Product Assessment Report

Biocidal product assessment report related to product authorisation under Regulation 528/2012

REPULSIF ANTI-MOUSTIQUES CORPOREL

SPRING

December 2013

Internal registration/file no:	PB-12-00204
R4BP no:	2012/4144/577/FR/APP/1832
Authorisation n°	FR-2014-0088
Granting date:	21st November 2014
Expiry date of authorisation:	21st November 2024
Active ingredient:	DEET (CAS 134-62-3)
Product type:	19 - Repellent

Competent Authority in charge of delivering the product authorisation:
French Ministry of Ecology
Department for Nuisance Prevention and Quality of the Environment
Chemical Substances and Preparation Unit
Grande Arche, Paroi Nord
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Authority in charge of the efficacy and risk assessment:
Anses – French agency for food, environmental and occupational health and safety
Regulated Products Directorate
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1 GENERAL INFORMATION ABOUT THE PRODUCT APPLICATION

1.1 Applicant

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City:	Saint-Martin-de -Crau
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Country:	France
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1.1.1 Person authorised for communication on behalf of the applicant

Name:	MORAITI OLIVIER
Function:	-
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1.2 Current authorisation holder[1]

Company Name:	SPRING
Address:	4, rue Blaise Pascal-ZI du bois de Leuze
City:	Saint-Martin-de -Crau
Postal Code:	13310
Country:	France

[1] Applies only to existing authorisations

Telephone:	+33 4.90.47.17.66
Fax:	+33 4.90.47.23.55
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Letter of appointment for the applicant to represent the authorisation holder provided (yes/no):	No

1.3 Proposed authorisation holder

Company Name:	SPRING
Address:	4, rue Blaise Pascal-ZI du bois de Leuze
City:	Saint-Martin-de -Crau
Postal Code:	13310
Country:	France
Telephone:	+33 4.90.47.17.66
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E-mail address:	www.spring-subito.com oliviersubito@aol.com
Letter of appointment for the applicant to represent the authorisation holder provided (yes/no):	No

1.4 Information about the product application

Application received:	31/07/2012
Application reported complete:	09/08/2012
Type of application:	Product authorisation
Further information:	New product

1.5 Information about the biocidal product

1.5.1 General information

Trade name:	REPULSIF ANTI-MOUSTIQUES CORPOREL
Manufacturer's development code number(s), if appropriate:	RAMC
Product type:	PT19
Composition of the product (identity and content of active substance(s) and substances of concern; full composition see confidential annex):	See Confidential annex.
Formulation type:	VIII.3 Liquid formulation

Ready to use product (yes/no):	Yes
Is the product the very same (identity and content) to another product already authorised under the regime of directive 98/8/EC (yes/no); If yes: authorisation/registration no. and product name: or Has the product the same identity and composition like the product evaluated in connection with the approval for listing of active substance(s) on to Annex I to directive 98/8/EC (yes/no):	No

1.5.2 Information on the intended use(s)

Overall use pattern (manner and area of use):	The product RAMC is presented as a ready-for-use product to be sprayed on uncovered human skin or on clothes to repel mosquitoes, for consumer use.
Target organisms:	- *Culex pipiens,* - *Aedes albopictus,* - *Aedes aegypti* - *Anopheles gambiae* - *Other mosquitoes*
Category of users:	Public
Directions for use including minimum and maximum application rates, application rates per time unit (e.g. number of treatments per day), typical size of application area:	The recommended rate of application of RAMC is 1.1 mg/cm² of skin, or 1.67 mg/cm² of clothes. The number of treatments is one application per day. The product can be used on children from 6 years old and adults. The number of sprays is to be adapted to the body surface to protect (*e.g.* 6 sprays for an application on an adult forearm).
Potential for release into the environment (yes/no):	No
Potential for contamination of food/feedingstuff (yes/no)	No No other study was performed on the biocidal product, since none of the non-active substances is a substance of concern and as RAMC will not be applied directly to feeding stuffs. In addition, intake of RAMC by animals producing food (eggs, milk, meat) is not expected based on the intended uses.
Proposed Label:	The product RAMC is packaged in a polypropylene flask with spray pump. There are three volumes of flask: 80 mL, 100 mL or 150 mL.

Use Restrictions:	The proposed label contains detailed instructions for use. The product must not be used for children under 6 years old. The product must not be applied on eyes. Number of applications must not exceed one per day. If applied with a sunscreen product, RAMC should be applied at least 30 minutes after.

1.5.3 Information on active substance(s)

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

1.5.4 Information on the substance(s) of concern

No substance of concern

1.6 Documentation

1.6.1 Data submitted in relation to product application

Identity, physicochemical and analytical method data

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

Efficacy data

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

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

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

Residues data:

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

Toxicology data

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

Ecotoxicology data

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

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

1.6.2 Access to documentation

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

2 Summary of the product assessment

2.1 Identity related issues

The source of the active substance used in the biocidal product REPULSIF ANTI-MOUSTIQUES CORPOREL (RAMC) is one of the source used for annex I inclusion.
There is no substance of concern in the biocidal product.
The formulation of the biocidal product RAMC is not the same as the formulation of the representative biocidal product assessed for the inclusion of the active substance in annex I of directive 98/8/EC.

2.2 Classification, labelling and packaging

2.2.1 Classification of the active substance

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

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

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

2.2.2 Classification of the biocidal product

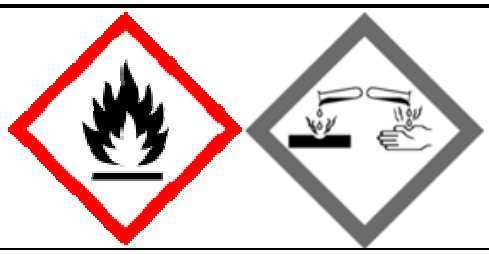
Classification - Directive 99/45/EEC	
Class of danger	Xi - Irritant
R phrases	R10: Flammable R41: Risk of serious damage to eyes
S phrases (proposed by the RMS)	S2: Keep out of the reach of children. S26: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice S39: Wear eye/face protection S46: If swallowed, seek medical advice immediately and show this container or label

Classification - Regulation (EC) 1272/2008	
Hazard statement	Flam. Liq. 3 - H226 : Flammable liquid and vapour Eye Dam. 1 - H318 : Causes serious eye damage
Precautionary statements (proposed by the RMS)	-

2.2.3 Labelling of the biocidal product

Labelling - Directive 67/548/EEC	
Symbols:	
Indications of danger:	Xi - Irritant
Risk phrases:	R10: Flammable. R41: Risk of serious damage to eyes
Safety phrases:	S2: Keep out of the reach of children. S26: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice S39: Wear eye/face protection S46: If swallowed, seek medical advice immediately and show this container or label

Labelling - Regulation (EC) 1272/2008

Pictograms:	
Signal words:	Flam. Liq. 3 ; Danger
Hazard statements:	Flam. Liq. 3 H226 : Flammable liquid and vapour Eye Dam. 1; H318 : Causes serious eye damage

2.2.4 Packaging of the biocidal product

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

2.3 Physico/chemical properties and analytical methods

2.3.1 Active ingredient

2.3.1.1 Identity, origin of active ingredient

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

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

Physical and chemical properties of the active substance and analytical methods for determination of active ingredient in the technical active ingredient have already been evaluated at EU level and are presented in the CAR of the active substance DEET (2009). The notifier of the product RAMC is not the applicant that supported the annex I inclusion dossier of the active substance but has a full letter of access to these data.

2.3.2 Biocidal product

2.3.2.1 Identity, composition of the biocidal product, packaging

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

Trade name: REPULSIF ANTI-MOUSTIQUES CORPOREL, SUBITO/BEAST-OFF

Code number: RAMC

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

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

2.3.2.2 Physico-chemical properties

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

Subsection (Annex Point IIB. 3/TNsG)	Method	Purity/ Specification	Results	Reference
3.1 Appearance (IIB3.1/Pt. I-B3.1) **3.1.1 Physical state and nature** **3.1.2 Colour** **3.1.3 Odour**	Visual	30% DEET Batch 965	limpid liquid Colourless Not performed	Study 402/12/1048F-e Legay 2012
3.2 Explosive properties (IIB3.2/Pt. I-B3.2)	Statement and DSC	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
3.3 Oxidising properties (IIB3.3/Pt. I-B3.3)	Statement	-	Based on structural considerations, RAMC is not expected to have oxidising properties. Not oxidizing	ASC report 12/04
3.4 Flash-point and other indications of flammability or spontaneous ignition (IIB3.4/Pt. I-B3.4)				
Flammability	EC A.9	30% DEET Batch 965	Flash point : 41.9°C Classified as R10 according to 99/45/EC Classified as flam liq 3; H226 according to CLP	Legay 2012
Self ignition temperature of solids	Statement	-	Based on composition considerations, RAMC is expected to have auto-flammability point higher than 360 °C.	ASC report 12/04
3.5 Acidity/Alkalinity (IIB3.5/Pt. I-B3.5)			Not required as pH of Biocidal product is > 4.0 and < 10.0	-
3.5 pH pure material	CIPAC MT 75.3	30% DEET Batch 965	pH of pure material: 8.1 at 20.6°C	Legay 2012
3.6 Bulk density (IIB3.6/Pt. I-B3.6)	EC A.3 OECD 109	30% DEET Batch 965	Liquid density : 0.950	Legay 2012
3.7 Storage stability - (IIB3.7/Pt. I-B3.7)	3 years at ambient temperature (ongoing	30% DEET Batch 965	Ongoing study. Final study report is required in post registration	Legay 2012

<table>
<tr><th>Subsection (Annex Point IIB. 3/TNsG)</th><th>Method</th><th>Purity/ Specification</th><th>Results</th><th>Reference</th></tr>
<tr><td></td><td>study)</td><td></td><td></td><td></td></tr>
<tr><td>3.7 Storage stability - (IIB3.7/Pt. I-B3.7)</td><td>CIPAC MT 46.3
14 days at 54 °C</td><td>30% DEET
Batch 965</td><td>After 14 days at 54°C in glass bottle:
<table><tr><td></td><td>T0</td><td>14d 54°C</td></tr><tr><td>Appearance</td><td></td><td>As initial, no phase separation</td></tr><tr><td>Content of DEET</td><td>298 g/L</td><td>302 g/L</td></tr><tr><td></td><td>Variation</td><td>+1%</td></tr><tr><td>pH value</td><td>8.1</td><td>8.0</td></tr></table>
Biocidal product is stable 14 days at 54 °C in glass container.</td><td>Legay 2012</td></tr>
<tr><td>Effect of low temperature</td><td>CIPAC MT 39.3
7 days at 0°C</td><td>30% DEET
Batch 965</td><td>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”.</td><td>Legay 2012</td></tr>
<tr><td>Effects of light</td><td></td><td></td><td>Not relevant as the product is not in contact with light acceptable</td><td></td></tr>
<tr><td colspan="5">3.8 Technical characteristics (IIB3.8/Pt. I-B3.8)</td></tr>
<tr><td>Wettability</td><td></td><td></td><td>Data not required as the product is a ready to use spray</td><td></td></tr>
<tr><td>Persistent foaming</td><td></td><td></td><td>Data not required as the product is a ready to use spray</td><td></td></tr>
<tr><td>Suspensibility</td><td></td><td></td><td>Data not required as the product is a ready to use spray</td><td></td></tr>
<tr><td>Spontaneity of dispersion</td><td></td><td></td><td>Data not required as the product is a ready to use spray</td><td></td></tr>
<tr><td>Dilution stability</td><td></td><td></td><td>Data not required as the product is a ready to use spray</td><td></td></tr>
<tr><td>Dry sieve test</td><td></td><td></td><td>Data not required as the product is a ready to use spray</td><td></td></tr>
<tr><td>Wet sieve test</td><td></td><td></td><td>Data not required as the product is a ready to use spray</td><td></td></tr>
</table>

