delay

*Please refer to the product assessment report related to REPULSIF ANTI-MOUSTIQUES CORPOREL product authorisation (FR-2014-0088) under Regulation (UE) n° 528/2012.*

#### Efficacy data

* **Major change application for REPULSIF ANTI-MOUSTIQUES ENFANT – 2017**

1) An arm-in-cage study (1859/1114) conducted with 3 human volunteers per test organism (3 replicates) with the product REPULSIF ANTI-MOUSTIQUES ENFANTSapplied 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 ENFANTS was tested under laboratory conditions (temperate 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 0.57 g / 600 cm² product, *ie* 0.95 mg / cm²).

This study demonstrated the efficacy of the product when used on skin at the application rate of 0.95 mg / cm² in temperate conditions.

1. An arm-in-cage study (1978/0815) conducted with 3 human volunteers per test organism (3 replicates) with the product REPULSIF ANTI-MOUSTIQUES ENFANTS 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 ENFANTS was tested under laboratory conditions (tropical 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 3 hours and then every 30 minutes until inefficacy. The time of protection is up to 3h30 for the 4 tested species at the application rate of 0.924 g/ 600 cm² product ie 1.54 mg / cm².

This study demonstrated the efficacy of the product when used on fabric (cotton only) at the application rate of 1.54 mg / cm² in tropical conditions.

1. An arm-in-cage study (1859/1114) conducted with 3 human volunteers per test organism (3 replicates) with the product REPULSIF ANTI-MOUSTIQUES ENFANTSapplied 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 ENFANTS was tested under laboratory conditions tropical 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 3.5 hours for the 4 tested species at the application rate of 0.57 g / 600 cm² product, *ie* 0.95 mg / cm²).

This study demonstrated the efficacy of the product when used on skin at the application rate of 0.95 mg / cm² in tropical conditions.

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

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

To confirm this approach, FR CA has launched a European consultation. Most of the consulted Member States think that field tests are not mandatory. Given the available literature on the active substance DEET and for reasons of standardization of testing and ethics, new field trials would not be justified.

Based on the results of this consultation and the efficacy data submitted in the dossier, FR CA agrees to consider the data presented as sufficient to demonstrate the efficacy of the product REPULSIF ANTI-MOUSTIQUES ENFANTS (**10** % w/w **DEET**).

* **Major change application for REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANT – 2020:**

Considering the addition of the use against ticks (*Ixodes ricinus)*, the modification of the composition with the solvent’s replacement by another one and the increase of the application rate claimed*,* the applicant has submitted 3 new studies performed with the product REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANT (10 % w/w DEET) to support these major change.

These studies demonstrate that the product REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANT is effective to repel:

* mosquitoes (*Culex spp., Aedes spp.)* in temperate conditions and mosquitoes (*Anopheles spp*.) in tropical conditions, during 6 hours, when applied on skin at an application rate of 1.2 mg/cm²
* mosquitoes (*Culex spp., Aedes spp.)* in temperate conditions and mosquitoes (*Anopheles spp.)* in tropical conditions, during 7 hours, when applied on fabric (cotton only) at an application rate of 1.8 mg/cm²
* ticks (*Ixodes ricinus*) during 7 hours, when applied on skin at an application rate of 1.2 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 product against target organism(s)** | | | | | | | |
| **Function** | **Field of use envisaged** | **Test substance** | **Test organism(s)** | **Test method** | **Test system / concentrations applied / exposure time** | **Test results: effects** | **Reference** |
| Repellent | skin | RCAME (DEET, 10% w/w)  Batch N°2630 | *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 1.2 mg/cm² of skin (i.e. 0.72 g/600 cm² forearm).  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), the treated forearm was inserted into the cage for 5 minutes (exposure time).  The same procedure was repeated every hour until 9 hours or inefficacy. Landings and bites were counted during each exposure time.  Climatic conditions:  For *C. pipiens* and *A. aegypti*:  temperature 25 ± 2 °C; relative humidity 65 % ± 5 %  For *A. gambiae:*  temperature 32 ±2 °C; relative humidity 90 % ± 5 % | After application of the product at 1.2 mg/cm² of skin, the duration of protection was:  - 6.2 hours for *C. pipiens*  - 7.1 hours for *A. aegypti*  - 6.1 hours for *A. gambiae*.  Based on the less sensitive species, the protection duration of the product is 6 hours when the product is applied on skin. | Serrano B., 2019  Report N° 2513a-RCAME/1019  S6.7\_01  R.I = 1 |
| Repellent | Textile (cotton) | RCAME (DEET, 10% w/w)  Batch N°2630 | *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 a 100% cotton fabric set on one forearm of each volunteer, the other one with an untreated fabric being used as a control. | Dose of product 1.8 mg/cm² of cotton fabric (i.e. 0.924 g/600 cm² forearm).  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), the treated forearm was inserted into the cage for 5 minutes (exposure time). The same procedure was repeated every hour until 3 hours and then every 30 minutes until inefficacy. Landings and bites were counted during each exposure time.  Climatic conditions:  For *C. pipiens* and *A. aegypti*:  temperature 25 ± 2 °C; relative humidity 65 % ± 5 %  For *A. gambiae:*  temperature 32 ±2 °C; relative humidity 90 % ± 5 % | After application of the product at 1.8 mg/cm² of fabric (cotton), the duration of protection was:  - 7.4 hours for *C. pipiens*  - 7 hours for *A. aegypti*  - 7.1 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 fabric (cotton). | Serrano B., 2019  Report N° 2513a2-RCAME/1019  S6.7\_02  R.I = 1 |
| Repellent | skin | RCAME (DEET 10% w/w)  Batch N°2630 | *Ixodes ricinus* (sheep tick): 60 nymphs | 6 ticks \* 10 volunteers  Temperature 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: 1.2 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 REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANT shows an efficacy period of 7 hours. | Dautel, H.  (2019)  STA\_IR\_0119\_01  S6.7\_02  R.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 REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS is is effective to repel:   * mosquitoes (*Culex spp., Aedes spp.)* in temperate conditions and mosquitoes (*Anopheles spp.)* in tropical conditions, during 6 hours, when applied on skin at an application rate of 1.2 mg/cm² * mosquitoes (*Culex spp., Aedes spp.)* in temperate conditions and mosquitoes (*Anopheles spp.)* in tropical conditions, during 7 hours, when applied on fabric (cotton only) at an application rate of 1.8 mg/cm² * ticks (*Ixodes ricinus*) during 7 hours, when applied on skin at an application rate of 1.2 mg / cm² 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. |

#### Occurrence of resistance and resistance management

*Please refer to the product assessment report related to REPULSIF ANTI-MOUSTIQUES CORPOREL product authorisation (FR-2014-0088) under Regulation (UE) n° 528/2012.*

#### Known limitations

The product REPULSIF ANTI-MOUSTIQUES ENFANTS has shown a sufficient efficacy for the uses claimed. Nevertheless, a monitoring of the resistance phenomenon must be put in place. The collected information must be sent every 5 years to FR CAs within the framework of a post-authorisation monitoring.

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

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

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

#### Evaluation of the label claims

* **First authorization - 2014**

The validated application rates that must be reported on the label are the following:

Mosquitoes (Aedes, Anopheles and Culex genus): 0.95 mg / cm² of skin and 1.54 mg / cm² of fabric (cotton).

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…

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

The product REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS is is effective to repel:

* mosquitoes (*Culex spp., Aedes spp.)* in temperate conditions and mosquitoes (*Anopheles spp.)* in tropical conditions, during 6 hours, when applied on skin at an application rate of 1.2 mg/cm²
* mosquitoes (*Culex spp., Aedes spp.)* in temperate conditions and mosquitoes (*Anopheles spp.)* in tropical conditions, during 7 hours, when applied on fabric (cotton only) at an application rate of 1.8 mg/cm²
* ticks (*Ixodes ricinus*) during 7 hours, when applied on skin at an application rate of 1.2 mg / cm² 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.

### Risk assessment for human health

#### Assessment of effects on Human Health

Except for dermal absorption all other toxicological properties are identical to the original formulation RAMC.

Therefore, regarding these properties, please refer to the original PAR.

* **Major Change application for REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS – 2020 :**

**Note to the reader:**

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

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.

For the assessment of the other endpoints (not detailed in this PAR), please refer to the PAR of REPULSIF CORPOREL ANTI-MOUSTIQUES and REPULSIF ANTI-MOUSTIQUE ENFANTS.

***Eye irritation***

* **Major Change application for REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS – 2020 :**

In order to avoid unnecessary testing, no study was performed with the product RCAME. The conclusions of studies conducted on similar product are extrapolated to the product RCAME according to the bridging principles (see confidential PAR for the justification of the read-across approach).

For eye irritation, two studies *in vitro* and *in vivo* are available.

| **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 438  Isolated chicken eye  GLP  Reliability: 1 | RAMC (DPG), 30 µL undiluted product | enucleated chicken eyes: 3  exposure during 10 seconds following by rinsing  positive and negative controls | Maximal mean score of corneal opacity: 2.0 corresponding to ICE class III  Mean score of fluorescein retention: 3.0 corresponding to ICE class IV  Maximal mean corneal swelling: 13% (240 min) corresponding to ICE class II  1\*IV, 1\*III, 1\*II  No prediction can be made | No deviations | XXXX |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **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 irritation  GLP  Reliability: 1 | New Zealand rabbits  Males  3 | RAMC (DPG) as supplied   * 1. mL | Average score (24, 48, 72h:  Conjunctivae chemosis: 0.0/0.0/0.0 redness: 1.3/0.3/0.3  - Iris :0.0 /0.0/0.0  - Cornea : 2.0/1.0/1.7  Reactions totally reversible.   * H319 | No deviations | XXXX |

|  |  |
| --- | --- |
| **Conclusion used in Risk Assessment – Eye irritation** | |
| Value/conclusion | Eye irritating of category 2  H319 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 2  H319 cause serious eye irritation |

***Information on dermal absorption***

|  |  |
| --- | --- |
| **Value(s) used in the Risk Assessment – Dermal absorption** | |
| Substance | DEET |
| Value(s) | 25% |
| Justification for the selected value(s) | For the original product containing 30% of a.s, the 20 % dermal absorption value from the CAR was used as it is based on a product containing 15% a.s.  The new formulation contains 10 % of a.s. As it is lower than the representative product from the CAR this approach can’t be used.  No new study was provided. The default dermal absorption value of 25 % from the EFSA guidance for product containing more than 5 % of a.s. is applied. |

|  |  |
| --- | --- |
| **Data waiving** | |
| Information requirement | Dermal absorption study |
| Justification | Application of default values from the EFSA guidance (2012). |

* **Major Change application for REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS – 2020 :**

The change has no impact on the dermal absorption.

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

*Please refer to the product assessment report related to REPULSIF ANTI-MOUSTIQUES CORPOREL product authorisation (FR-2014-0088) under Regulation (UE) n° 528/2012.*

* **Major Change application for REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS – 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.

***Available toxicological data relating to a mixture***

*Not relevant.*

***Other***

*None*

#### Exposure assessment

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 1 year and over.

**Inhalation exposure:**

RAME will be applied by spraying. In this context an exposure by inhalation could be considered. However, the aerosol droplets generated by the original product 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.

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

Moreover, according to consumer spraying model 2 for trigger spray, the user will be exposed to 35.9 mg of product /m3 during few minutes when he will be exposed to approximately 8g of product on skin with a dermal absorption of 25 %. Therefore, inhalation exposure is really negligible

**Oral exposure:**

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

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 RAME on him or herself and of a person who applies the product on another person are considered.

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

| **Summary table: relevant paths of human exposure** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Exposure path** | **Primary (direct) exposure** | | | **Secondary (indirect) exposure** | | | |
| **Industrial use** | **Professional use** | **Non-professional use** | **Industrial use** | **Professional use** | **General public** | **Via food** |
| Inhalation | n.a. | n.a. | negligible | n.a. | n.a. | negligible |  |
| Dermal | n.a. | n.a. | Yes | n.a. | n.a. | Yes |  |
| Oral | n.a. | n.a. | No | n.a. | n.a. | Yes |  |

* **Major Change application for REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS – 2020:** The major change corresponds to an increase of the claimed doses for the intended uses. This change has an impact on the exposure and risk assessment for human health. These sections are consequently reviewed taking into account the new claimed application rates.

The product RCAME is a RTU insect repellent containing 10% w/w DEET as active substance.

The product is intended to be used by non-professional users:

-on human skin (by adults and children up to 1 year old) at an application rate of 1.2 mg of product/ cm2; once per day.

-on clothes at an application rate of 1.8 mg/ cm2 for adults and children up to 1 years old;

* once per day for children from 1 to 6 year-old
* up to twice a day for child > 6 year-old and adults.

-on human skin and clothes simultaneously at an application rate of 1.2 mg/ cm2 for skin application and 1.8 mg/cm2 for clothes spraying only for adults and children older 12 years; once per day.

| **Summary table: relevant paths of human exposure** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Exposure path** | **Primary (direct) exposure** | | | **Secondary (indirect) exposure** | | | |
| **Industrial use** | **Professional use** | **Non-professional use** | **Industrial use** | **Professional use** | **General public** | **Via food** |
| Inhalation | n.a. | n.a. | Negligible | n.a. | n.a. | Negligible | n.a. |
| Dermal | n.a | n.a. | Yes | n.a. | n.a. | Yes | n.a. |
| Oral | n.a. | n.a. | n.a | n.a. | n.a. | Yes | n.a. |

***Primary exposure:***

For application on skin, dermal and inhalation exposure occur. It is considered that the exposure of the person spraying the product is covered by the exposure after application on the skin.

According to the Pest Control Product Fact Sheet, “the inhalation route is excluded due to the use outdoors, and because use indoors only takes place in the summer in situations where there is a high ventilation rate”. On these grounds, the inhalation exposure to aerosol sprays is also considered to be negligible. This applies to RCAME which is intended to be used preferentially in summer or under hot climate where insects proliferate, outdoor or in well ventilated area (see the label).

Based on these data, inhalation exposure to RCAME is estimated to be negligible and not taken into account in the exposure assessment. Therefore, the primary exposure is limited to the dermal route.

S***econdary exposure:***

For skin application, despite the fact that the product contains a bittering agent, oral exposure is taken into account for infants and toddlers (hand-to-mouth behaviour) and children and adults which can be incidentally exposed orally to the biocidal product.

***List of scenarios***

| **Summary table: scenarios** | | | |
| --- | --- | --- | --- |
| **Scenario number** | **Scenario**  (e.g. mixing/ loading) | **Primary or secondary exposure**  **Description of scenario** | **Exposed group**  (e.g. professionals, non-professionals, bystanders) |
| 1. | Application by spraying on skin | Primary exposure, dermal  The product is spread on the exposed area of human skin. In order to mimic a systemic exposure for consumer, an internal dose of DEET (in mg/kg b.w./day) is calculated from a dose of product first applied on skin and then absorbed. | Non professional  (adults and children < 6 years old) |
| 2 | Application by spraying on clothes | Primary exposure, dermal  The product is spread on clothes. In order to mimic a systemic exposure for consumer, an internal dose of DEET (in mg/kg b.w./day) is calculated from a dose of product first applied on clothes and then absorbed following transfer from the clothes to the skin. | Non professional  (adults and children < 6 years old) |
| 3. | Hand-to-mouth behaviour. | Secondary exposure, oral  The product is accidentally ingested following hand-to-mouth behaviour. A reverse scenario is performed to calculate the surface of hands to mouth to reach the acute AEL. | Non professional  (adults and children < 6 years old) |

**MAJOR CHANGE FOR RCAME – 2020**

| **Summary table: scenarios** | | | |
| --- | --- | --- | --- |
| **Scenario number** | **Scenario** | **Primary or secondary exposure**  **Description of scenario** | **Exposed group** |
| 1. | Skin application (dermal exposure) | **Primary exposure**:  Dermal exposure assessment for adults, children, toddlers when the product is spread on the exposed area of human skin.  Inhalation exposure is covered by dermal exposure. | **General public**  (adults, children, toddlers) |
| 2. | Application of product on clothes  (dermal exposure) | **Primary exposure**: Dermal exposure assessment for adults, children and toddlers when the product is spraying on clothes. | **General public**  (adults, children, toddlers) |
| 3. | Application of product on skin and clothes | **Primary exposure:** Dermal exposure assessment for adults and children up to 12 years old when the product is spraying on skin and clothes simultaneously | **General public** (adults) |
| 4. | Post-application phase - Hand-to-mouth transfer after skin application | **Secondary exposure:**  Hand-to-mouth transfer for adults, children, toddlers. | **General public**  (adults, children, toddlers) |

***Industrial exposure***

RAME is an insect repellent containing 10 % 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 industrial exposure is not relevant.

***Professional exposure***

RAME is an insect repellent containing 10 % DEET as active substance and is intended to be used by adult and child aged 1 year and over consumers (non-professional exposure). Therefore the assessment of professional exposure is not relevant.

***Non-professional exposure***

*Scenario [1] Application on skin*

| **Description of Scenario [1]** | | | |
| --- | --- | --- | --- |
| It is considered that the exposure of the person spraying the product is covered by the exposure to the product he applies on his skin.  The exposure by dermal route to RAME can be calculated according to the following equation:    where:  ID Internal dose (mg/kg b.w./day)  ARp Average dose of product applied on skin (mg/cm²)  CDEET Average concentration of substance in product (%)  BS Body surface exposed to the product (cm²)  DA Dermal absorption (%)  N Number of product application per day (/day)  BW Body weight (kg)  This equation can be applied to adults and to children.  ARp, CDEET, Dermal absorption and N remain the same, body parameters (such as body surface exposed to the product and body weight) vary according to age range.  The body parameters are issued from HEEG opinion 17.  The product is not intended to be applied on the total body surface but on the following body segments corresponding to uncovered parts: **head + ¾ arms + hands + ½ legs.**  No protection factor is taken into account | | | |
|  | Parameters1 | Value | Reference |
| Tier 1 | Average dose of product applied on skin (mg/cm²) | 0.95 | Efficacy data |
|  | Average concentration of substance in product | 10% w/w | Applicant data |
|  | Body surface exposed to the product (cm²) | See Table below | Heeg opinion 17 and US EPA factor handbook |
|  | Dermal absorption (%) | 25 | Efsa guidance on dermal absorption |
| Number of product applications per day (/day) | 2 | Applicant data |
|  | Body weight (kg) | See Table below | Heeg opinion 17 |

***Exposure estimate for 1 application***

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Body surface area cm2 (heat + 3/4 arm + hands + 1/2 legs)** | **Body weight (kg)** | **Mass of applicated product (mg)** | **Mass of applicated active substance (mg)** | **Mass of absorbed active substance (mg)** | **Estimated dermal uptake  (mg a.s./kg bw)** |
| Adult | 6297.5 | 60 | 5982.6 | 598.3 | 149.6 | 2.49 |
| Child (6 to 11 years old) | 3279.8 | 23.9 | 3115.8 | 311.6 | 77.9 | 3.26 |
| Child (3 to 6 years old) | 2165.25 | 16 | 2057.0 | 205.7 | 51.4 | 3.21 |
| Child (2 to 3 years old) | 1906.75 | 12 | 1811.4 | 181.1 | 45.3 | 3.77 |
| Toddler (1-2 years old) | 1707.15 | 10 | 1621.8 | 162.2 | 40.5 | 4.05 |

**Calculations for Scenario [1]**

| **Summary table: systemic exposure from non-professional uses** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake** | **Estimated dermal uptake** | **Estimated oral uptake** | **Estimated total uptake** |
| Adult  1 application on skin | 1 | n.a. | 2.49 | n.a. | 2.49 |
| Adult  2 applications on skin | 1 | n.a. | 4.99 | n.a. | 4.99 |
| Child (6 to 11 years old) 1 application on skin | 1 | n.a. | 3.26 | n.a. | 3.26 |
| Child (6 to 11 years old) 2 Application on skin | 1 | n.a. | 6.52 | n.a. | 6.52 |
| Child (3 to 6 years old) 1 application on skin | 1 | n.a. | 3.21 | n.a. | 3.21 |
| Child (3 to 6 years old) 2 Application on skin | 1 | n.a. | 6.43 | n.a. | 6.43 |
| Child (2 to 3 years old) 1 application on skin | 1 | n.a. | 3.77 | n.a. | 3.77 |
| Child (2 to 3 years old) 2 Application on skin | 1 | n.a. | 7.55 | n.a. | 7.55 |
| Toddler 1 application on skin | 1 | n.a. | 4.05 | n.a. | 4.05 |
| Toddler 2 Application on skin | 1 | n.a. | 8.11 | n.a. | 8.11 |

In order to determine the dermal exposure, an exposure according to the recommendation N°11 of the BPC Ad hoc WG on human exposure[[1]](#footnote-1) is also applied. Therefore, it is considered that the person will be exposed to the efficacy dose and wear a short-sleeved shirt (T-shirt) and a short.