Subsection (Annex Point IIB. 3/TNsG)	Method	Purity/ Specification	Results	Reference
Dustiness			Data not required as the product is a ready to use spray	
Attrition/friability of granules; integrity of tablets			Data not required as the product is a ready to use spray	
Emulsifiability / Emulsion stability / Re-emulsifiability			Data not required as the product is a ready to use spray	
Stability of dilute emulsions			Data not required as the product is a ready to use spray	
Flowability			Data not required as the product is a ready to use spray	
Pourability (including rinsed residue)			Data not required as the product is a ready to use spray	
3.9 Compatibility with other products (IIB3.9/Pt. I-B3.9)			Data not required as the product is a ready to use spray	
3.10 Surface tension (Pt. I-B3.10)	EC A5 OECD 115	30% DEET Batch 965	32.0 mN/m Biocidal product is surface active	Legay 2012
3.11 Viscosity (Pt. I-B3.10)	OECD 114	30% DEET Batch 965	< 5 mP a.s at 20.0°C	Legay 2012
3.12 Particle size distribution (Pt. I-B3.11)	CIPAC MT 187	30% DEET Batch 965 150 mL PET-bottles with PP/POM spray head	Particle size distribution of droplet when sprayed: 1 % of particles < 9.4 µm 10 % of particles < 34 µm 50 % of particles < 66 µm 90 % of particles < 104 µm	Biogenus study Mo4415
Other			Volume delivered by pump is 0.12 mL/ spray	Legay 2013

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

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

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

Validation data

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

The provided method is acceptable for the product RAMC.

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

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

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

Considering the use pattern of the biocidal product REPULSIF ANTI-MOUSTIQUES CORPOREL and the properties of DEET, the contamination of air compartment during application is not significant and no method of analysis in air is required.
According to Assessment report N,N- diethyl-meta-toluamide (DEET) Product-type 19 (repellents and attractants), 2010/03/11, analytical methods for residues in food/feed of plant and animal origins are not required as the use pattern of DEET will not result in any contact with food or feeding stuffs.

2.4 Risk assessment for Physico-chemical properties

REPULSIF ANTI-MOUSTIQUES CORPOREL is a ready-to-use TP 19. It is under the form of limpid liquid, not auto-flammable (up to 360°C), not explosive and does not have oxidizing properties but classified as flammable R10 according to regulation 99/45/EC and flam. Liq. 3 / H226 according to CLP regulation.
The product is stable 14 days at 54°C. a shelf life of 2 years is granted. As biocidal product is suseptible to be used in tropical countries, the following recommandation is added : do not store more than 2 weeks at 54°C.

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

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

Risk mitigation measures linked to assessment of physico-chemical properties

The product must be shaken before use

Do not store more than 2 weeks at 54°C

Required information linked to assessment of physico-chemical properties

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

2.5 Effectiveness against target organisms

2.5.1 Function

Main Group 03: Pest Control
Product Type 19: Repellents and attractants

REPULSIF ANTI-MOUSTIQUES CORPOREL 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.

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

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

<u>The application rates recommended by the applicant are the following:</u>
The number of spraying recommended is ranged from 4 to 6 sprays per forearm (average 600 cm²). The recommended application rates are 1.1 mg / cm² on skin and 1.67 mg / cm² on fabric.

It has to be noted that the tested arthropods are not all present in France and in the overseas territories but RMS consider than they are representative of their genus:
- *Aedes aegypti (Stegomya aegypti):* this species occurs in overseas territories of France (Reunion, Mayotte, Guadeloupe, Martinique islands and in Guyane). This species is a vector of Dengue and Chikungunya in the French Antilles.
- *Anopheles gambiae:* this species is a vector of malaria (paludism) in tropical areas.
- *Culex pipiens:* mosquitoes of the Culex genus are the most present in France.
- *Aedes albopictus:* this species occurs in the Indian Ocean, including Reunion island, and Southern Europe, including France. This species is a vector of Dengue and Chikungunya.

2.5.3 Effects on target organisms and efficacy

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

The applicant submitted following studies:

For the use against mosquitoes:

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

The duration of efficacy of the product REPULSIF ANTI-MOUSTIQUES CORPOREL was tested under laboratory conditions against 4 mosquito species: *Aedes aegypti, Anopheles gambiae, Aedes albopictus* and *Culex pipiens*.
The product was sprayed on the forearm and spread, from the wrist to the elbow, for an average surface area of 600 cm².
The trial began 30 minutes after the product had been applied. The control forearm was inserted into the cage, and after validation of this control (10 landings in 30 seconds or 5 bites), the treated forearm was inserted into the cage for 3 minutes (exposure time).
The same procedure was repeated every hour until 9 hours or inefficacy. The time of protection is up to 8 hours for the 4 tested species at the application rate of 1.67 mg / cm² product (0.5 mg / cm² DEET). Even if this application rate demonstrated the efficacy of the product, this application rate is not claimed by the applicant and will not be taken into account regarding this product.

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

The duration of efficacy of the product REPULSIF ANTI-MOUSTIQUES CORPOREL was tested under laboratory conditions against 4 mosquito species: *Aedes aegypti, Anopheles gambiae, Aedes albopictus* and *Culex pipiens*.
The product was sprayed on the forearm and spread, from the wrist to the elbow, for an average surface area of 600 cm².
The trial began 30 minutes after the product had been applied. The control forearm was inserted into the cage, and after validation of this control (10 landings in 30 seconds or 5 bites), the treated forearm was inserted into the cage for 3 minutes (exposure time).
The same procedure was repeated every hour until 9 hours or inefficacy. The time of protection is up to 4 hours for the 4 tested species at the application rate of 1.1 mg / cm² product (0.33 mg / cm² DEET).

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

The duration of efficacy of the product REPULSIF ANTI-MOUSTIQUES CORPOREL was tested under laboratory conditions against 4 mosquito species: *Aedes aegypti, Anopheles gambiae, Aedes albopictus* and *Culex pipiens*.
The product was sprayed on a cotton fabric used to cover the forearm, from the wrist to the elbow.
The trial began 30 minutes after the product had been applied. The control forearm, with untreated fabric, was inserted into the cage, and after validation of this control (10 landings in 30 seconds or 5 bites), the treated forearm was inserted into the cage for 3 minutes (exposure time).
The same procedure was repeated every hour until 9 hours or inefficacy. The time of protection is up to 8 hours for the 4 tested species at the application rate of 1.67 mg / cm² product on cotton fabric (0.5 mg / cm² DEET).

All efficacy studies are presented in annex 3.

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

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

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

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

To confirm this approach, FR CA has launched an European consultation. Most of the consulted Member States think that field tests are not mandatory. Given the available literature on the active substance DEET and for reasons of standardization of testing and ethics, new field trials would not be justified. Based on the results of this consultation, FR CA agrees to consider the data presented as sufficient to demonstrate the efficacy of the product REPULSIF ANTI-MOUSTIQUES CORPOREL.

2.5.4 Mode of action including time delay

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

Two main hypotheses are presented in available bibliography.

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

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

By using toxicological, biochemical and electrophysiological techniques, Corbel *et al*.[2] show that DEET is not simply a behaviour-modifying chemical but that it also inhibits cholinesterase activity, in both insect and mammalian neuronal preparations. DEET is commonly used in combination with insecticides and Corbel *et al.* show that DEET has the capacity to strengthen the toxicity of carbamates, a class of insecticides known to block acetylcholinesterase.

In 2011, Lavialle-Defaix *et al*.[3] developed a new biological model based on mosquito neurons isolated from adults *Anopheles gambiae* heads and revealed that AgNav channeland AChE enzymes which are targeted by insecticide and/or repellent were sensitive to the pyrethroid permethrin and to the repellent DEET, respectively.

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

In 2003, Xue *et al.*[4] wrote an article on a laboratory evaluation of toxicity of sixteen commercial insect repellents (6 botanical and l0 synthetic organic products) in aerosol sprays to adult mosquitoes. These repellents (including 8 insect repellent products containing 6.65 to 38% of DEET) were evaluated in the laboratory for adult knockdown (KD) and mortality of laboratory-reared female *Aedes aegypti*, *Aedes*

[2] V.Corbel, M. Stankiewicz, C. Pennetier, D. Fournier, J. Stojan, E. Girard, M. Dimitrov, J. Molgó, J-M. Hougard, B. Lapied, *Evidence for inhibition of cholinesterases in insect and mammalian nervous systems by the insect repellent deet*, *BMC Biology* 2009, **7**:47.

[3] C. Lavialle-Defaix, V.Apaire-Marchais, C. Legros, C. Pennetier, A. Mohamed, P. Licznar, V. Corbel, B.Lapied, *Anopheles gambiae mosquito isolated neurons: A new biological model for optimizing insecticide/repellent efficacy*, Journal of Neuroscience Methods, 200 (2011) 68-73

[4] R. D. Xue, A. Ali, D. R. Barnard, *Laboratory evaluation of toxicity of sixteen insect repellents in aerosol sprays to adult mosquitoes*, Journal of the American Mosquito Control Association, 19(3) :271-274, 2003

albopictus, and *Anopheles quadrimaculatus*. All tested formulations except 2 botanical repellent products caused 100% 24-h mortality of *Ae. aegypti* and all but 1 caused 100% 24-h mortality of *Ae. albopictus* and *An. quadrimaculatus*.
In 2006, Licciardi *et al.*[5] evaluated the knock-down, mortality and ' irritancy ' effects of three synthetic repellents (DEET, IR3535 and KBR 3023) on *Aedes aegypti* (L) (Diptera: Culicidae) in the laboratory in the absence of animal bait. Filter paper tests were carried out to assess the knock-down effect (KDt_{50} and KDt_{95}) and mortality (LC_{50} and LC_{95}) induced by each repellent. Irritancy tests were carried out to compare the flight response (time to first take-off, or FT) to increasing concentrations of repellents (2 – 7%) and at five distances from the treated surface (0 – 40 mm). DEET had an insecticidal effect at 7% (KDt_{50} = 9.7 min; CL_{50} = 1165 mg/m^2). Relative to an untreated control, DEET was an irritant at 2% (RI = 12.3).

2.5.5 Occurrence of resistance – resistance management / Unacceptable Effect

Resistance to DEET is still uncertain as only one study on this subject has been identified yet.
In 2010, Stanczyk *et al*[6]*.* wrote an article on some mosquitoes' insensitivity to DEET behaviour. Studies were performed in order to show insensitive characters. Over a group of *Aedes aegypti* females, 13% were identified as insensitive to DEET by using the "arm-in-cage test". The breeding of these insensitive females with males which sensitivity is unknown led to an increase of insensitive individuals along generations. Second generation was composed of more than 50% of insensitive individuals.
This test shows that there might be a resistance effect against DEET and that the insensitivity to DEET would be a heritable trait. The way how resistance works is not clearly identified.
Two hypotheses are presented. There could be a mutation of DEET-sensitive ORNs (Olfactory Receptor Neurons) so that receptors could no longer recognize DEET. Another hypothesis is a mutation in the gene encoding for an odorant-binding protein in charge of transporting DEET to receptors. This mutation would lead to a smaller amount of DEET transported to ORNs and thus a lower sensitive response to this substance (see Document IV Stanczyk *et al*., 2010).