The exposed body surface corresponds to 55% of the total body surface: head, neck, hands (palms and backs), lower arms, lower legs, feet and 70% of upper arms and thighs according to Pest Control Products Fact Sheet of Consexpo.

| **Description of Scenario** | | | |
| --- | --- | --- | --- |
| Application on the skin of repellent.  The exposure by dermal route 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)  CIR3535 Average concentration of substance in product (%)  BS Body surface exposed to the product (cm²)  DA Dermal absorption (%)  BW Body weight (kg)  This equation can be applied to adults and to children. | | | | |
|  | | Parameters | Value |
|  | | Body surface exposed to the product for **adult** considering exposure to head, neck, hands (palms and backs), lower arms, lower legs, feet and 70% of upper arms and thighs (cm2) | 9023 |
| Body surface exposed to the product for **child (6-11 years)** considering exposure to head, neck, hands (palms and backs), lower arms, lower legs, feet and 70% of upper arms and thighs (cm2) | 4794 |
| Body surface exposed to the product for **child (2-6 years)** considering exposure to head, neck, hands (palms and backs), lower arms, lower legs, feet and 70% of upper arms and thighs (cm2) | 3565 |
| Body surface exposed to the product for **child (1-2 years)** considering exposure to head, neck, hands (palms and backs), lower arms, lower legs, feet and 70% of upper arms and thighs (cm2) | 2532 |
|  | | Body weight of an **adult** (kg) | 60 |
| Body weight of **child (6-11 years)** (kg) | 23.9 |
| Body weight of **child (2-6 years)** (kg) | 16 |
| Body weight of **child (1-2 years)** (kg) | 10 |
| **Specific parameters** | | | | |
| Scenario 1 | Average dose of product applied on skin (mg/cm2) | | 0.95 |
| Average concentration of substance in product (%) | | 10 |
| Dermal absorption (%) | | 25 |

**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 | 3.57 | NR | 3.57 |
| Scenario [1]  child 6-11 years | Tier 1 | NR | 4.76 | NR | 4.76 |
| Scenario [1]  child 2-6 years | Tier 1 | NR | 5.43 | NR | 5.43 |
| Scenario [1]  child 1-2 years | Tier 1 | NR | 6.01 | NR | 6.01 |

**Further information and considerations on scenario**

*None*

**MAJOR CHANGE FOR RCAME – 2020**

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

| **Description of Scenario [1]** | | | |
| --- | --- | --- | --- |
| Adults, children and toddlers 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 RCAME 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[[2]](#footnote-2), 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).  Considering that the product is not intended to be used to treat hands of children, a refinement is developed considering the uncovered body surface are of 55% without hands for children exposure assessment.  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 | 25% | Efsa guidance on dermal absorption |
| % of active substance in biocidal product | 10% | Applicant’s data |
| Number of product application/day | 1 | Applicant’s data |
| **Body weight (kg)** | | Recommendation no. 14, 2017[[3]](#footnote-3) |
| Adult | 60 |  |
| Child (6 to <12 years old) | 23.9 |
| Child (2 to <6 years old) | 15.6 |
| Toddler (1 to <2 years old) | 10 |
| **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 |  |
| Child (6 to <12 years old) | 5096 |
| Child (2 to <6 years old) | 3779 |
| Toddler (1 to <2 years old) | 2676 |
| Tier 2 | **Body surface**  **exposed (cm²)** | | Recommendation no. 11, 2018  Recommendation no. 14, 2017  **Body surface** considering exposure to head, neck, arms (lower arms and 70% of upper arms), lower legs, 70% of thighs and feet. |
| Child (6 to <12 years old) | 4669 |  |
| Child (2 to <6 years old) | 3448 |
| Toddler (1 to <2 years old) | 2446 |

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 | 4.94 | NR | 4,94 |
| Scenario [1]  child 6-12 years | Tier 1 | NR | 6.60 | NR | 6.60 |
| Tier 2 | NR | 6.04 | NR | 6.04 |
| Scenario [1]  child 2-6 years | Tier 1 | NR | 7.49 | NR | 7.49 |
| Tier 2 | NR | 6.84 | NR | 6.84 |
| Scenario [1]  child 1-2 years | Tier 1 | NR | 8.28 | NR | 8.28 |
| Tier 2 | NR | 7.57 | NR | 7.57 |

*Scenario [2] Application on clothes*

| **Description of Scenario [2]** | | | |
| --- | --- | --- | --- |
| 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 RAME can be calculated according to the following equation:    where:  ID Internal dose (mg/kg b.w./day)  ARp Average dose of product applied on skin (mg/cm²)  CDEET Average concentration of substance in product (%)  BS Body surface exposed to the product (cm²)  DA Dermal absorption (%)  N Number of product application per day (/day)  BW Body weight (kg)  This equation can be applied to adults and to children.  ARp, CDEET, Dermal absorption and N remain the same, body parameters (such as body surface exposed to the product and body weight) vary according to age range.  The body parameters are issued from HEEG opinion 17.  When RAME is applied on clothes, the following body segments corresponding to dressed parts: **trunk + ¼ arms + ½ legs** are in contact with the product.  According to HeadHoc recommendation 8, as the product is applied on the exterior of clothes, only 50% of the product will penetrate the cloth and reach the skin | | | |
|  | Parameters1 | Value | Reference |
| Tier 1 | Average dose of product applied on skin (mg/cm²) | 1.54 | Efficacy data |
| Average concentration of substance in product | 10% w/w | Applicant data |
| Cloth penetration factor | 50% | Headhoc recommenadation 8 |
| Body surface in contact with treated cloth (cm²) | See Table below | Heeg opinion 17 and US EPA factor handbook |
| Dermal absorption (%) | 25 | Efsa guidance on dermal absorption |
| Number of product applications per day (/day) | 2 | Applicant data |
| Body weight (kg) | See Table below | Heeg opinion 17 |

***Exposure estimate for 1 application***

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Surface area (dressed parts) cm2 (trunk + 1/4 arm + hands + 1/2 legs)** | **Body weight (kg)** | **Mass of applicated product (mg)** | **Mass of applicated active substance (mg)** | **Mass of absorbed active substance (mg)** | **Estimated dermal uptake  (mg a.s./kg bw)** |
| Adult | 8942.5 | 60 | 13771.5 | 1377.1 | 172.1 | 2.87 |
| Child (6 to 11 years) | 5064.2 | 23.9 | 7798.9 | 779.9 | 97.5 | 4.08 |
| Child (3 to 6 years old) | 3325 | 16 | 5120.1 | 512.0 | 64.0 | 4.00 |
| Child (2 to 3 years old) | 2971 | 12 | 4575.0 | 457.5 | 57.2 | 4.77 |
| Toddler (1 to 2 years) | 2559.25 | 10 | 3941.2 | 394.1 | 49.3 | 4.9 |

**Calculations for Scenario [2]**

| **Summary table: systemic exposure from non-professional uses** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake** | **Estimated dermal uptake** | **Estimated oral uptake** | **Estimated total uptake** |
| Adult  1 application on clothes | 1 | n.a. | 2.87 | n.a. | 2.49 |
| Adult  2 applications on clothes | 1 | n.a. | 5.74 | n.a. | 5.74 |
| Child (6 to 11 years old) 1 application on skin | 1 | n.a. | 4.08 | n.a. | 4.08 |
| Child (6 to 11 years old) 2 Application on skin | 1 | n.a. | 8.16 | n.a. | 8.16 |
| Child (3 to 6 years old) 1 application on skin | 1 | n.a. | 4.00 | n.a. | 4.00 |
| Child (3 to 6 years old) 2 Application on skin | 1 | n.a. | 8.00 | n.a. | 8.00 |
| Child (2 to 3 years old) 1 application on skin | 1 | n.a. | 4.77 | n.a. | 4.77 |
| Child (2 to 3 years old) 2 Application on skin | 1 | n.a. | 9.53 | n.a. | 9.53 |
| Toddler  1 application on clothes | 1 | n.a. | 4.9 | n.a. | 4.9 |
| Toddler  2 Application on clothes | 1 | n.a. | 9.85 | n.a. | 9.85 |

If the product is applied on skin and on simultaneous on the clothes and that the recommendation 11 is followed, it is considered that trunk, arms (30% of upper arms), 30% of thighs are covered (45% of the body surface ).

*Application on clothes*

| **Description of Scenario [2]** | | | |
| --- | --- | --- | --- |
| 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 RAME can be calculated according to the following equation:    where:  ID Internal dose (mg/kg b.w./day)  ARp Average dose of product applied on clothes (mg/cm²)  CDEET Average concentration of substance in product (%)  BS Body surface exposed to the product (cm²)  DA Dermal absorption (%)  N Number of product application per day (/day)  BW Body weight (kg)  This equation can be applied to adults and to children.  ARp, CDEET, Dermal absorption and N remain the same, body parameters (such as body surface exposed to the product and body weight) vary according to age range.  The body parameters are issued from HEEG opinion 17.  When RAME is applied on clothes, 45% of the body surfaceis in contact with the product.  According to HeadHoc recommendation 8, as the product is applied on the exterior of clothes, only 50% of the product will penetrate the cloth and reach the skin | | | |
|  | Parameters1 | Value | Reference |
| Tier 1 | Average dose of product applied on skin (mg/cm²) | 1.54 | Efficacy data |
| Average concentration of substance in product | 10% w/w | Applicant data |
| Cloth penetration factor | 50% | Headhoc recommenadation 8 |
| Body surface in contact with treated cloth (cm²) | See Table below | Heeg opinion 17 and US EPA factor handbook |
| Dermal absorption (%) | 25 | Efsa guidance on dermal absorption |
| Body weight (kg) | See Table below | Heeg opinion 17 |

***Exposure estimate for 1 application***

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Surface area (dressed parts) cm2 (**trunk, arms (30% of upper arms), 30% of thighs**)** | **Body weight (kg)** | **Mass of applicated product (mg)** | **Mass of applicated active substance (mg)** | **Mass of absorbed active substance (mg)** | **Estimated dermal uptake  (mg a.s./kg bw)** |
| Scenario [2]  adult | 7012 | 60 | 10798 | 1080 | 135 | 2.25 |
| Scenario [2]  child 6-11 years | 4794 | 23.9 | 7383 | 738 | 92.3 | 3.86 |
| Scenario 2]  child 2-6 years | 3565 | 16 | 5490 | 549 | 68.6 | 4.40 |
| Scenario [2]  child 1-2 years | 2532 | 12 | 3900 | 390 | 48.8 | 4.88 |

**Calculations for Scenario [2]**

| **Summary table: systemic exposure from non-professional uses** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake** | **Estimated dermal uptake** | **Estimated oral uptake** | **Estimated total uptake** |
| Adult  1 application on clothes | 1 | n.a. |  | n.a. | 2.25 |
| Adult  2 applications on clothes | 1 | n.a. |  | n.a. | 4.5 |
| Child (6 to 11 years old) 1 application on skin | 1 | n.a. |  | n.a. | 3.86 |
| Child (6 to 11 years old) 2 Application on skin | 1 | n.a. |  | n.a. | 7.72 |
| Child (2 to 6 years old) 1 application on skin | 1 | n.a. |  | n.a. | 4.40 |
| Child (2 to 6 years old) 2 Application on skin | 1 | n.a. |  | n.a. | 8.79 |
| Child (1 to 2 years old) 1 application on skin | 1 | n.a. |  | n.a. | 4.88 |
| Child (1 to 2 years old) 2 Application on skin | 1 | n.a. |  | n.a. | 9.75 |

**MAJOR CHANGE FOR RCAME – 20*20***

*Scenario [2]: Primary exposure –* ***application of the product on clothes:*** *Dermal exposure assessment for adults, children and toddlers*

| **Description of Scenario 2** | | | |
| --- | --- | --- | --- |
| The ready to use product is a ready to use lotion to be sprayed on clothing.  Adults, children, toddlers could be exposed when wearing treated clothes.  The exposure by dermal route to RCAME can be calculated according to the following equation:    where:  ID Internal dose (mg/kg b.w./day)  ARp Average dose of product applied on clothes (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)  This equation can be applied to adults and to children.  ARp, CDEET, Dermal absorption and N remain the same, body parameters (such as body surface exposed to the product and body weight) vary according to age range.  In order to determine the exposure during the wear of treated cloth, as a worst case situation, it is considered that the person wears long clothes and that the treated surface is the total body surface area removing surface of the head, hands and neck.  For this use, a maximum of one application per day has been considered for child from 1 to 6 years-old and a maximum of two applications per day for child older 6 years and adults as claimed by the applicant.  According to Recommendation no.8[[4]](#footnote-4), a protection factor of 50% is used as the product is applied on the exterior of clothes and so only 50% of the product will penetrate the cloth and reach the skin. | | | |
|  | **Parameters** | **Value** | **References** |
| Tier 1 | Application rate (mg product/cm2) | 1.80 | Applicant’s data |
| Number of product applications per day (/day) | 2 for child > 6 year-old and adults  1 for children from 1 to 6 year-old | Applicant’s data |
| % of active substance in biocidal product | 10% | Applicant’s data |
| Reduction in exposure (long sleeve shirt and long pants) | 50% | Recommendation no. 8, 2015 |
| Dermal absorption (%) | 25% | Efsa guidance on dermal absorption |
| **Body weight (kg)** | | Recommendation no. 14, 2017 |
| Adult | 60 |
| Child (6 to <12 years old) | 23.9 |
| Child (2 to <6 years old) | 15.6 |
| Toddler (1 to <2 years old) | 10 |
|  |  |
| **Treated clothing surface (cm²)**  **LONG TROUSERS + LONG SHIRT = total BS - (head + hands + neck) (cm²)** | | Recommendation no. 14, 2017 |
| Adult | 14440 |
| Child (6 to <12 years old) | 7993 |
| Child (2 to <6 years old) | 5705 |
| Toddler (1 to <2 years old) | 3984 |

**Calculations for Scenario [2]**

| **Summary table: systemic exposure from non-professional uses** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake** | **Estimated dermal uptake** | **Estimated oral uptake** | **Estimated total uptake** |
| Adult  2 application on clothes | 1 | n.a. | 11.15 | n.a. | 11.15 |
| Adult  1 application on clothes | 2 | n.a. | 5.58 | n.a. | 5.58 |
| Child (6 to 12 years old) 2 application on clothes | 1 | n.a. | 15.50 | n.a. | 15.50 |
| Child (6 to 12 years old) 1 application on clothes | 2 | n.a. | 7.75 | n.a. | 7.75 |
| Child (2 to 6 years old) 1 Application on clothes | 1 | n.a. | 8.48 | n.a. | 8.48 |
| Toddler (1 to 2 years old) 1 application on clothes | 1 | n.a. | 9.23 | n.a. | 9.23 |

*Combined scenarios*

| **Summary table: combined systemic exposure from non-professional uses** | | |
| --- | --- | --- |
| **Scenarios combined** | **Estimated dermal uptake** | **Estimated total uptake** |
| Adult  1 application on skin and clothes | 5.36 | 5.36 |
| Adult  2 applications on skin and clothes | 10.72 | 10.72 |
| Child (6 to 11 years old) 1 application on skin and clothes | 7.34 | 7.34 |
| Child (6 to 11 years old) 2 applications on skin and clothes | 14.68 | 14.68 |
| Child (3 to 6 years old) 1 application on skin and clothes | 7.21 | 7.21 |
| Child (3 to 6 years old) 2 applications on skin and clothes | 14.43 | 14.43 |
| Child (2 to 3 years old) 1 application on skin and clothes | 8.54 | 8.54 |
| Child (2 to 3 years old) 2 applications on skin and clothes | 17.08 | 17.08 |
| Toddler (1 to 2 years old) 1 application on skin and clothes | 8.98 | 8.98 |
| Toddler (1 to 2 years old) 2 applications on skin and clothes | 17.96 | 17.96 |

1 Please include the Tier where relevant

*Combined scenarios for European approach*

| **Summary table: combined systemic exposure from non-professional uses** | | |
| --- | --- | --- |
| **Scenarios combined** | **Estimated dermal uptake** | **Estimated total uptake** |
| Adult  1 application on skin and clothes | 5.8 |  |
| Adult  2 applications on skin and clothes | 11.6 |  |
| Child (6 to 11 years old) 1 application on skin and clothes | 8.6 |  |
| Child (2 to 6 years old) 1 application on skin and clothes | 9.8 |  |
| Toddler (1 to 2 years old) 1 application on skin and clothes | 10.9 |  |

**MAJOR CHANGE FOR RCAME – 2020**

*Scenario [3]: Primary exposure –* ***application of the product on skin and clothes:*** *Dermal exposure assessment for adults and children older 12 years*

| **Description of Scenario 3** | | | |
| --- | --- | --- | --- |
| The ready to use product is a ready to use lotion to be sprayed and spread on the exposed area of human skin, and to be sprayed on clothes (Use # 3 – Combined spraying on skin and clothes).  According to the SPC, the RCAME product cannot be used on children under 12 year-old simultaneously on skin and clothes. That is the reason why only an adult and children older 12 years exposure assessment is developed for this use.  The dermal exposure of an adult during skin application of RCAME product is developed in the scenario 1 (see above for more details on the calculations).  Concerning the treatment on clothes, when the application is combined to the application on skin the harmonised surfaces for covered areas proposed in the Recommendation no. 11, 2018 (short-sleeved shirt (i.e. T-shirt) and shorts) are considered.  According to Recommendation no.8[[5]](#footnote-5), a protection factor of 50% is used as the product is applied on the exterior of clothes and so only 50% of the product will penetrate the cloth and reach the skin.  The dermal exposure is calculated by adding the dermal exposure during skin application and the dermal exposure during application on clothes. | | | |
|  | **Parameters** | **Value** | **References** |
| Tier 1 | Application rate (mg product/cm2) | 1.80 for clothes and 1.2 for skin | Applicant’s data |
| Number of product applications per day (/day) | 1 | Applicant’s data |
| % of active substance in biocidal product | 10% | Applicant’s data |
| Reduction in exposure | 50% | Recommendation no. 8, 2015 |
| Dermal absorption (%) | 25% | Efsa guidance on dermal absorption |
| **Body weight (kg)** | | Recommendation no. 14, 2017 |
| Adult | 60 |
| **Treated clothing surface (cm²)** :  Tee shirt and short | | Recommendation no. 11, 2018 |
| Adult | 7011.8 |
| **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 |  |

**Calculations for Scenario [3]**

| **Summary table: systemic exposure from non-professional uses** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake** | **Estimated dermal uptake** | **Estimated oral uptake** | **Estimated total uptake** |
| Adult   application on skin | 1 | n.a. | 4.94 | n.a. | 4.94 |
| Adult application on clothes (short-sleeved shirt (i.e. T-shirt) and shorts) | 1 | n.a. | 2.71 | n.a. | 2.71 |
| Adult application on skin and clothes | 1 | n.a. | 7.65 | n.a. | 7.65 |