2.5.6 Evaluation of the Label Claims

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

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

The application rates validated are the following:
Mosquitoes (*Aedes*, *Anopheles* and *Culex genus*): 1.1 mg/cm² of skin and 1.67 mg/cm² of fabric

2.5.7 Conclusion of the efficacy assessment

The product REPULSIF ANTI-MOUSTIQUES CORPOREL has shown a sufficient efficacy for the uses proposed in annex 0b. Nevertheless, a monitoring of the resistance phenomenon must be put in place. The

[5] S. Licciardi, J.P. Herve, F. Darriet, J.-M. Hougard, V. Corbel,, *Lethal and behavioural effects of three synthetic repellents (DEET, IR3535 and KBR3023) on Aedes aegypti mosquitoes in laboratory assays*, Medical and Veterinary Entomology, 20 :288-293, 2006
[6] Stanczyk, N. M., et al. (2010). "Behavioral insensitivity to DEET in *Aedes aegypti* is a genetically determined trait residing in changes in sensillum function." Proceedings of the National Academy of Sciences of the United States of America **107**(19): 8575-8580.

collected information must be sent every 5 years to Anses within the framework of a post-authorisation monitoring.

Conditions of use linked to efficacy assessment

- Respect the recommended application doses.
- The users should report straightforward to the registration holder any alarming signals which could be assumed to be resistance development.
- The label has to respect the recommended conditions of use and the biocidal products labelling guide[7].
- The use of the product with other biocidal products or sunscreen products is not recommended.
- Protection time can be lowered by sweating, water wash off, rubbing, high temperature (>30°C), wind velocity, etc.

Required information linked to efficacy assessment

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

2.6 Description of the intended use(s)

The validated application rates and intended uses are the following:

MG/PT	Field of uses envisaged	Likely doses at which product will be used
Main Group 03; Pest Control PT19: Repellents and attractants	Repellent against mosquitoes *Aedes aegypti, Anopheles gambiae, Aedes albopictus and Culex pipiens*	1.67 mg/cm^2 on fabric (cotton), protection time up to 8 hours 1.1 mg/cm² on skin, protection time up to 4 hours

Method of application

The product REPULSIF ANTI-MOUSTIQUES CORPOREL is an insect repellent lotion containing 30 % DEET as active substance and intended to be applied on human skin and on fabric (cotton) to repel mosquitoes.
The product is sprayed on the exposed area of the skin (*i.e.* face, neck, arms, hands and legs) or or sprayed on clothes.
Since the product is formulated as a ready-for-use product, no dilution or other preparation is necessary.

[7] Guide à l'intention des responsables de la mise sur le marché des produits biocides. Lignes directrices sur l'étiquetage des produits biocides mis sur le marché. Version du 28 août 2007.

2.7 Risk assessment for human health

2.7.1 Hazard potential

2.7.1.1 Toxicology of the active substance

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

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

The absorption, distribution, metabolism, and excretion studies (ADME) show that, more than 80% of DEET given orally to rats is absorbed and excreted in the urine. DEET showed no evidence for accumulation. When applied dermally to rats 74-78% is absorbed and excreted in the urine. The dermal absorption of DEET occurred at a slower rate than oral absorption (peak plasma concentration ≥4 hr vs.<1 hr, respectively). Seventy-four to ninety-one percent of the administered radioactivity was excreted via urine and about 3-7% was excreted via the faeces. DEET was metabolised completely in all oral and dermal treatment groups with little or no parent compound excreted in the urine. DEET is extensively metabolized to 2 major metabolites, m-[(N,N-diethylamino)carbonyl] benzoic acid and m-[(ethylamino)carbonyl] benzoic acid. DEET is absorbed slowly (peak plasma concentration ≥8 hr), metabolised completely, and excreted rapidly when applied to human skin. Less than 20% (when corrected for total recovery) of a dermally applied dose of DEET, either as a 15% (w/w) solution in ethanol or as the undiluted technical grade material, is absorbed through the skin during an 8-hour exposure period. Plasma level studies were performed in rats (oral and dermal exposure) and in dogs (oral exposure) to compare plasma levels and area under the curve (AUC) at NOAEL levels with human plasma levels and AUC (dermal exposure).

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

2.7.1.2 Toxicology of the substance(s) of concern

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

2.7.1.3 Toxicology of the biocidal product

The toxicology of the biocidal product was examined appropriately according to standard requirements.
The basis for the health assessment of the biocidal product is laid out in Annex 5 "Toxicology – biocidal product"

2.7.1.3.1 Percutaneous absorption

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

2.7.1.3.2 Acute toxicity

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

No mortality was observed in the dermal acute toxicity study (LD_{50} > 2000 mg/kg bw). Neither cutaneous reactions nor systemic clinical signs related to the administration of RAMC were observed. The body weight evolution of the animals remained normal throughout the study. The macroscopical examination of the animals at the end of the study did not reveal treatment-related changes.

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

Route	Species Strain Sex No/group	Dose levels Duration of exposure	Value LD_{50}/LC_{50}	Remarks
Oral	Rat Sprague Dawley (SPF Caw) 6 female/group	Single dose at 2000 mg/kg bw Post exposure period: 14 days	LD_{50}>2000 mg/kg bw Clinical signs noted during the first minutes of the test: decrease in spontaneous activity (4/6), and piloerection (3/6) No effect on body weight No macroscopical changes	
Dermal	Rat Sprague Dawley 5/sex/group	Single dose of 2000 mg/kg bw, applied to 10% body surface for 24 hours	LD_{50}>2000 mg/kg bw No clinical signs No cutaneous reactions No effect on body weight No macroscopical changes	

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

2.7.1.3.3 Irritation and corrosivity

- Irritation and corrosivity

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

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

Species Strain	Average score 24, 48, 72h	Reversibility?	Result

No/group	erythema	oedema		
Rabbit Albino New Zealand 3 females	0.00	0.00	No (no cutaneous reactions)	Not irritating to the skin

Species Strain No/group	Average score				Reversibility?	Result
	cornea	iris	Conjunctiva			
			Redness	Chemosis		
Rabbit Albino New Zealand 3 males	1.3 2.0 2.0	0.3 1.0 1.0	1.7 2.3 2.0	1.3 1.3 2.0	No. Moderate corneal opacity, noted 24 hours after the test item instillation remaining on the last day of the test (day 21: same intensity) in one animal	R41 Cat.1, H318.

2.7.1.3.4 Sensitisation

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

Species Strain Sex	Method	Number of animals sensitized/total number of animals	Result
Guinea pigs Albino Dunkin-Hartley Females	GPMT assay	Controls: 0/5 females Test group: 0/10 females	Not sensitising

2.7.1.3.5 Other studies

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

2.7.2 Human exposure assessment

RAMC is an insect repellent containing 30% DEET as active substance and intended to be applied on human skin or on clothes to repel mosquitoes. Since the product is formulated as a ready-for-use product, no dilution or other preparation is necessary.
Applicant required authorisation for consumer adults and children aged 6 years and over.

MG/PT	Field of uses envisaged	Likely concentrations at which a.s. will be used
Main Group 03; Pest Control PT19: Repellents and attractants	Professional uses	
	No	Not relevant
	Non-professional uses	
	Repellent for use by consumers (non-professional users/adults and children older than 6 years, dermal application) against mosquitoes' attacks	30% (w/w)

Method of application:

RAMC is intended to be applied by spraying on human skin or clothes to repel mosquitoes.
The product is formulated as a ready-to-use product, no dilution or other preparation is necessary.

RAMC is packaged in 80 mL, 100 mL or 150 mL bottles for use by consumers.
During one spray, 120 µL of product with a density of 0.95 were released.

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

Inhalation exposure:

RAMC will be applied by spraying. In this context an exposure by inhalation could be considered. However, the aerosol droplets generated by RAMC were assessed in a study. A mass median aerodynamic diameter (MMAD) of 66 µm was measured and only 1% of particles was < 9.4 µm.
RAMC is not expected to generate particles which are deposited in tracheobronchial and alveolar regions therefore the respirable fraction could be considered as negligible.

Although this dose was not considered as respirable, it could be swallowed after reflex of the body to remove product from the body by natural clearance (coughing, sneezing etc.).

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

Oral exposure:

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

Oral exposure to RAMC, especially by hand-to-mouth transfer, is not expected to be a significant and regular route of exposure. Moreover the product RAMC contains the active substance DEET and also a co-formulant (denatonium benzoate), which are both known to act as strong deterrents for ingestion.
Hand-to-mouth transfer scenario concerns mainly the infant between 3 months and 3 years.
However, adults and children aged 6 years and over may be incidentally exposed orally to the product. In this context, a reverse scenario calculation was included to show the importance of deterrents for ingestion in the product. This scenario was assessed as an acute exposure.

Dermal exposure:

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

Exposure path	Industrial use	Professional use	General public	*via* the environment
Inhalation	Not relevant	Not relevant	negligible	Not relevant
Dermal	Not relevant	Not relevant	yes	Not relevant
Oral	Not relevant	Not relevant	yes	Not relevant

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

2.7.2.2.1 Exposure of professional users

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

2.7.2.2.2 Exposure of non-professional users

For the inhalation exposure, as quoted above, considering the aerosol droplet diameter, the amount of substance could not be respirable but swallowed.
In a worst case, it was considered that all the amount of substance is swallowed without taking into account the respirable fraction. An absorption of 100% is used for oral route.

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

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

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

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

$$ID = \frac{(AR_p \times C_{DEET} \times BS \times DA \times N)}{100 \times 100 \times BW}$$

where:
ID Internal dose (mg/kg b.w./day)
AR_p Average dose of product applied on skin (mg/cm^2)
C_{DEET} Average concentration of substance in product (%)
BS Body surface exposed to the product (cm^2)

DA Dermal absorption (%)
N Number of product application per day (/day)
BW Body weight (kg)

This equation can be applied to male and female adults and to children.
AR_p, $C_{DEET,}$ Dermal absorption and N remain the same, body parameters (such as body surface exposed to the product and body weight) vary according to gender and to age range.