***Exposure of the general public***

*Scenario [3] hand to mouth behaviour*

| **Description of Scenario [3]** | | | |
| --- | --- | --- | --- |
| Adults and children aged 6 years and over may be incidentally exposed orally to RAME via hand-to-mouth behavior. Even if the product contains a bittering agent, a reverse scenario calculation has been included. | | | |
|  | Parameters1 | Value | Reference |
| Tier 1 | Short term AEL (mg as.s/kg) | 0.75 | a.s. CAR |
| Average dose of product applied on skin (mg/cm²) | 0.95 | Efficacy data |
| Average concentration of substance in product | 10% w/w | Applicant data |
| Hands surface exposed to the product (cm²) | See Table below | Heeg opinion 17 and US EPA exposure factor handbook |
| Transfer from hand to mouth | 100% | Default |
| Oral absorption | 100% | Default |
| Body weight | See Table below | Heeg opinion 17 |

**Calculations for Scenario [3]**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Summary table: systemic exposure from non-professional uses** | | | | | | |
|  | **Body weight** | **Hands 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 short-term** | **% hand surface area to put in the mouth to reach the AEL short-term** |
| **Age group** | **kg** | **cm²** | **mg** | **mg** | **cm²** | **%** |
| Adult | 60 | 820 | 45.0 | 450.0 | 473.7 | 58 |
| Child (6<11) | 23.9 | 428 | 17.9 | 179.3 | 188.7 | 44 |
| Child (3<6) | 16 | 415 | 12.0 | 120.0 | 126.3 | 30 |
| Child (2<3) | 12 | 297 | 9.0 | 90.0 | 94.7 | 32 |
| Toddler (1<2) | 10 | 230 | 7.5 | 75.0 | 78.9 | 34 |

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

*None*

* **MAJOR CHANGE FOR RCAME – 2020**

*Scenario [4]: Post-application phase - Hand-to-mouth transfer*

| **Description of Scenario 4** | | | |
| --- | --- | --- | --- |
| After application on the skin, a person can be exposed orally to the biocidal product *via* hand-to-mouth behaviour. Even if the product contains a bittering agent, a reverse scenario calculation was included, with the new application rate of 1.2 mg/cm². | | | |
|  | **Parameters** | **Value** | **References** |
| Tier 1 | Oral absorption | 100% | Default value |
| % of active substance in biocidal product | 10% | Applicant’s data |
| Application rate (mg/cm²) | 1.2 | Applicant’s data |
| **Body weight (kg)** | | Recommendation no. 14, 2017 |
| Adult | 60 |
| Child (6 to <12 years old) | 23.9 |
| Child (2 to <6 years old) | 15.6 |
| Toddler (1 to <2 years old) | 10 |
| **Hand surface area (one hand) (cm²)** | | Recommendation no. 14, 2017 |
| Adult | 410 |
| Child (6 to <12 years old) | 213.9 |
| Child (2 to <6 years old) | 165.9 |
| Toddler (1 to <2 years old) | 115.2 |

Calculations for Scenario [4]

| **Summary table: estimated exposure for Dermal Primary exposure** | | | |
| --- | --- | --- | --- |
| **Exposure scenario** | **Maximum external quantity of DEET (mg)** | **Skin surface area to put in the mouth to reach the AEL short-term (cm2)** | **% hand surface area to put in the mouth to reach the AEL short-term** |
| Adult (1 application) | 45 | 364,1 | 88.8% |
| Child (6 to <12 years old)  (1 application) | 17.9 | 145.0 | 67.8% |
| Child (2 to <6 years old)  (1 application) | 11.7 | 94.7 | 57.2% |
| Toddler (1 to <2 years old)  (1 application) | 7.5 | 60.7 | 52.7% |

*Combined scenarios*

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

***Monitoring data***

None

***Dietary exposure***

As regards the intended use of the product REPULSIF ANTI-MOUSTIQUES ENFANTS on clothes by spraying, no contamination of food is expected.

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

Residue definitions

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

*List of scenarios*

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

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

2 e.g. chicken, milk, beer

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

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

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

Regarding the intended use of the product REPULSIF ANTI-MOUSTIQUES ENFANTS, no livestock exposure to DEET (N,N-diEthyl-m-Toluamide) is expected.

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

The product REPULSIF ANTI-MOUSTIQUES ENFANTS is only intended as non-professional use.

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

**Scenario 1**

Scenario 1 was performed for toddler, children and adult considering reference values mentioned in HEEG opinion 17(1) (US EPA Exposure Factors Handbook (2011 Issue), which are derived from US EPA Analysis of NHANES 1999-2006).

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

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

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

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

|  |  |
| --- | --- |
| Ratio surface factor of the palm compared to whole hand | 0.5 |
| transfer factor (hand to food) in % | 100% |
| transfer factor (food to mouth) in % | 100% |
| handwash after use (i.e rinsing factor)[[6]](#footnote-6) | 3 (considering that this recommendation could not be applicable and regarding the practical use, this factor is considered not relevant for children) |

Considering the intended use of REPULSIF ANTI-MOUSTIQUES ENFANTS, its concentration of DEET, and the reference values mentioned above, the exposure was estimated as:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Product application rate (mg product/cm²) (effective) | 0,95 | | | | |
| Concentration (a.s in % w/w in the product) | 10 | | | | |
| Applicated active substance (mg a.s/cm²) (effective) | 0,095 | | | | |
| age | Toddler  1-2 years | Child  2-3 years | Child  3-6 years | Child  6-11 years | adult |
| hands (palms and back of both hands) (cm2) | 230 | 297 | 415 | 428 | 820 |
| Intended/authorized number of application | 2 | 2 | 2 | 2 | 2 |
| Ratio surface factor of the palm compared to whole hand | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| exposure per application (transfered a.s in mg) | 11 | 14 | 20 | 20 | 39 |
| transfer factor (hand to food) in % | 100 | 100 | 100 | 100 | 100 |
| transfer factor (food to mouth) in % | 100 | 100 | 100 | 100 | 100 |
| ingested a.s in mg and per application | 11 | 14 | 20 | 20 | 39 |
| **total ingested a.s in mg** | **22** | **28** | **39** | **41** | **78** |
| Body weight in kg | 10 | 12 | 16 | 23.9 | 60 |
| Exposure per application in mg a.s/kg b.w./day | 1.1 | 1.2 | 1.2 | 0.9 | 0.6 |
| **Total exposure in mg a.s/kg b.w./day** | **2.2** | **2.4** | **2.5** | **1.7** | **1.3** |
| handwash after use (i.e rinsing factor) | nr | nr | nr | nr | 3 |
| **Total exposure in mg a.s/kg b.w./day including hand washing** | **-** | **-** | **-** | **-** | **0.43** |

nr: Not relevant

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

If recommendation 11 of the HHEG is followed the product is applied on skin twice a day for adults and once a day for children < 12 years. This would result in the following exposure calculations:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Product application rate (mg product/cm²) (effective) | 0.95 | | | | |
| Concentration (a.s in % w/w in the product) | 10 | | | | |
| Applicated active substance (mg a.s/cm²) (effective) | 0.095 | | | | |
| age | Toddler  1-2 years | Child  2-3 years | Child  3-6 years | Child  6-11 years | adult |
| hands (palms and back of both hands) (cm2) | 230 | 297 | 415 | 428 | 820 |
| Intended/authorized number of application | 1 | 1 | 1 | 1 | 2 |
| Ratio surface factor of the palm compared to whole hand | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| exposure per application (transfered a.s in mg) | 11 | 14 | 20 | 20 | 39 |
| transfer factor (hand to food) in % | 100 | 100 | 100 | 100 | 100 |
| transfer factor (food to mouth) in % | 100 | 100 | 100 | 100 | 100 |
| ingested a.s in mg and per application | 11 | 14 | 20 | 20 | 39 |
| **total ingested a.s in mg** | **11** | **14** | **20** | **20** | **78** |
| Body weight in kg | 10 | 12 | 16 | 23.9 | 60 |
| Exposure per application in mg a.s/kg b.w./day | 1.1 | 1.2 | 1.2 | 0.9 | 0.6 |
| **Total exposure in mg a.s/kg b.w./day** | **1.1** | **1.2** | **1.2** | **0.9** | **1.3** |
| handwash after use (i.e rinsing factor) | nr | nr | nr | nr | 3 |
| **Total exposure in mg a.s/kg b.w./day including hand washing** | **-** | **-** | **-** | **-** | **0.43** |

**Conclusion**

As regards the intended use of the product REPULSIF ANTI-MOUSTIQUES ENFANTS on clothes by spraying, no contamination of food is expected.

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

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

*Not relevant*

***Aggregated exposure***

*Not relevant*

#### Risk characterisation for human health

**Reference values to be used in Risk Characterisation**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Reference** | **Study** | **NOAEL (LOAEL)** | **AF** | **Correction for oral absorption** | **Value** |
| AELshort-term oral | 8 weeks oral capsule study in dogs. | 75 mg/kg/bw/day | 100 | 100% | 0.75 mg/kg b.w. |
| AELlong-term dermal | 90 days dermal study in rats | 1000 mg/kg/bw/day | 100 | 82% (dermal absorption in rats) | 8.2 mg/kg b.w. |
| ARfD | n.a | | | | |
| ADI | n.a | | | | |