The body parameters are issued from RIVM. The data for range 9-14 years cover a child of 11 years, and the data for range 3-9 years cover a child of 6 years.
The product is not intended to be applied on the total body surface but on the following body segments which correspond to uncovered parts: **head + ¾ arms + hands + ½ legs.** When RAMC is applied on clothes, the following body segments which correspond to dressed parts: **trunk + ¼ arms + ½ legs** . No protection factor is taken into account

Summary of parameters for RAMC application

Table: Parameters for the calculation of consumer exposure to RAMC

Parameter	Value	Source
Average dose of product applied on skin (mg/cm^2)	1.1	Applicant data
Average concentration of substance in product	30% w/w	Applicant data
Body surface exposed to the product (cm^2)	See Table below	RIVM General Fact Sheet
Dermal absorption (%)	20	DEET Assessment Report
Number of product applications per day (/day)	1	Applicant data
Body weight (%)	See Table below	RIVM General Fact Sheet

Table: results of exposure by dermal route after application of **RAMC** at 1.1 mg/cm^2 (application on skin)

	BS Body surface area cm^2 (head + 3/4 arm + hands + 1/2 legs)	**BW Body weight (kg)**	**Mass of applied product (mg)**	**C_{DEET} Active substance concentration (%)**	**Mass of applied active substance (mg)**	**Dermal absorption (%)**	**Mass of absorbed active substance (mg)**	**ID Active substance per kg mg/kg**
Man	7215	74	7936.5	30%	2381.0	20%	476.2	6.4
Woman	6451	61	7096.1	30%	2128.8	20%	425.8	7.0
Child 3-9 years	3040	16.3	3344.0	30%	1003.2	20%	200.6	12.3
Child 9-14 years	5361	39.3	5897.1	30%	1769.1	20%	353.8	9.0

Table: results of exposure by dermal route after application of **RAMC** at 1.67 mg/cm^2 (application on clothes)

	Body surface area cm^2 (trunk + 1/4 arm + 1/2 legs) BS	**Body weight (kg) BW**	**Mass of applied product (mg)**	**Active substance concentration (%) C_{DEET}**	**Mass of applied active substance (mg)**	**Dermal absorption (%)**	**Mass of absorbed active substance (mg)**	**Active substance per kg mg/kg ID**
Man	10643	74	17774.6	30	5332.4	20	1066.5	14.4
Woman	9190	61	15346.6	30	4604.0	20	920.8	15.1
Child 3-9 years	3547	16.3	5923.1	30	1776.9	20	355.4	21.8
Child 9-14 years	6763	39.3	11294.0	30	3388.2	20	677.6	17.2

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

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

Hand to mouth transfer

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

The hand surface area to put in the mouth to reach the AEL short-term has been determined by a reverse scenario.
The following parameters were taken into account in the calculations:

- Quantity of RAMC applied to the skin: 1.1 mg/cm^2;
- Concentration of DEET in RAMC: 30%;
- Hand surface area; this value depends on the type of population (RIVM).
- Body weight; this value depends on the type of population (RIVM).

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

Based on the short-term AEL of 0.75 mg/kg bw/day, the lowest percentage of hand surface to put in the mouth to reach the AEL is 34% (woman) or 36% (man) of the surface of one hand of an adult. For children, the lowest percentage of hand surface to put in the mouth to reach the AEL is 19% (child 6-9 years old) or 24% (child 9-14 years old) of the surface of one hand.

Chewing treated clothes (infants/children)

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

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

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

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

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

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

2.7.2.4 Indirect exposure via residues in food

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

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

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

REPUSIF ANT-MOUSTIQUES CORPOREL									
TP19									
PB-12-00204									
SPRING									
Product application rate (mg product/cm²) (effective)	1,1								
Concentration (a.s in % w/w in the product)	30								
Applicated active substance (mg a.s/cm²) (effective)	0,330								
age	≤ 4.5 months	≤ 7.5 months	≤ 13.5 months	≤ 1.5 years	≤ 4.5 years	≤ 6.5 years	≤ 12.5 years	Adult (man)	Adult (woman)
hands surface (cm²) (up+down)	176	207	248	247	390	463	747	936	823
intended number of application	not supported	not supported	not supported	not supported	not supported	not assessed : first exposure not acceptable	not assessed : first exposure not acceptable	1	
factor for the whole hand = 1 or only the palm = 0.5								0,5	0,5
exposure per application (transfered a.s in mg)								154,4	135,8
transfer factor (hand to food) in %								100	
transfer factor (food to mouth) in %								100	
ingested a.s in mg and per application								154,4	135,8
Body weight in kg								74	61
ARfD (mg a.s/kg b.w./day)								0,75	
Exposure per application in mg a.s/kg b.w./day								2,1	2,2
Proposed restriction : handwash after use (i.e rinsing factor)								3	
% of ARfD (per application)								278	297
% of ARfD (per application) including hand washing								93	99
Exposure (in %) according to proposed statements proposed on the label : - no application on children's hand - washing hands for adults after each application								93	99

Comment : this calculation include a dilution factor of "3" following a washing hand preconised as a restriction of use to be realized after application and before eating foods. This default value was collected from the ConsExpo model[8]. This dilution factor is not deemed to be an overestimation according to physico-chemical properties of the active substance with water :

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

Resulted acute exposure is slightly 100% for adults. This assessment includes several worst case estimations (transfer factor of 100% from hand to food and food to mouth) which in all likelihood are overestimations. It can be considered also that the smell and taste of the product can act as a self deterrent against repetitive ingestion.

After completing a comprehensive re-assessment of DEET, US-EPA also concluded that, as long as consumers follow label directions and take proper precautions, insect repellents containing DEET do not present a health concern. Human exposure is expected to be brief, and long-term exposure is not expected. Based on extensive toxicity testing, the Agency believes that the normal use of DEET does not present a health concern to the general population. EPA completed this review and issued its re-registration decision (called a RED) in 1998.[9]

U.S. EPA label requirements state that[10] :

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

[8] 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 and 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

[9] U.S. EPA (Environmental Protection Agency).Re-registration Eligibility Decision (RED) for the insect repellent DEET:
http://www.epa.gov/pesticides/factsheets/chemicals/deet.htm
http://www.epa.gov/oppsrrd1/REDs/0002red.pdf

[10] U.S. EPA (Environmental Protection Agency).Toxicity and Exposure Assessment for Children's Health, Diethyltoluamide (DEET), Chemical Summary Last revised 4/24/2007:
http://www.epa.gov/teach/chem_summ/DEET_summary.pdf

Consequently

Following assessment based on supported uses for the product REPULSIF ANTI MOUSTIQUES CORPOREL and EPA label requirements, the following restrictions of use are proposed:

- Do not applied near food
- Avoid palm hand contamination or DEET-contaminated hands should be washed carefully prior to eating.

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

2.7.2.5 Combined exposure

No combined exposure is assessed.

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

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

2.7.3 Risk assessment for human health

2.7.3.1 Risk for direct exposure

2.7.3.1.1 Professional users

Not applicable.

2.7.3.1.2 Non-professional users

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

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

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

	Systemic exposure active substance per kg mg/kg	**AEL (mg/kg/d)**	**% AEL (%)**
Man	6.4	8.2	78
Woman	7.0	8.2	85
Child 3-9 years	12.3	8.2	150
Child 9-14 years	9.0	8.2	110

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

	Systemic exposure active substance per kg mg/kg	**AEL (mg/kg/d)**	**% AEL (%)**
Man	14.4	8.2	176
Woman	15.1	8.2	184
Child 3-9 years	21.8	8.2	266
Child 9-14 years	17.2	8.2	210

An acceptable risk is identified for adults (men and women) when RAMC is applied on skin directly. However, the risk is unacceptable when RAMC is applied on clothes, considering a worst-case penetration factor from cloth of 100%.
In addition, the results demonstrate that the risk is unacceptable for children since the estimated systemic exposure for children aged 6 years or over is above the proposed systemic AEL of 8.2 mg/kg b.w./day.
Moreover, a reverse scenario has demonstrated that an adult can apply RAMC only once a day. Therefore, an adult will not be able to apply RAMC on another adult.

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

2.7.3.2 Risk for indirect exposure

Hand-to-mouth transfer

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

Chewing treated clothes (infants/children)

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

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

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

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

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

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

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

2.7.3.3 Risk for indirect exposure

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

2.7.3.4 Risk for consumers via residues in food

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

Based on proposed conditions of use from acceptable primary exposure and as long as consumers follow label directions detailed above and take proper precautions, acute exposure to residues in food resulting from the intended uses for REPULSIF ANTI MOUSTIQUES CORPOREL is unlikely to cause a significant dietary risk to the adults.

2.7.3.5 Conclusion of risks assessment for human health

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

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

Risk mitigation measures linked to risk assessment for human health

- Only use by adults
- Do not exceed one application per day
- Only applied on uncovered skin
- Do not put hands in mouth after application
- Keep out of the reach of children
- Do not spray directly in the face
- Wash the palm of hands after application
- Do not use the spray near food and surfaces that may come into contact with food or drink intended for human consumption.

2.8 Risk assessment for the environment

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

The summary of information about the active substance DEET is carried out with the data from the CAR of DEET supplied by the notifier McKenna, Long & Aldridge (Competent Authority Report According to Directive 98/8/EC, Active substance in Biocidal Products, N,N-diethyl-*m*-toluamide (DEET) CAS 134-62-3, Product Type 19 (Repellents), RMS Sweden, march 2010).

2.8.1.1 Degradation

2.8.1.1.1 Abiotic degradation

2.8.1.1.1.1 Hydrolysis in function of pH

According to the test OECD 111, DEET is considered stable to hydrolysis. It was concluded that the hydrolytic half-life (DT_{50}) was above one year at environmentally relevant temperature at pH 4, 7 and 9. The hydrolytic degradation is deemed negligible.

2.8.1.1.1.2 Photolysis in water

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

2.8.1.1.1.3 Photolysis in soil

Not relevant for DEET according to the active substance CAR.

2.8.1.1.1.4 Photodegradation in air

The photo-oxidative degradation of DEET in air was estimated by a structural activity relationship (QSAR) method using the Atmospheric Oxidation Program v1.91 (AOPWIN). The estimated half-live for the hydroxyl reactions in air is 0.63 days or 15.2 hours. DEET has a low volatility (Henry's law constant = $3.93 * 10^{-3}$ $Pa.m^3.mol^{-1}$) and emissions to the air compartment are expected be low. Thus, an extensive accumulation of DEET in air and long range transport is unlikely.

2.8.1.1.2 Biotic degradation

2.8.1.1.2.1 Aquatic compartment

- Ready biodegradation / inherent biodegradation

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

- Degradation in water/sediment system

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

2.8.1.1.2.2 Degradation in STP

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

2.8.1.1.2.3 Terrestrial compartment

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

2.8.1.2 Distribution

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

2.8.1.3 Accumulation

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

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

BCF_{fish} = 22 L/kg (according to TGDII Equation 74)
$BCF_{earthworm}$ = 63.1 L/kg (according to TGDIII 4.6)

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

2.8.1.4 Behaviour in air

The vapour pressure of DEET has been determined to be 0.23 Pa at 25°C. Furthermore, Henry's law constant for DEET has been calculated to 3.93 * 10^{-3} $Pa.m^3.mol^{-1}$ based on a water solubility of 11.2 g/L. In addition, DEET is expected to be quickly degraded by photo-oxidation, the atmospheric photochemical half-life was 15.2 hours (cf 2.8.1.1.1.4). Based on these data, DEET is not expected to volatilise or persist in air.

2.8.2 Effects on environmental organisms for active substance DEET

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

2.8.2.1 Aquatic compartment (including water, sediment and STP)

2.8.2.1.1 Aquatic organisms

Based on the results of acute toxicity studies, DEET is not very toxic to aquatic organisms. The EC/LC_{50} values for the tested organisms (*Oncorhynchus mykiss, Daphnia magna, and Pseudokirchneriella subcapitata)* are all in the same range (10-100 mg/L), although algae represented the most sensitive (ErC_{50} = 43 mg/L) of the three aquatic trophic levels tested. No long-term tests have been performed.

Test item	Species	Guideline	Endpoints	Toxicity (mg as/L)	Reference
Fish					

DEET	*Onchorhynchus mykiss*	OECD 203 Static conditions	LC_{50} – 96h	97[1]	CAR DEET III-A 7.4.1.(1)
Invertebrates					
DEET	*Daphnia magna*	U.S. EPA Ecol;Res; Series 660/375009; Standard methods for the Examination of Water and Wastewater (1980) Static conditions	EC_{50} – 51h	75[1]	CAR DEET III-A 7.4.1.2(1)
Algae					
DEET	*Pseudokirchneriella subcapitata*	OECD 201 Static conditions	ErC_{50} – 96h EbC_{50} – 72h	43[1] 17	CAR DEET III-A 7.4.1.3(1)

[1] Measured concentrations

Additional endpoints: Not relevant

Justification of $PNEC_{water}$

According to the TGD for Risk Assessment (2003), if only short-term toxicity data are available, an assessment factor of 1000 will be applied on the lowest $L(E)C_{50}$ of the relevant available toxicity data. The $PNEC_{water}$ is derived from the ErC_{50} values (43 mg a.s./L) for *Pseudokirchneriella subcapitata* exposed to the active substance divided by an assessment factor of 1000. Therefore,

$PNEC_{water}$ = 0.043 mg a.s./L

2.8.2.1.2 Sediment dwelling organisms

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

$PNEC_{sedEP}$ = 0.0741 mg/kg wet weight sediment

2.8.2.1.3 STP micro-organisms

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

Test item	Guideline/Test method	Species/inoculums	Endpoint / type of test	Exposure design duration	Result [mg a.s./L]			reference
					EC_{20}	EC_{50}	EC_{80}	
DEET	OECD 209; EEC Method C11	Activated sludge	Inhibition of oxygen consumption	3h	N.D.[1]	>1000[2]	N.D.	CAR DEET A7.4.1.4

[1] at 300 mg/l there was 13.8 % stimulation

[2] at 1000 mg/l there was 26.8% inhibition

Additional endpoints: not relevant

Justification of $PNEC_{microorganisms}$

According to TGD for Risk Assessment (2003), considering the EC_{50} toxicity data, an assessment factor of 100 will be applied to derive the PNEC from the EC_{50} value for the activated sludge exposed to the product. Therefore,

$PNEC_{STP\ microorganisms}$ = 10 mg/L

2.8.2.2 Atmosphere

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

2.8.2.3 Terrestrial compartment

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

$PNEC_{soilEP}$ = 0.0379 mg/kg wet weight soil

2.8.2.4 Summary of PNECs of the active substance DEET

Compartment	Species	Endpoint (mg DEET/L)	Safety factor	PNEC
(*Fresh*) Water	*Pseudokirchneriella subcapitata*	ErC_{50}=43	1000	0.043 mg /L
Sediment	EPM	-	-	0.0741 mg /kg ww
Microorganisms (STP)	Activated sludge	EC_{50}>1000	100	10 mg /L
Soil	EPM	-	-	0.0379 mg /kg ww

2.8.2.5 Non compartment specific effect relevant to the food chain

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

2.8.2.6 PBT Assessment

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

2.8.3 Effects on environmental organisms for biocidal product

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

The applicant provides ecotoxicological data on algae which is the most sensitive species for the active substance DEET, exposed to the biocidal product RÉPULSIF ANTI-MOUSTIQUES CORPOREL. All the other available data are obtained from the active substance DEET (McKenna, Long & Aldridge, Competent Authority Report According to Directive 98/8/EC, Active substance in Biocidal Products, N,N-diethyl-*m*-toluamide (DEET) CAS 134-62-3, Product Type 19 (Repellents), RMS Sweden, march 2010).

A bittering agent is used in the biocidal product. This substance is classified as “Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment” in the frame of the Directive 91/414/EEC. Nevertheless at the concentration used in RÉPULSIF ANTI-MOUSTIQUES CORPOREL, the substance does not contribute to the classification of the biocidal product.

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

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

2.8.3.1 Aquatic compartment (including water, sediment and STP)

2.8.3.1.1 Aquatic organisms

The product RÉPULSIF ANTI-MOUSTIQUES CORPOREL is not toxic to algae (ErC_{50} >100 mg/L).

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

Test item	Species	Guideline	Endpoints	Toxicity (mg product/ L)	Reference
Algae					
SUBITO RÉPULSIF ANTI-MOUSTIQUES ADULTE SUBITO	*Pseudokirchneriella subcapitata*	OECD 201 Static conditions	ErC_{50} – 72h EbC_{50} – 72h	>100[1] >100[1]	III-B 7.2.2.2

[1] based on nominal concentration and checked by analytical analysis

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

Title	Growth inhibition test on *Pseudokirchneriella subcapitata* with RÉPULSIF ANTI-MOUSTIQUES CORPOREL SUBITO / BEAST-OFF	
Author, date, N° reference	Martin C., 2013, Algae *Pseudokirchneriella subcapitata*, 72h-growth inhibition test performed on the test item "SUBITO REPULSIF MOUSTIQUES ADULTE", according to the OECD 201 guideline, Limit test, FCBA, Report No.402/12/1048F/g-e.	
GLP	Yes	
Deviation	No	
Validity/ Acceptability	- In the controls, cell density increased by an average factor of > 16 within three days (161). - The mean coefficient of variation for section-by-section specific growth rates in the control cultures did not exceed 35% (15.3%). - The coefficient of variation of average specific growth rates during the whole test period in replicate control cultures did not exceed 7% (0.85%) - the pH did not change by more than 1.5 units (0.3).	
Method	Guideline	OECD Guideline No.201, 2006; Annex 5 corrected 28/07/2011.
	Organisms	*Pseudokirchneriella subcapitata*
	Test item	Trade name: SUBITO REPULSIF MOUSTIQUES ADULTE (Batch number 965) Chemical name: N,N-diethyl-m-toluamide (DEET) CAS No 134-62-3
	Treatments	- 6 replicates of the exposed algae to 100 mg SUBITO REPULSIF MOUSTIQUES ADULTE /L (limit test due to result of preliminary test), - 6 replicates of the control.
	Exposure	250 mL Erlenmeyer flasks, containing 100 mL of test solution placed in incubator where algal cells were kept in suspension by continuous shaking, under continuous light for 72 hours
Results	Analysis	The algae concentrations have been measured during the test at 24, 48 and 72 hours with a particle counter or under a microscope with a Malassez counting cell (in order to distinguish test substance particles from *Pseudokirchneriella subcapitata* alga cells). In order to verify the initial concentrations and maintenance of the exposure concentrations during the ecotoxicological testing, chemical analyses of test item in algae medium solutions have been performed according to the following protocol: - at the beginning of the test (T = 0h) for the Control (*i.e.* algae medium), and for the six replicates of the test concentration (100 mg/L); - at the end of the test (T = 72h), for the Control and for the six replicates of the test concentration (100 mg/L). A total of 14 analyses have been carried out.
	Lethal effects	Not detected. No inhibition of growth rate was observed after 72 hours of exposure. The inhibition of average specific growth rate was -1.21%, indicating thus an increase compared to the control. The inhibition of yield was -6.40%, indicating also an increase compared to the control.
	Sub-lethal effects	The EC_{50} for growth rate reduction (E_rC_{50}: 0-72h) and the EC_{50} for yield inhibition (E_yC_{50}: 0-72h) were beyond the range tested, *i.e.* exceeded 100 mg test item/L.
Conclusion	Endpoints	**ErC_{50} and E_yC_{50}: > 100 mg SUBITO REPULSIF MOUSTIQUES ADULTE /L (>30 mg DEET/L).**
Reliability	1	This study is considered as acceptable by RMS

index		

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

2.8.3.1.2 Sediment dwelling organisms

Refer to section 2.8.2.1.2

2.8.3.1.3 STP micro-organisms

Refer to section 2.8.2.1.3

2.8.3.2 Atmosphere

See section 2.8.2.2

2.8.3.3 Terrestrial compartment

See section 2.8.2.3

2.8.3.4 Non compartment specific effect relevant to the food chain

See section 2.8.2.5

2.8.3.5 Summary of PNECs

Refer to section 2.8.2.4

2.8.4 Environmental exposure assessment

2.8.4.1 Assessment of exposure to the environment

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

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

The direct outdoor emissions to surface water *via* some direct flow of DEET from skin during direct contact with water while swimming can be assumed. This route of entry to the aquatic compartment must be assessed.For both routes (direct and indirect), sediment compartment is not considered as relevant for DEET due to its low adsoprtion potential (log Pow<3).

In the following sections, PEC values for indirect exposure are derived by using the Emission Scenario Document (ESD) for PT01 (Human hygiene products)[11] and equations from the TGD Part II (since there is no specific ESD developed for PT 19). These calculations are based on maximum amount of product consumed by individual per day as described in the intended uses. The PEC values for groundwater are calculated using FOCUS-PEARL modelling performed on the submitted information on the EU tonnage of DEET as described in the CAR for the active substance.

Direct releases to surface water are estimated according to the DE proposed "swimming scenario" (Klein, 2011[12]) with some modifications in order to be conservative enough.

2.8.4.2 Environmental emission calculations and PEC derivations

2.8.4.2.1 Indirect emission through the STP ("Scenario ESD PT01")

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

- Skin: An application on skin only, at the dose rate of 1.1 mg product.cm^{-2} of skin considering a treated body surface of 7 215 cm^2 according to the human exposure section, corresponding to 7.94 g product per application.

- Clothes: An application on clothes only considering that the quantity applied on clothes represents 25% of the total quantity applied by one person, corresponding to 2.65 g product per application (= 7.94 x (25/75)). No adsorption by fabric is taken into account in order to extrapolate the calculation to all kind of materials (Fwater=1).

- Skin and clothes: A simultaneous application on skin and clothes considering both application types cumulated

Consumption based approach for PEC STP, surface water, soil

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

$$\mathbf{Elocal_{water} = Nlocal * Finh * F_{water} * Qform_{inh} * Cform_{weight} * Fpenetr * 10^{-6}}$$

Where

Nlocal	Number of inhabitants feeding one STP (default ESD PT01 = 10 000)
Finh	Fraction of inhabitants using an insect repellent (CAR value = 0.37)
$F_{water\ skin}$	Fraction released to wastewater during skin cleaning (adapted CAR value for DEET applied on skin only = 0.865)
$F_{water\ clothes}$	Fraction released to wastewater during clothes washing (adapted CAR value for DEET applied on clothes only = 0.95)
$Qform_{inh\ skin}$	Consumption per inhabitant per day (g.day^{-1}; Nappl* $Qform_{appl\ skin}$*BS)
$Qform_{inh\ clothes}$	Consumption per inhabitant per day (g.day^{-1}; Nappl*2.65 g product)
$Qform_{inh\ skin\ and\ clothes}$	Consumption per inhabitant per day (g.day^{-1}; $Qform_{inh\ skin}$ + $Qform_{inh\ clothes}$
$Cform_{weight}$	Concentration of the active substance in the product (specific value for RÉPULSIF ANTI-MOUSTIQUES CORPOREL = 300 g.kg^{-1})

[11] Environmental Emission Scenarios for biocides used as human hygiene biocidal products (Product type 1). European Commission DG ENV/RIVM. January 2004.
[12] Klein M. (2011). Proposals for standard scenarios and parameter setting of the FOCUS groundwater scenarios when used in biocide exposure assessments. FKZ: 360 04 035, pp 1-40

Fpenetr	Market share for DEET-containing repellent products (CAR value for DEET based products = 0.28)
Nappl	Number of applications (specific value for RÉPULSIF ANTI-MOUSTIQUES CORPOREL = 1 day^{-1})
$Qform_{appl\ skin}$	Consumption per application (specific value for RÉPULSIF ANTI-MOUSTIQUES CORPOREL = 1.1 mg $product.cm^{-2}$ for skin)
BS	Body surface treated (7215 cm^2)

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

A fraction of 0.865 released to wastewater (F_{water}) is considered for the exposure assessment of RÉPULSIF ANTI-MOUSTIQUES CORPOREL. The evaporation reported in the CAR (5%) and the dermal absorption rate specific to RÉPULSIF ANTI-MOUSTIQUES CORPOREL (9%) are subtracted from the amount of DEET applied on skin only. In fact, when the product RÉPULSIF ANTI-MOUSTIQUES CORPOREL is used on skin only, applications on clothes are not considered and the emission reduction due to dermal penetration can be applied on the total quantity of RÉPULSIF ANTI-MOUSTIQUES CORPOREL used on skin. It should be noted that considering the lower dermal absorption value of 9% used in the CAR (specific to the active substance DEET regardless to the product properties) compared to the specific value for RÉPULSIF ANTI-MOUSTIQUES CORPOREL (20%; see toxicology section) represents a worst case approach for the environmental exposure assessment. Concerning the applications on clothes only, no dermal adsorption is considered and only the evaporation allows lowering the fraction of emission which is therefore stated at 0.95.