**Maximum residue limits or equivalent**

Residue definitions

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

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

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

***Risk for industrial users***

Not relevant

***Risk for professional users***

Not relevant

***Risk for non-professional users***

**Systemic effects**

| **Task/**  **Scenario** | **Tier** | **Systemic NOAEL**  **mg/kg bw/d** | **AEL**  **mg/kg bw/d** | **Estimated uptake**  **mg/kg bw/d** | **Estimated uptake/ AEL**  **(%)** | **Systemic risk**  **Acceptable**  **(yes/no)** |
| --- | --- | --- | --- | --- | --- | --- |
| **Scenario [1] application on skin** | | | | | | |
| Adult 1 application | 1 | 1000 | 8.2 | 2.49 | 30.4 | Yes |
| Adult 2 applications | 1 | 1000 | 8.2 | 4.99 | 60.8 | Yes |
| Child (6 to 11 years old) 1 application | 1 | 1000 | 8.2 | 3.26 | 39.7 | Yes |
| Child (6 to 11 years old) 2 applications | 1 | 1000 | 8.2 | 6.52 | 79.5 | Yes |
| Child (3 to 6 years old) 1 application | 1 | 1000 | 8.2 | 3.21 | 39.2 | Yes |
| Child (3 to 6 years old) 2 applications | 1 | 1000 | 8.2 | 6.43 | 78.4 | Yes |
| Child (2 to 3 years old) 1 application | 1 | 1000 | 8.2 | 3.77 | 46.0 | Yes |
| Child (2 to 3 years old) 2 applications | 1 | 1000 | 8.2 | 7.55 | 92.0 | Yes |
| Toddler (1 to 2 years old) 1 application | 1 | 1000 | 8.2 | 4.05 | 49.4 | Yes |
| Toddler (1 to 2 years old) 2 applications | 1 | 1000 | 8.2 | 8.11 | 98.9 | Yes |
| **Scenario [2] application on cloth** | | | | | | |
| Adult 1 application | 1 | 1000 | 8.2 | 2.87 | 35.0 | Yes |
| Adult 2 applications | 1 | 1000 | 8.2 | 5.74 | 70.0 | Yes |
| Child (6 to 11 years old) 1 application | 1 | 1000 | 8.2 | 4.08 | 49.7 | Yes |
| Child (6 to 11 years old) 2 applications | 1 | 1000 | 8.2 | 8.16 | 99.5 | Yes |
| Child (3 to 6 years old) 1 application | 1 | 1000 | 8.2 | 4.00 | 48.8 | Yes |
| Child (3 to 6 years old) 2 applications | 1 | 1000 | 8.2 | 8.00 | 97.6 | Yes |
| Child (2 to 3 years old) 1 application | 1 | 1000 | 8.2 | 4.77 | 58.1 | Yes |
| Child (2 to 3 years old) 2 applications | 1 | 1000 | 8.2 | 9.53 | **116.2** | **No** |
| Toddler (1 to 2 years old) 1 application | 1 | 1000 | 8.2 | 4.93 | 60.1 | Yes |
| Toddler (1 to 2 years old) 2 applications | 1 | 1000 | 8.2 | 9.85 | **120.2** | **No** |

*Conclusion on risk assessment according to the European approach (55% of body is exposed)*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Task/**  **Scenario** | **Tier** | **AEL**  **mg/kg bw/d** | **Estimated uptake**  **mg/kg bw/d** | **Estimated uptake/ AEL**  **(%)** | **Number of application claimed by applicant** | **Number of application acceptable** | **Acceptable**  **(yes/no) compared to applicant requirement for systemic risk** |
| **Scenario 1** | | | | | | | |
| Scenario [1]  adult | 1 | 8.2 | 3.57 | 43.6 | 2 | 2 | Acceptable |
| Scenario [1]  child 6-11 years | 1 | 8.2 | 4.76 | 58.1 | 2 | 1 | Acceptable if one application only |
| Scenario [1]  child 2-6 years | 1 | 8.2 | 5.43 | 66.2 | 2 | 1 | Acceptable if one application only |
| Scenario [1]  child 1-2 years | 1 | 8.2 | 6.01 | 73.3 | 2 | 1 | Acceptable if one application only |

**Combined scenarios**

| **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 application on skin and clothes** | | | | | | |
| Adult 1 application | 1 | 1000 | 8.2 | 5.36 | 65.4 | Yes |
| Adult 2 applications | 1 | 1000 | 8.2 | 10.72 | **130.8** | **No** |
| Child (6 to 11 years old) 1 application | 1 | 1000 | 8.2 | 7.34 | 89.5 | Yes |
| Child (6 to 11 years old) 2 applications | 1 | 1000 | 8.2 | 14.68 | **179.0** | **No** |
| Child (3 to 6 years old) 1 application | 1 | 1000 | 8.2 | 7.21 | 88.0 | Yes |
| Child (3 to 6 years old) 2 applications | 1 | 1000 | 8.2 | 14.43 | **176.0** | **No** |
| Child (2 to 3 years old) 1 application | 1 | 1000 | 8.2 | 8.54 | **104.1** | **No** |
| Child (2 to 3 years old) 2 applications | 1 | 1000 | 8.2 | 17.08 | **208.3** | **No** |
| Toddler (1 to 2 years old) 1 application | 1 | 1000 | 8.2 | 8.98 | **109.5** | **No** |
| Toddler (1 to 2 years old) 2 applications | 1 | 1000 | 8.2 | 17.96 | **219.0** | **No** |

*Conclusion on combined risk assessment according to the European approach*

| **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 application on skin and clothes** | | | | | | |
| Adult  1 application on skin and clothes | 1 | 1000 | 8.2 | 5.8 | 71% | Yes |
| Adult  2 applications on skin and clothes | 1 | 1000 | 8.2 | 11.6 | 142% | No |
| Child (6 to 11 years old) 1 application on skin and clothes | 1 | 1000 | 8.2 | 8.6 | 105% | No |
| Child (2 to 6 years old) 1 application on skin and clothes | 1 | 1000 | 8.2 | 9.8 | 120% | No |
| Toddler (1 to 2 years old) 1 application on skin and clothes | 1 | 1000 | 8.2 | 10.9 | 133% | No |

The risk is acceptable for adult considering only one application per day on skin and clothes. The combined risk is unacceptable for children.

* **MAJOR CHANGE FOR RCAME – 2020**

**Systemic effects**

| **Task/**  **Scenario** | **Tier** | **Systemic NOAEL**  **mg/kg bw/d** | **AEL**  **mg/kg bw/d** | **Estimated uptake**  **mg/kg bw/d** | **Estimated uptake/ AEL**  **(%)** | **Systemic risk**  **Acceptable**  **(yes/no)** |
| --- | --- | --- | --- | --- | --- | --- |
| **Scenario [1] application on skin** | | | | | | |
| Adult | 1 | 1000 | 8.2 | 4.94 | 60.3 | Yes |
| Child (6 to 12 years old) | 1 | 1000 | 8.2 | 6.60 | 80.4 | Yes |
| Child (6 to 12 years old) | 2 | 1000 | 8.2 | 6.04 | 73.7 | Yes |
| Child (2 to 6 years old) | 1 | 1000 | 8.2 | 7.49 | 91.4 | Yes |
| Child (2 to 6 years old) | 2 | 1000 | 8.2 | 6.84 | 83.4 | Yes |
| Toddler (1 to 2 years old) | 1 | 1000 | 8.2 | 8.28 | 101.0 | **NO** |
| Toddler (1 to 2 years old) | 2 | 1000 | 8.2 | 7.57 | 92.3 | Yes |
| **Scenario [2] application on clothes** | | | | | | |
| Adult 1 application | 1 | 1000 | 8.2 | 5.58 | 68 | Yes |
| Adult 2 applications | 1 | 1000 | 8.2 | 11.15 | 136.0 | **NO** |
| Child (6 to 12 years old) 1 application | 1 | 1000 | 8.2 | 7.75 | 94.51 | Yes |
| Child (6 to 11 years old) 2 applications | 1 | 1000 | 8.2 | 15.50 | 189 | **NO** |
| Child (2 to 6 years old) 1 application | 1 | 1000 | 8.2 | 8.48 | 103.4 | **NO** |
| Toddler (1 to 2 years old) 2 applications | 1 | 1000 | 8.2 | 9.23 | 112.6 | **NO** |
| **Scenario [3] application on skin and clothes** | | | | | | |
| Adultand child older 12 years 1 application | 1 | 1000 | 8.2 | 7.65 | 93 | YES |

**Conclusion on the risk assessment for human health:**

* **Application on the skin**: the systemic risk is acceptable for adults, children (2 to < 12 years old) and toddlers (1 to < 2 years old) provided that the product is applied by an adult and the application do not exceed one application per day. Moreover, the product has not to be applied on the hands of children between one and 2 years.
* **Application on clothes**: the systemic risk is acceptable for adults and children (6 to < 12 years old) provided that the application do not exceed one per day. For children and toddlers (1 to < 6 years old), the risk is unacceptable so the product can’t be used in this condition for this category of users.
* **Application on clothes and skin:** the systemic risk is acceptable for adults and children of 12 years old and more provided that the applications do not exceed one application per day.

**Local effects**

Due to the classification of the product (H318 - Eye Dam. 1.) and the risk of exposure of eyes during spray application , this product will not be authorized in accordance with Article 19 (1) of the BPR.

* **Major Change application for REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS – 2020**

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 until 12 years: the repellent must be applied by adults

**Conclusion**

Due to the classification of the product (H318 - Eye Dam. 1.) and the risk of exposure of eyes during spray application , this product will not be authorized in accordance with Article 19 (1) of the BPR

**In France, given the need to repel mosquitoes from human to prevent vector borne disease, the product REPULSIF ANTI MOUSTIQUE ENFANT will be authorized for use on humans against mosquitoesbased on article 19(5) with appropriated risk mitigation measures. It has to be applied on adults and on children above 3 years old, for the skin application twice a day, for the clothes application twice a day and for the combined application once a day. For children younger than 3 years old, skin application can be done twice a day and clothes application once a day. No combined application can be done for children under 3 years old.**

***Risk for the general public***

**Systemic effects**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Skin surface area to put in the mouth to reach the AEL (cm²)** | **% hand surface area to put in the mouth to reach the AEL** | **Acceptable**  **(yes/no)** |
| **Scenario [3] hand to mouth behaviour** | | | |
| Adult | 473.7 | 58% | Yes |
| Child (6<11 years) | 188.7 | 44% | Yes |
| Child (3<6 years) | 126.3 | 30% | Yes |
| Child (2<3 years) | 94.7 | 32% | Yes |
| Toddler (1<2 years) | 78.9 | 34% | Yes |

Due to the presence of a bittering agent, it is considered that treated hands will not be mouthed on large surfaces. So secondary exposure via hand to mouth behaviour is considered acceptable.