The applicant supplied a document justifying the use of a market share (Fpenetr) specific to RÉPULSIF ANTI-MOUSTIQUES CORPOREL product, instead of the default value of 0.5 from the ESD. No detailed information on the methods applied to calculate this market share is available and it is therefore not possible to consider this value for the risk assessment. A market share of 0.28 for DEET-containing repellents is considered according to the same survey study (Boomsma and Parathasarathy, 1990) reported in the CAR and used to conclude on the Finh. Following analysis of confidential data on the market of insect repellents in France, it can be concluded that the CAR value of 0.28 covers the market share of all the DEET-containing products put on the French market.

It is worth noting that the average amount of DEET consumed per application (skin only) used in the CAR (0.9 g) is covered by the amount of DEET per application calculated as presented above on the basis of the intended uses for RÉPULSIF ANTI-MOUSTIQUES CORPOREL ($Qform_{appl} \times Cform_{weight} \times BS \times 10^{-6}$= 7.94 g). For the comparison, the average amount of DEET consumed by the general population (0.9 g/application on skin only) has to be chosen rather than the 75th percentile of dermal exposure estimated for subgroups (for instance male adult, female adult, children...), since this value is more relevant in the context of the environmental exposure assessment conducted at the STP scale. Nevertheless, the value for RÉPULSIF ANTI-MOUSTIQUES CORPOREL covers also the 75th percentile values (1.5 g or 1.66 g of DEET per skin application for male adult or children respectively). The total quantity of DEET for applications on skin and clothes used for the assessment of RÉPULSIF ANTI-MOUSTIQUES CORPOREL also covers the quantity used in the CAR (1.2 g).

Then,

$Elocal_{water\ skin}$= 2.13 kg DEET.d^{-1}
$Elocal_{water\ clothes}$= 0.78 kg DEET.d^{-1}

$Elocal_{water\ skin\ and\ clothes}$= 2.91 kg DEET.$d^{-1}$

The concentration in the untreated wastewater, $Clocal_{inf}$, is calculated considering a daily sewage volume of 2 × 10^6 L (TGD II, eq.32), therefore,

$Clocal_{inf\ skin}$ = 1.07mg DEET.L^{-1}
$Clocal_{inf\ clothes}$ = 0.39 mg DEET.L^{-1}
$Clocal_{inf\ skin\ and\ clothes}$ = 1.46 mg DEET.L^{-1}

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

Table 2.8.4.2-1: Fractions of emission by the STP

Symbol	Parameter	Value	Unit
INPUTS			
	Characterisation of biodegradability	Readily biodegradable	[-]
VP	Vapour pressure	0.23 (at 20°C)	[Pa]
Sol	Solubility in water	11.2	[$g.L^{-1}$]
Koc	Partition coefficient organic carbon-water	43.3	[$L.kg^{-1}$]
HENRY	Henry's law constant	3.93E-03 (at 25°C)	[$Pa.m^3.mol^{-1}$]
OUTPUTS			
$F_{STP\ air}$	Fraction of emission to air by STP	8.15E-04	[%]
$F_{STP\ water}$	Fraction of emission to effluent by STP	12.6	[%]
$F_{STP\ sludge}$	Fraction of emission to sludge by STP	0.407	[%]

DEET concentrations in the STP effluent and in surface water are calculated according to the TGD equations considering the $Elocal_{water}$ calculated above and the different parameters presented in the following table:

Table 2.8.4.2-2: Input and output values for calculation of concentrations in STP and surface water

Local emission of active substance to waste water during episode:		Skin	Clothes	Skin and clothes	Unit	Reference
INPUTS						
$Elocal_{water}$	Emission rate to wastewater	2.13	0.78	2.91	[$kg.d^{-1}$]	-
$Clocal_{inf}$	Concentration in sewage water to default STP	1.07	0.39	1.46	[$mg.L^{-1}$]	TGD Eq. 32
$Fstp_{water}$	Fraction emitted to water by STP	12.6			[%]	Table 2.8.4.2-1
Koc	Partition coefficient organic carbon-water	43.3			[$L.kg^{-1}$]	-

Kp_{susp}	Solids-water partitioning coefficient	4.33			[L.kg-1]	TGD Eq. 23
OUPUTS						
PEC_{STP}	PEC in the treated wastewater	0.13	4.92E-02	0.18	[$mg.L^{-1}$]	TGD Eq. 33
$PEClocal_{water}$	PEC in water during emission episode	1.34E-02	4.92E-03	1.84E-02	[$mg.L^{-1}$]	TGD Eq. 45

The concentrations in agricultural soil, following the spreading of contaminated STP sludge, are calculated according to the TGD equations considering the emissions $Elocal_{water}$ and the different parameters presented in Table 2.8.4.2-3. Degradation of the substance in soil is considered based on its ready biodegradability ($DT_{50\ soil}$: 30 days at 12°C); dissipation by leaching and volatilisation is also taken into account based on the TGD equations.

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

Local emission of active substance to soil during episode:		**Skin**	**Clothes**	**Skin and clothes**	**Unit**	**Reference**
INPUTS						
$Elocal_{water}$	Emission rate to wastewater	2.13	0.78	2.91	[$kg.d^{-1}$]	-
$Fstp_{\ sludge}$	Fraction emitted to sludge by STP	0.407			[%]	Table 2.8.4.2-1
k_{soil}	Rate constant for removal in soil based on biodegradation and dissipation	0.0249			[-]	TGD Eq. 56 TGD Eq. 57
Koc	Partition coefficient organic carbon-water	43.3			[$L.kg^{-1}$]	-
SLUDGERATE	Rate of sewage sludge production	710			[$kg.d^{-1}$]	TGD Eq. 37
$K_{soil\ water}$	Soil-water partitioning coefficient	1.5			[$m^3.m^{-3}$]	TGD Eq. 24
OUTPUT						
Csludge	Concentration in dry sewage sludge	12.23	4.48	16.71	[$mg.kg^{-1}_{dwt}$]	TGD Eq. 36
PEC local soil	PEC in soil after 10 years of application - Twa over 30 d	1.27E-02	4.64E-03	1.73E-02	[$mg.kg^{-1}_{wwt}$]	TGD Eq. 55

<u>Tonnage based approach for PEC groundwater</u>

DEET concentrations in groundwater are estimated using the leaching model FOCUS-PEARL 4.4.4., which integrate transformation and dilution of the active substance in deeper soil layers. Modeling is based on the annual tonnage of DEET placed on the EU market as proposed in the CAR for the active substance inclusion, given that it was verified that the annual tonnage of DEET placed on the French market (representing 3 EU regions) is covered by the EU tonnage considered in the CAR.

A tonnage approach has been favored for groundwater compared to a consumption approach for different reasons. The consumption approach represents a peak of release with worst case assumptions which can be considered realistic in case of daily emission to environmental compartments (surface water downstream the STP for instance). Nevertheless, sludge applied as a

soil enrichment product is collected in the STP over weeks or months. This matter is stored and sometimes mixed with other additives (for instance during composting). However, no dilution or degradation can be taken into account in the exposure calculations without validated data. The actual assessment model probably overestimates the concentration of DEET in sludge at the time of land spreading considering the ready biodegradability property of the substance. It was therefore considered more relevant to follow a tonnage approach that allows taking into consideration a mean emission to the sludge which seems more realistic for exposure of groundwater.

The model used, input data and assumptions presented below are chosen according to DE proposals (Klein, 2011[13]). Two representative crops for arable lands (maize and winter cereals) and one for grassland (grass/alfalfa) are investigated to estimate the potential leaching to groundwater. The overall assumption being that the only exposure route to groundwater is *via* the application of sludge from STPs.

Application rate is calculated from DEET concentration in dry sewage sludge proposed in the CAR (2.63 $mg.kg^{-1}_{dwt}$), and the maximum sewage sludge application of 5000 kg $_{dry\ sludge}.ha^{-1}.yr^{-1}$ on arable land and 1000 kg $_{dry\ sludge}.ha^{-1}.yr^{-1}$ on grassland (at a single event as suggested in the TGD, Part II 2.3.8.5), leading to dose rates of $1.31.10^{-2}$ $kg.ha^{-1}.yr^{-1}$ and $2.63.10^{-3}$ $kg.ha^{-1}.yr^{-1}$ respectively. The DT_{50} soil value used is in accordance with EUSES/TGD, Part II 2.3.6.5, for readily biodegradable substances (30 days at 12°C).

Table 2.8.4.2-4: Summary of data used and assumptions made to calculate PECgw for DEET in FOCUS scenariosParameters

	Values for arable land	**Values for grassland land**
Model used	FOCUS PEARL 4.4.4.	FOCUS PEARL 4.4.4.
Years of simulation	26 (including 6 yrs "warming-up" period)	26 (including 6 yrs "warming-up" period)
Application rate	**0.0131 $kg.ha^{-1}$**	**0.00263 $kg.ha^{-1}$**
Application depth	20 cm	10 cm
Date of application	one application per year, 20 days before crop emergence	1 March 1901
Standard crop for arable land	Maize & Winter Cereals	Grass/alfalfa
Molar mass	191.3 g/mol	191.3 g/mol
Vapour pressure	0.23 Pa	0.23 Pa
Water solubility	11200 mg/L, 25°C	11200 mg/L, 25°C
Kom	25.1 L/kg	25.1 L/kg
Freundlich exponent	0.9 (FOCUS Default)	0.9 (FOCUS Default)
DT_{50}soil	30d	30d
Coefficient for uptake by plant	0	0

Results in **Erreur ! Source du renvoi introuvable.** show that the predicted groundwater concentrations of DEET are all below the threshold value of 0,1 $\mu g.L^{-1}$ for all the tested conditions.

Table 2.8.4.2-5: 80th percentile annual average PEC of DEET in groundwater (at 1 m depth) calculated with FOCUS assuming application of sewage sludge from STP to agricultural land and grassland

[13] Klein M. (2011). Proposals for standard scenarios and parameter setting of the FOCUS groundwater scenarios when used in biocide exposure assessments. FKZ: 360 04 035, pp 1-40

Scenario	$PEC_{Groundwater}$		
	Maize	**WinterCereals**	**Grass/alfalfa**
Chateaudun	< 0.001	0.001	< 0.001
Hamburg	0.003	0.026	< 0.001
Jokioinen	-	0.011	< 0.001
Kremsmuenster	0.003	0.017	< 0.001
Okehampton	0.006	0.032	< 0.001
Piacenza	0.001	0.011	< 0.001
Porto	< 0.001	0.014	< 0.001
Sevilla	< 0.001	< 0.001	< 0.001
Thiva	< 0.001	< 0.001	< 0.001

*2.8.4.2.2 **Direct exposure - "swimming scenario"***

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

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

- In the proposed DE scenario, the assumed volume of a lake is set to 1 million m^3 (1 000 000 000 L) as a worst case assumption, which is seen representative for a medium quarry pond and for small natural and other freshwater lakes for swimming, based on some inquiries of ponds and lakes near to urban areas in Saxony and Bavaria, known to be used by the public for swimming during bathing season.
  This volume seems to be applicable to the total volume of a pond and is further used in the long-term assessment of the product RÉPULSIF ANTI-MOUSTIQUES CORPOREL over the bathing season.