* **MAJOR CHANGE FOR RCAME – 2020**

**Systemic effects**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Skin surface area to put in the mouth to reach the AEL (cm²)** | **% hand surface area to put in the mouth to reach the AEL** | **Acceptable**  **(yes/no)** |
| **Scenario [3] hand to mouth behaviour** | | | |
| Adult | 364.1 | 88.8% | Yes |
| Child (6<12 years) | 145.0 | 67.8% | Yes |
| Child (2<6 years) | 94.7 | 57.2% | Yes |
| Child (1<2 years) | 60.7 | 52.7% | Yes |

Due to the presence of a bittering agent, it is considered that treated hands will not be mouthed on large surfaces. So secondary exposure via hand to mouth behaviour is considered acceptable. However, the applicant has proposed the following RMM: Do not treat hands of children.

**Combined scenarios**

*Not relevant are toxicological effects are specific to the route of exposure.*

**Local effects**

*Not relevant*

**Conclusion**

An acceptable risk is identified for secondary exposure of general public.

* **Major Change application for REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS – 2020**

An acceptable risk is identified for secondary exposure of general public.

If the product is authorized in accordance with Article 19(1), the following instruction of uses should be applied:

* the product is applied on skin twice a day for adults and once a day for children < 12 years
* the product is apllied on clothes twice a day for adults and children > 6 years and once a day for children < 6 years
* the product is applied on skin and clothes once a day for adults and the combined scenario can be used by adults only.
* **Major Change application for REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS – 2020**

**Conclusion:**

The risk for human health is acceptable considering the following scenario:

* the product is applied on skin once a day for adults, children from 2 to 12 years old and toddlers from 1 to 2 years old. The product has not be applied on the hands of children between one and 2 years.
* the product is applied on clothes once a day for adults and children from 6 to 12 years old. For children and toddlers (1 to < 6 years old), the risk is unacceptable
* the product is applied on skin and clothes once a day for adults and children older 12 years.

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

As regards the intended use of the product REPULSIF ANTI-MOUSTIQUES ENFANTS on clothes by spraying, no contamination of food is expected.

Considering the exposure estimated for the intended use on skin of REPULSIF ANTI-MOUSTIQUES ENFANTS, and the ARfD proposed for DEET, the following dietary risk assessments were performed:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| age | Toddler  1-2 years | Child  2-3 years | Child  3-6 years | Child  6-11 years | adult |
| Exposure per application in mg a.s/kg b.w./day | 1.1 | 1.2 | 1.2 | 0.9 | 0.6 |
| **Total exposure in mg a.s/kg b.w./day** | **2.2** | **2.4** | **2.5** | **1.7** | **1.3** |
| **Total exposure in mg a.s/kg b.w./day including hand washing** | nr | nr | nr | nr | **0.43** |
| ARfD (mg a.s/kg b.w./day ) | 0.75 | 0.75 | 0.75 | 0.75 | 0.75 |
| % of ARfD (per application) | 146 | 157 | 164 | 113 | 87 |
| % of ARfD (in total) | 292 | 314 | 329 | 227 | 173 |
| % of ARfD (per application) including hand washing | nr | nr | nr | nr | 29 |
| **% of ARfD (in total) including hand washing** | **-** | **-** | **-** | **-** | **58** |

nr: Not relevant

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

If recommendation 11 of the HHEG is followed the product is applied on skin twice a day for adults and once a day for children < 12 years. This would result in the following risk calculations:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| age | Toddler  1-2 years | Child  2-3 years | Child  3-6 years | Child  6-11 years | adult |
| Exposure per application in mg a.s/kg b.w./day | 1.1 | 1.2 | 1.2 | 0.9 | 0.6 |
| **Total exposure in mg a.s/kg b.w./day** | **1.1** | **1.2** | **1.2** | **0.9** | **1.3** |
| **Total exposure in mg a.s/kg b.w./day including hand washing** | nr | nr | nr | nr | **0.43** |
| ARfD (mg a.s/kg b.w./day ) | 0.75 | 0.75 | 0.75 | 0.75 | 0.75 |
| % of ARfD (per application) | 146 | 157 | 164 | 113 | 87 |
| % of ARfD (in total) | 143 | 157 | 164 | 113 | 173 |
| % of ARfD (per application) including hand washing | nr | nr | nr | nr | 29 |
| **% of ARfD (in total) including hand washing** | **-** | **-** | **-** | **-** | **58** |

**Conclusion**

As regards the intended use of the product REPULSIF ANTI-MOUSTIQUES ENFANTS on clothes by spraying, no contamination of food is expected.

Considering the intended use on skin of REPULSIF ANTI-MOUSTIQUES ENFANTS and based on the assumption and the reference values used, a dietary risk was identified for toddler and for children with a single application per day. However, no dietary risk adults for 2 applications per day considering hand washing factor.

As a consequence the following label recommendations are proposed:

* “Wash hands before handling food”
* “Do not treat hands of children”
* “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”

Moreover a co-formulant (denatonium benzoate) is a strong deterrent contained in REPULSIF ANTI-MOUSTIQUES ENFANTS to limit any ingestion of this biocide product.

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

Not Relevant.

### Risk assessment for animal health

Not Relevant.

### Risk assessment for the environment

*Please refer to the product assessment report related to REPULSIF ANTI-MOUSTIQUES CORPOREL product authorisation (FR-2014-0088) under Regulation (UE) n° 528/2012.*

**Major Change application for REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS – 2020**

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

Considering the revision of the dose rates for this product, the risk assessment for the environment has been revised considering

- two applications on skin alone at the application rate of 1.2 mg product / cm² (scenario 1 and 2),

- two applications on clothes alone at the application rate of 1.8 mg product / cm² (scenario 3).

- a combined unique application on skin and clothes at the respective above application rates (scenario 4).

**Exposure assessment for the major change**

**Scenario 1: Repellent treatment applied on skin – STP release scenario**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Input parameters for calculating the local emission** | | | | |
| **Input** | **Nomenclature** | **Value** | **Unit** | **Remarks** |
| Number of inhabitants per STP | Nlocal | 10 000 | [-] | Default value |
| Active substance in product | (B) Cformweight | 103.1 | g.kg-1 | (10.31% technical) |
| Consumption per application | (D2) Qformappl | 1.2 | mg.cm-² | Maximum efficient dose |
| Number of applications per day | Nappl | 2 | d-1 | Intended use |
| Treated area of human skin | AREAskin | 9130 | cm² | HEAdoc recommendation (January 2018) |
| Fraction released to wastewater | Fwater | 0.887 | [-] | CAR DEET |
| Fraction of inhabitants using a repellent product | Finh | 0.2 | [-] | Default value (ESD PT19, Table 3.5) |
| Market share of repellent | Fpenetr | 0.5 | [-] | Default value |

Calculations for Scenario 1: Repellent treatment s applied on skin – STP release scenario

| **Resulting local emission to relevant environmental compartments** | | |
| --- | --- | --- |
| **Compartment** | **Local emission (Elocalcompartment) [kg/d]** | **Remarks** |
| STP | 2.00 | / |

**Scenario 2: Repellent treatment applied on skin – Swimming scenario**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Input parameters for calculating the local emission** | | | | |
| **Input** | **Nomenclature** | **Value** | **Unit** | **Remarks** |
| Daily number of swimmers | Nswimmer | 1500 | [-] | Default value |
| Fraction of swimmers using the repellent product | Fswim | 0.1 | [-] | Default value for infested areas |
| Number of applications per day | Nappl | 1 | d-1 | Default value |
| Fraction released to surface water body | Fwaterbody | 0.887 | [-] | CAR DEET |
| Active substance in the product | (B) Cformweight | 103.1 | g/kg | (10.31% technical) |
| Consumption per application | (D2) Qformappl | 1.2 | mg.cm-² | Maximum efficient dose |
| Treated area of human skin | AREAskin | 9130 | cm² | HEAdoc recommendation (January 2018) |

Calculations for Scenario 2: Repellent treatments applied on skin – swimming scenario

| **Resulting local emission to relevant environmental compartments** | | |
| --- | --- | --- |
| **Compartment** | **Local emission (Elocalcompartment) [kg/d]** | **Remarks** |
| Surface water | 1.50E-01 | / |

**Scenario 3: Repellent treatment applied on clothes – STP release scenario**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Input parameters for calculating the local emission** | | | | |
| **Input** | **Nomenclature** | **Value** | **Unit** | **Remarks** |
| Number of inhabitants per STP | Nlocal | 10 000 | [-] | Default value |
| Active substance in product | (B) Cformweight | 103.1 | g.kg-1 | (10.31% technical) |
| Consumption per application | (D2) Qformappl | 1.80 | mg.cm-² | Maximum efficient dose |
| Number of applications per day | Nappl | 2 | d-1 | Intended use |
| Treated area of clothes | AREAclothes | 17838 | cm² | Default value for human clothes (ESD PT19, Table 3.4) |
| Fraction released to wastewater | Fwater | 1 | [-] | Default value |
| Fraction of inhabitants using a repellent product | Finh | 0.2 | [-] | Default value (ESD PT19, Table 3.5) |
| Market share of repellent | Fpenetr | 0.5 | [-] | Default value |

Calculations for Scenario 3: Repellent treatment applied on clothes – STP release scenario

| **Resulting local emission to relevant environmental compartments** | | |
| --- | --- | --- |
| **Compartment** | **Local emission (Elocalcompartment) [kg/d]** | **Remarks** |
| STP | 6.62 | / |

Calculations for Scenario 4: Repellent treatment applied on skin and clothes (only one application) – STP release scenario

| **Resulting local emission to relevant environmental compartments** | | |
| --- | --- | --- |
| **Compartment** | **Local emission (Elocalcompartment) [kg/d]** | **Remarks** |
| STP | 4.31 | (Elocal STP skin + Elocal clothes) / 2 |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Input parameters (only set values) for calculating the fate and distribution in the environment** | | | | | |
| **Input** | | **Value** | **Unit** | | **Remarks** |
| Molecular weight | | 191.27 | g/mol | |  |
| Vapour pressure (at 25°C) | | 0.23 | Pa | |  |
| Water solubility (at 25°C) | | 11 200 | mg/l | |  |
| Log Octanol/water partition coefficient | | 2.40 | Log 10 | |  |
| Organic carbon/water partition coefficient (Koc) | | 43.3 | l/kg | |  |
| Biodegradability | | Readily biodegradable with the 10 day window | - | |  |
| DT50 soil (at 12°C) | | 30 | d | |  |
| ksoil (total removal soil depth of 0.2 m) | | 2.49E-02 | d-1 | |  |
| DT50 surface water (at 12°C) | | 15 | d | |  |
| **Calculated fate and distribution in the STP** | | | | | |
| Compartment | Percentage [%] – Simple Treat 4.0 | | | Remarks | |
| Air | 9.00E-04 | | | - | |
| Water | 7.992 | | |
| Sludge | 0.403 | | |
| Degraded in STP | 91.6 | | |

***PEC calculations***

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Summary table on calculated PEC values** | | | | | |
|  | **PECSTP** | **PECwater** | **PECsed** | **PECsoil** | **PECGW** |
| [mg/l] | [mg/l] | [mg/kgwwt] | [mg/kgwwt] | [µg/l] |
| Scenario 1 | 8.01E-02 | 8.01E-03 | Risk assessment covered by surface water | 1.06E-02 | 3.76E+00 |
| Scenario 2 | Not relevant | 7.54E-03 | Not relevant | Not relevant |
| Scenario 3 | 2.65E-01 | 2.65E-02 | 3.50E-02 | 1.24E+01 |
| Scenario 4 | 1.72E-01 | 1.72E-02 | 2.28E-02 | 8.09E+00 |

**Risk assessment for the major change**

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

***PEC/PNEC calculations***

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Summary table on calculated PEC values** | | | | | |
|  | **PEC/PNECSTP** | **PEC/PNECwater** | **PEC/PNECsed** | **PEC/PNECsoil** | **PECGW** |
| Scenario 1 | 8.01E-03 | 1.86E-01 | Risk assessment covered by surface water | 2.79E-01 | 3.76E+00\* |
| Scenario 2 | Not relevant | 1.75E-01 | Not relevant | Not relevant |
| Scenario 3 | 2.65E-02 | 6.15E-01 | 9.23E-01 | 1.24E+01\* |
| Scenario 4 | 1.72E-02 | 4.01E-01 | 6.01E-01 | 8.09E+00\* |

\* < 0.1 µg/L when refined by a tonnage approach (see confidential PAR)

**Conclusions for the Major Change application for REPULSIF CORPOREL ANTI-MOUSTIQUES ENFANTS – 2020**

Considering the revision of the dose rates for this product, the revised risk assessment for the environment leads to acceptable risks for:

- two applications on skin alone at the application rate of 1.2 mg product / cm² (scenario 1 and 2),

- two applications on clothes alone at the application rate of 1.8 mg product / cm² (scenario 3).

- a combined unique application on skin and clothes at the respective above application rates (scenario 4).

Concerning groundwater, the refinement based on tonnage data from the first authorisation is presented in the confidential PAR and leads to acceptable level of DEET in groundwater.

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

*Please refer to summary of the product assessment and to the relevant sections of the assessment report.*

### Assessment of a combination of biocidal products

Not Relevant.

### Comparative assessment

Not Relevant.

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

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Experimental data on the efficacy**  **of the biocidal product against target organism(s)** | | | | | | | |
| **Function** | **Field of use envisaged** | **Test substance** | **Test organism(s)** | **Test method** | **Test system / concentrations applied / exposure time** | **Test results: effects** | **Reference** |
| Repellent | skin | RAME (DEET, 10% w/w) | *Culex pipiens*  *Aedes albopictus*  *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.  3 volunteers and 3 replicates per volunteer.  Product applied on one forearm of each volunteer, the other untreated one being used as a control. | Dose of product 0.95 mg/cm² of skin (i.e. 0.57 g/600 cm² forearm).  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), 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.  Climatic conditions: temperature 27 ±2 °C; relative humidity 62 % ± 10 % | After application of the product at 0.95 mg/cm² of skin, the duration of protection was:  - 4 hours for *C. pipiens*  - 4 hours for *A. albopictus*  - 4 hours for *A. aegypti*  - 4 hours for *A. gambiae*.  Based on the less sensitive species, the protection duration of the product is 4 hours when the product is applied on skin. | Serrano B., 2014  S6.7\_01  R.I = 2 |
| Repellent | Textile (cotton) | RAME (DEET, 10% w/w) | *Culex pipiens*  *Aedes albopictus*  *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. 3 volunteers and 3 replicates per volunteer.  Product applied on a 100% cotton fabric set on one forearm of each volunteer, the other one with an untreated fabric being used as a control. | Dose of product 1.54 mg/cm² of skin (i.e. 0.924 g/600 cm² forearm).  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), the treated forearm was inserted into the cage for 3 minutes (exposure time). The same procedure was repeated every hour until 3 hours and then every 30 minutes until inefficacy. Landings and bites were counted during each exposure time.  Climatic conditions: temperature 30 ±2 °C; relative humidity 70 % ± 10 % | After application of the product at 1.54 mg/cm² of fabric (cotton), the duration of protection was:  - 4 hours for *C. pipiens*  - 4 hours for *A. albopictus*  - 4 hours for *A. aegypti*  - 3.5 hours for *A. gambiae* Based on the less sensitive species, the protection duration of the product is 3.5 hours when the product is applied on fabric (cotton). | Serrano B., 2015  S6.7\_02  R.I = 2 |
| Repellent | skin | RAME (DEET 10% w/w) | *Culex pipiens*  *Aedes albopictus*  *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.  3 volunteers and 3 replicates per volunteer.  Product applied on one forearm of each volunteer, the other untreated one being used as a control. | Dose of product 0.95 mg/cm² of skin (i.e. 0.57 g/600 cm² forearm).  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), 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.  Climatic conditions: temperature 32 ±2 °C; relative humidity 75 % ± 10 % | After application of the product at 0.95 mg/cm² of skin, the duration of protection was:  - 4 hours for *C. pipiens*  - 4 hours for *A. albopictus*  - 4 hours for *A. aegypti*  - 3.5 hours for *A. gambiae*.  Based on the less sensitive species, the protection duration of the product is 3.5 hours when the product is applied on skin. | Serrano B., 2016  S6.7\_03  R.I = 2 |

**Annex 9 List of new data submitted in support of the evaluation of the biocidal product – major change 2020**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Section No** | **Reference No** | **Author** | **Year** | **Title** | **Owner of data** | **Letter of access** | | **Data protection claimed** | |
| **Physico-chemistry** | |  |  |  |  | **Yes** | **No** | **Yes** | **No** |
| S3.1, S3.2, S3.4.1, S3.5 | 19-919062-006 | 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 RCAME in compliance with CIPAC MT 46.3 CIPAC Handbook J (2000) | Spring |  | **X** | **X** |  |
| S3.4.1 | 19-919062-007 | 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 RCAME In compliance with Technical Monograph No. 17, 2nd edition CropLife International | Spring |  | **X** | **X** |  |
| S3.5 | 19-919062-010 | Halbwachs P. | 2020 | Spray droplet size distribution by laser diffraction on the product RCAME In compliance with the CIPAC Handbook K – MT 187 method (2003) and ISO 13320:2009 | Spring |  | **X** | **X** |  |
| S3.8 | 19-919062-001 | Halbwachs P. | 2019 | Physico-chemical tests on the product VRCAM | Spring |  | **X** | **X** |  |
| S3.4.1, S3.9 | 19-919062-005 | Halbwachs P. | 2019 | Physico-chemical tests on the product RCAME | Spring |  | **X** | **X** |  |
| S4.6 | 20-919062-001 | Padilla P. | 2020 | Flash point test on the product VRCAM | Spring |  | x | x |  |

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Method validation** | |  |  |  |  | **Yes** | **No** | **Yes** | **No** |
| S5.1 | 19-919062-008 | Ricau H. | 2019 | Validation of the analytical method for the determination of N,N-diethyl-meta-toluamide (DEET) in RCAME in compliance with SANCO/3030/99 rev.5 from 22/03/2019 | Spring |  | **X** | **X** |  |
| S5.1 | 19-919062-004 | Ricau H. | 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** |  |

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Efficacy** |  |  |  |  |  | **Yes** | **No** | **Yes** | **No** |
| S6.7\_01 | 2513a1-RCAME/1019 | Serrano B. | 2019 | Laboratory assessment of a personal skin repellent against mosquitoes | Spring |  | **X** | **X** |  |
| S6.7\_02 | 2513a2-RCAME/1019 | Serrano B. | 2019 | Laboratory assessment of a repellent against mosquitoes - application on clothes | Spring |  | **X** | **X** |  |
| S6.7\_03 | STA\_IR\_0119\_01 | Dautel H. | 2019 | Evaluation of the repellent efficacy of two products against the European Sheep Tick Ixodes ricinus on human volunteers | Spring |  | **X** | **X** |  |

1. Proposal for harmonising the assessment of human exposure to repellents (PT19) Agreed at the HH WH III 2016 [↑](#footnote-ref-1)
2. Recommendation no. 11 of the BPC Ad hoc Working Group on Human Exposure: Proposal for harmonising the assessment of human exposure to repellents (PT19), 2018. [↑](#footnote-ref-2)
3. Recommendation no. 14 of the BPC Ad hoc Working Group on Human Exposure: Default human factor values for use in exposure assessments for biocidal products, 2017. [↑](#footnote-ref-3)
4. Recommendation no. 8 of the BPC Ad hoc Working Group on Human Exposure Consumer use of biocidal product and protection from typical clothing, 2015. [↑](#footnote-ref-4)
5. Recommendation no. 8 of the BPC Ad hoc Working Group on Human Exposure Consumer use of biocidal product and protection from typical clothing, 2015. [↑](#footnote-ref-5)
6. Dilution factor from ConsExpo 4.0, Consumer Exposure and Uptake Models. Program Manuel. Bilthoven, The Netherlands: National Institute for Public Health and the Environment (RIVM). Report no. 320104004. & RIVM report 320104001/2006 : Cosmetics Fact Sheet To assess the risks for the consumer (Updated version for ConsExpo 4) H.J. Bremmer, L.C.H. Prud’homme de Lodder, J.G.M. van Engelen [p34 : "Weight fraction dilution Wf / 3" " Estimate dilution factor 3 (wetting hands)] [↑](#footnote-ref-6)