  Nevertheless, this proposed volume of 1 million m^3 seems underestimated if the risk is evaluated at short term in the bathing area, which can be reduced compared to the total volume of a water body. Considering published data on the attendance ratio of several lakes located in France[14,15], a more realistic water volume of 70 000 m^3, which corresponds to the specific swimming area, has been chosen for the short term assessment.

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

[14] Profil de la zone de baignade Lac Kir "plage Est" (2011). Rivage Protech, pp 1-99.
[15] Réalisation du profil de baignade du lac des Vannades, Avril 2011, SCE Aménagement et Environnement, pp 1-58.

Published data on the attendance ratio of several lakes located in France showed that the maximum average number of swimmers is 780 per day. Considering the fraction of inhabitants (Finh) using a repellent product of 0.37 and the market share (Fpenetr) of 0.28 (see indirect exposure section), the number of swimmers using the repellent product RÉPULSIF ANTI-MOUSTIQUES CORPOREL per day should be:
Nswim = 780 * 0.37 * 0.28
Nswim = 81 swimmers.day^{-1}

- The fraction of the product which is emitted to the swimming water is set as default to Fwater = 0.865. The same emission factor as in the scenario for body cleaning is used.

- The rate constant for biodegradability in surface water is set according to Table 7 (EU TGD, 2003) considering the ready biodegradability of the active substance: k=0.047 d^{-1} ($DT_{50\ water}$= 15 days at 12°C).

- The time of swimming during the year is limited by the temperature of the air and the water, therefore it was estimated that swimming will take place once a day on 150 days per year as a maximum limit. The assessment time is set as T_{1d} for a short term assessment and $T_{emission}$ for a long-term emission corresponding to 150 days.

- For PEC localwater, two situations are calculated: $Clocal_{water}$ after 1 day in the bathing area (without considering degradation) and $Clocal_{water\_annual}$ over 150 days in the total volume of the lake considering the constant release of the product and the degradation over time, which can be considered as a background concentration.
  A cumulative assessment is further conducted for the bathing area in order to consider the release during one day in this restricted zone with the background calculated over 150 days.

Calculation steps:

1) The daily emission to the lake, $Elocal_{water}$ (kg.d^{-1}), is estimated from the formula:

$$\mathbf{Elocal_{water} = Nswim * Fwater * Qform_{inh} * Cform_{weight} * 10^{-6}}$$

Where

Nswim	Number of swimmers using the repellent product RÉPULSIF ANTI-MOUSTIQUES CORPOREL per day (81 d^{-1})
$Qform_{inh}$	Consumption per inhabitant per day (g.d^{-1}; Nappl* $Qform_{appl}$*BS)
$Cform_{weight}$	Concentration of the active substance in the product (specific value for RÉPULSIF ANTI-MOUSTIQUES CORPOREL = 300 g.kg^{-1})
Nappl	Number of applications (specific value for RÉPULSIF ANTI-MOUSTIQUES CORPOREL = 1 day^{-1})
$Qform_{appl}$	Consumption per application (specific value for RÉPULSIF ANTI-MOUSTIQUES CORPOREL = 1.1 mg product.cm^{-2})
BS	Body surface treated (7215 cm^2; see Section Human exposure)
Fwater	Fraction of the product emitted to the swimming water (0.865)

Then,

$$\mathbf{Elocal_{water} = 0.17\ kg\ DEET.d^{-1}}$$

2) **Short-term assessment**:
Calculation of $Clocal_{water}$ is done considering with the volume of $V_{bathing\ area}$ = 70 000 000 L for the bathing area, after the first day of bathing, without taking into account the degradation in surface water.

$$\mathbf{Clocal_{water} = Elocalwater * 10^{6} / V_{bathing\ area}}$$

Then,

$$\mathbf{Clocal_{water} = 2.38E\text{-}03\ mg\ DEET.L^{-1}}$$

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

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

With

k = rate constant for biodegradation in surface water (readily biodegradable substance = 0.047 d^{-1})
$V_{waterbody}$ = 1 000 000 000 L
$T_{emission}$ = 150 days

Then,

$$\mathbf{Clocal_{water\_annual} = 3.08E\text{-}03\ mg\ DEET.L^{-1}}$$

4) **Cumulative assessment**:
Calculation of the total concentration in the bathing area considering the $Clocal_{water}$ and the $Clocal_{water\_annual}$ as a background concentration.

$$\mathbf{Total\ Clocal_{water} = Clocal_{water\_annual} + Clocal_{water}}$$

Where

$Clocal_{water\_annual}$	Background water concentration after a season
$Clocal_{water}$	Local concentration at the last swimming day in the bathing area

Then,

Total $Clocal_{water}$ = 5.46E-03 mg DEET.L^{-1}

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

2.8.4.3 Summary of PEC values

2.8.4.3.1 Aquatic compartment (including water and STP)

Table 2.8.4.3-1: Summary of PEC values for DEET considering the indirect and direct emissions to the aquatic compartment

	PEC	Unit
Indirect emissions (via the STP* – ESD PT01*) - Skin application		
STP	0.13	[mg.L^{-1}]
Surface water	1.34E-02	[mg.L^{-1}]
Indirect emissions (via the STP* – ESD PT01*) - Clothes application		
STP	4.92E-02	[mg.L^{-1}]
Surface water	4.92E-03	[mg.L^{-1}]
Indirect emissions (via the STP* – ESD PT01*) - Clothes and skin application		
STP	0.18	[mg.L^{-1}]
Surface water	1.84E-02	[mg.L^{-1}]
Direct emissions (Swimming scenario) - Skin application		
Surface water – $Clocal_{water}$ *Short term assessment in the bathing area*	2.38E-03	[mg.L^{-1}]
Surface water – $Clocal_{water\_annual}$ *Long term assessment in the lake*	3.08E-03	[mg.L^{-1}]
Surface water – Total Clocalwater *Cumulative assessment*	5.46E-03	[mg.L^{-1}]

2.8.4.3.2 Atmospheric compartment

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

2.8.4.3.3 Terrestrial compartment (soil and groundwater)

Table 2.8.4.3-2: Summary of PEC values for DEET for the terrestrial compartment only for indirect emissions (via the STP)

	PEC	Unit
Indirect emissions (via the STP)-Skin application		
Soil	1.27E-02	[$mg.kg^{-1}_{wwt}$]
Groundwater Focus PEARL 4.4.4	< 0.1	[$\mu g.L^{-1}$]
Indirect emissions (via the STP)-Clothes application		
Soil	4.64E-03	[$mg.kg^{-1}_{wwt}$]
Groundwater Focus PEARL 4.4.4	< 0.1	[$\mu g.L^{-1}$]
Indirect emissions (via the STP)-Skin and clothes application		
Soil	1.73E-02	[$mg.kg^{-1}_{wwt}$]
Groundwater Focus PEARL 4.4.4	< 0.1	[$\mu g.L^{-1}$]

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

The low calculated BCF values of DEET suggest that RÉPULSIF ANTI-MOUSTIQUES CORPOREL has a low potential to bioaccumulate into aquatic and terrestrial organisms.

2.8.5 Risk characterisation for the environment

2.8.5.1 Skin application

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

2.8.5.1.1 Aquatic compartment (including water and STP)

Table 2.8.5.1-1: Risk characterization in the aquatic compartment

	PEC	PNEC	Unit	PEC/PNEC
Indirect emissions (via the STP* – ESD PT01*) - Skin application				

STP	0.13	10	[mg.L^{-1}]	1.34E-02
Surface water	1.34E-02	4.3E-02	[mg.L^{-1}]	0.31
Indirect emissions (via the STP* – ESD PT01*) - Clothes application				
STP	4.92E-02	10	[mg.L^{-1}]	4.92E-03
Surface water	4.92E-03	4.3E-02	[mg.L^{-1}]	0.11
Indirect emissions (via the STP* – ESD PT01*) - Clothes and skin application				
STP	0.18	10	[mg.L^{-1}]	1.84E-02
Surface water	1.84E-02	4.3E-02	[mg.L^{-1}]	0.43
Direct emissions (Swimming scenario) - Skin application				
STP	NR	10	[mg.L-1]	
Surface water – Clocal$_{water}$ Short term assessment in the bathing area	2.38E-03	4.3E-02	[mg.L^{-1}]	5.53E-02
Surface water – Clocal$_{water_annual}$ Long term assessment in the lake	3.08E-03		[mg.L-1]	7.17E-02
Surface water – Total Clocalwater Cumulative assessment	5.46E-03		[mg.L-1]	0.13

NR: Not relevant

The PEC/PNEC ratios are all below the trigger value of 1. Then, risks for aquatic organisms and for STP microorganisms are acceptable for both indirect and direct emissions, after 1 daily skin and/or clothes applications of RÉPULSIF ANTI-MOUSTIQUES CORPOREL.

2.8.5.1.2 Atmospheric compartment

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

2.8.5.1.3 Terrestrial compartment (including soil and groundwater)

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

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

	PEC	PNEC	Unit	PEC/PNEC
Indirect emissions (via the STP) - Skin application				
Soil	1.27E-02	3.79E-02	[$mg.kg^{-1}_{wwt}$]	0.33
Groundwater Focus PEARL 4.4.4	<0.1	0.1	[$\mu g.L^{-1}$]	<0.1 µg/L Threshold value in groundwater
Indirect emissions (via the STP) - Clothes application				
Soil	4.64E-03	3.79E-02	[$mg.kg^{-1}_{wwt}$]	0.12
Groundwater Focus PEARL 4.4.4	<0.1	0.1	[$\mu g.L^{-1}$]	<0.1 µg/L Threshold value in groundwater
Indirect emissions (via the STP) - Skin and clothes application				
Soil	1.73E-02	3.79E-02	[$mg.kg^{-1}_{wwt}$]	0.43
Groundwater – Tier II Focus PEARL 4.4.4	<0.1	0.1	[$\mu g.L^{-1}$]	< 0.1 µg/L Threshold value in groundwater

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

The predicted groundwater concentrations of DEET are lower than the trigger value of 0.1 $\mu g.L^{-1}$ for all the conditions tested in Focus PEARL 4.4.4. Consequently, the risk for groundwater is acceptable.

FR underlines that the presence of DEET in the groundwater compartment has been demonstrated in several monitoring studies performed all around the world. Although not peer reviewed, groundwater monitoring data from The Netherland (149 molecules at 189 locations), showed that in 1.6% of the samples, DEET concentrations ranged between 0.36-1.48 µg/L (DEET CAR[16], 2010). Therefore, monitoring data of DEET should be performed and included in national programs.

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

The low BCF values suggest that DEET has a low bioaccumulation potential. Therefore, no risk of secondary poisoning via ingestion of potentially contaminated food (e g earthworms or fish) by birds or mammals is expected.

2.8.5.1.5 Conclusions

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

[16] Competent Authority Report According to Directive 98/8/EC, Active substance in Biocidal Products, N,N-diethyl-m-toluamide (DEET) CAS 134-62-3, Product Type 19 (Repellents), RMS Sweden, march 2010

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

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

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

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

Risk mitigation measures linked to risk assessment for environment

- Do not use the product before bathing or showering.
- Do not exceed 1 application of the product per day.

2.9 Measures to protect man, animals and the environment

See Summary of product characteristics.

3 Proposal for decision to be adopted by the French CA (Ministry of Ecology)

This section is a proposal from the authority in charge of the risk assessment (Anses) for the decision to be adopted by the competent authority in charge of the decision (French Ministry of Ecology).

In case of inconsistency between the risk assessment and the decision, only the original and signed decision has a legal value. The decision specifies the terms and conditions to the making available on the market and use of the biocidal product.

Conclusions of efficacy and risk assessment

Summary of risk assessment for Physico-chemical properties

REPULSIF ANTI-MOUSTIQUES CORPOREL is a ready-to-use TP 19. It is under the form of limpid liquid, not auto-flammable (up to 360°C), not explosive and does not have oxidizing properties but classified as flammable R10 according to regulation 99/45/EC and flam. Liq. 3 / H226 according to CLP regulation.
The product is stable 14 days at 54°C. a shelf life of 2 years is granted. As biocidal product is suseptible to be used in tropical countries, the following recommandation is added : do not store more than 2 weeks at 54°C.

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

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

Summary of efficacy assessment

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

Summary of risks characterisation of the product for human health

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

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

Summary of risks characterisation of the product for the environment

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

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

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

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

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

Risk mitigation measures and conditions of use

Risk mitigation measures linked to assessment of physico-chemical properties

- The product must be shaken before use
- Do not store more than 2 weeks at 54°C

Conditions of use linked to efficacy assessment

- 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.
- The label has to respect the recommended conditions of use and the biocidal products labelling guide[17].
- The use of the product with other biocidal products or sunscreen products is not recommended.
- Protection time can be lowered by sweating, water wash off, rubbing, high temperature (>30°C), wind velocity, etc.

Risk mitigation measures linked to risk assessment for human health

- Only use by adults
- Do not exceed one application per day
- Only apply on uncovered skin
- Do not put hands in mouth after application
- Keep out of the reach of children
- Do not spray directly in the face

[17] Guide à l'intention des responsables de la mise sur le marché des produits biocides. Lignes directrices sur l'étiquetage des produits biocides mis sur le marché. Version du 28 août 2007.

- Wash the palm of hands after application
- Do not use the spray near food and surfaces that may come into contact with food or drink intended for human consumption.

Risk mitigation measures linked to risk assessment for environment

- Do not use the product before bathing or showering.
- Do not exceed 1 application of the product per day.

Required information

Required information linked to assessment of physico-chemical properties

Long term storage stability in commercial packaging study including data on volume delivered by pump after 2 years

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.

4 Appendices

Annex 0a: Practical use claimed by the applicant

Name of the product and type of formulation (gel, paste, spray, dust, powder, …)	Target organisms (common species and genus) and development stages (larvae, nymph, adults, female or male…)*	User category (professional/non professional)*	Application aim (human or animal protection)	Area of use (dermal, clothes, indoor or outdoor buildings…)	Method of application including description of system used (spraying, padding treatment…)	Application rate (expressed in g/m^3, g/m^2, ml/m^2…) Maximum and minimum dosage (if appropriate)	Mode of action including time delay (repellent or attractant)	Time delay of residual efficacy (hours, days, weeks and months)	Time delay for human , food and animals reentrance after treatment (if appropriate)	Frequency and duration of application (number of application, time between each application…)	Package details : Individual packaging (yes/no)**	Primary packaging : type : bulk, individual wrapping…/ nature: bucket, bottle, sachet…/ material: paper, polyethylene…/	Size of each packaging	Secondary packaging
NAME : Répulsif anti-moustiques corporel SUBITO / BEAST-OFF Formulation: VIII.3 Liquid formulation VIII.3.2 Ready-for-use	Mosquitoes I.3.12.1 Culicidae II.1.5 Adults	V.1 Non-professional user / consumer	Human protection VII.2 Health protection	IV.3 use on skin, or use on clothes	VI.1 Spraying Spread on the exposed skin's area or sprayed on clothes.	1.1 mg of product/cm² of skin Number of sprayings recommended: 2 per adult forearm (as an example). The number of sprays is then to be adapted to the body surface to protect.	III.2.6 Repellent Immediate effect	III.4.2 Residual activity (long time effect) Protection against mosquitoes for a period of 8 hours.	n.a.	1 application per day	Yes	Individual polypropylene flask	3 different sizes : 80 mL, 100 mL and 150 mL	n.a.

Annex 0b: Proposed uses for authorisation

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

Users	Field of uses envisaged	Likely doses at which product will be used
Public - Adults only	Repellent against mosquitoes *Aedes aegypti, Anopheles gambiae, Aedes albopictus and Culex pipiens*	1.1 mg/cm² on skin only, protection time up to 4 hours Max. one application per day

Annex 1: Summary of product characteristics

See separated file.

Annex 2: List of studies reviewed

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

Section No	Reference No	Author	Year	Title	Owner of data	Letter of access		Data protection claimed	
Doc IIIB									
Physico-chemistry						**Yes**	**No**	**Yes**	**No**
B3.1 B3.4 B3.5 B3.6 B3.7 B3.10 B3.11	B3.1	S. Legay	2012	Physico-chemical tests on a ready-to-use anti mosquito solution "REPULSIF ANTI-MOUSTIQUES CORPOREL, SUBITO / BEAST-OFF": Validation of analytical method and chemical analysis of active substance declared in the test item Identification criteria Stability test at 54°C during 14 days Stability test at 0°C during 7 days, FCBA, Report No.n°402/12/1048F-e, Draft report	SPRING		**X**	**X**	
B3.2 B3.3 B3.4	B3.2-01	D. Bour, H. Detrimont, D. Ambrosi	2012	Literature survey on explosive properties, oxidising properties and auto-flammability of the ingredients of the product SUBITO (30% DEET), A.S.C., Report No.12/04	SPRING		**X**	**X**	
B3.2	B3.2-02	B. Demangel	2012	Determination of exothermic reactions by DSC of SUBITO, Défitraces, Report No.12-919062-001, Draft report	SPRING		**X**	**X**	
B3.7	B3.7	S. Legay	2012	Storage stability at ambient temperature on 3 years, on a ready-to-use anti mosquito solution "REPULSIF ANTI-MOUSTIQUES CORPOREL, SUBITO / BEAST-OFF": (GIFAP monograph n°17), FCBA, testing schedule	SPRING		**X**	**X**	
B3.12	B3.12	H.J. Kroh	2012	Determination of the Particle Size Distribution for SUBITO ANTI-MOUSTIQUE CORPOREL in 150 mL PET Bottles with PP/POM Spray Head, BioGenius, Study No.Mo4415, Draft report	SPRING		**X**	**X**	

Method validation						**Yes**	**No**	**Yes**	**No**
B4.1	B4.1	S. Legay	2012	Physico-chemical tests on a ready-to-use anti mosquito solution “REPULSIF ANTI-MOUSTIQUES CORPOREL, SUBITO / BEAST-OFF”: Validation of analytical method and chemical analysis of active substance declared in the test item Identification criteria Stability test at 54°C during 14 days Stability test at 0°C during 7 days, FCBA, Report No.n°402/12/1048F-e, Draft report	SPRING		**X**	**X**	
Efficacy						**Yes**	**No**	**Yes**	**No**
B5.10	B5.10/01	B. Serrano	2012	Laboratory assessment of a personal skin repellent against mosquitoes. Répulsif anti-moustiques corporel SUBITO / BEAST-OFF - 300 g/L, Laboratoire TEC, Report 1506/0512.	SPRING		**X**	**X**	

B5.10	B5.10/01	B. Serrano	2012	Laboratory assessment of a personal skin repellent against mosquitoes. Répulsif anti-moustiques corporel SUBITO / BEAST-OFF - 300 g/L, Laboratoire TEC, Report 1506/0512.	SPRING		**X**	**X**	
Toxicity						**Yes**	**No**	**Yes**	**No**
B6.1.1	B6.1.1	Richeux F.	2012	RAMC-Evaluation of Acute Oral Toxicity in rats – Acute toxic class method Phycher Bio Développement, Study No:TAO423-PH-12/0195	SPRING		**X**	**X**	
B6.1.2	B6.1.2	Richeux F.	2012	RAMC-Evaluation of Acute Dermal Toxicity in rats, Phycher Bio Développement, Study No.: TAD-PH-12/0195.	SPRING		**X**	**X**	
B6.2.1	B6.2.1	Richeux F.	2012	RAMC-Assessment of acute dermal irritation, Phycher Bio Développement, Study No.: IC-OCDE-PH-12/0195	SPRING		**X**	**X**	
B6.2.2	B6.2.2/01	Richeux F.	2012	RAMC-Assessment of acute eye irritation, Phycher Bio Développement, Study No.: IO-OCDE-PH-12/0195	SPRING		**X**	**X**	

Ecotoxicity						**Yes**	**No**	**Yes**	**No**
B7.2.2	B7.2.2/01	Martin C.	2012	Algae *Pseudokirchneriella subcapitata* , 72h-growth inhibition test performed on the test item "SUBITO REPULSIF MOUSTIQUES ADULTE", according to the OECD 201 guideline, Limit test, FCBA Report No.402/12/1048F/g-e, Draft report	SPRING		**X**	**X**	
B7.2.2	B7.2.2/02	Legay S.	2012	Validation of analytical method for the chemical analysis of DEET (N,N-diethyl-meta-toluamide) in algae ecotoxicology solutions, FCBA Report No.402/12/1048F/d-e, Draft report	SPRING		**X**	**X**	
Doc II						**Yes**	**No**	**Yes**	**No**
3.2	IIB_3.2/01	Vabre V.	2012	Taste evaluation of mosquito spray "Subito Anti-Moustiques Corporel", Report #11888, Alpha-Mos	SPRING		**X**	**X**	
3.3	IIB_3.3	EUSES	2012	Full report EUSES calculations	SPRING		**X**	**X**	

Annex 3: Analytical methods residues – active substance

DEET

Matrix, action levels, relevant residue and reference

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

Methods suitable for the determination of residues (monitoring methods)

Methods for products of plant origin
Not required as the use pattern of DEET will not results in any contact with food or feeding stuffs

Methods for foodstuffs of animal origin
Not required as the use pattern of DEET will not results in any contact with food or feeding stuffs

Methods for soil

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

Methods for drinking water and surface water

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

Methods for air

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

Methods for body fluids/tissue

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

Annex 4 : Toxicology and metabolism –active substance

<DEET>

Threshold Limits and other Values for Human Health Risk Assessment

Summary			
	Value	Study	SF
AEL long-term	Not relevant		
AEL medium-term	8.2 mg/kg/d	90 day study (rat, dermal)	100
AEL acute	0.75 mg/kg/d	8 week study (dogs, oral)[18]	100
ADI Not applicable			
ARfD Not applicable			

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

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

[18] Study terminated at day 5 due to severe toxicity

Annex 5 : Toxicology – biocidal product

<RAMC>

General information

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

Acute toxicity, irritancy and skin sensitisation of the preparation (Annex IIIB, point 6.1, 6.2, 6.3)	
Rat LD50 oral (OECD 423)	LD_{50}>2000 mg/kg
Rat LD50 dermal (OECD 402)	LD_{50}>2000 mg/kg
Rat LC50 inhalation (OECD 403)	No study submitted
Skin irritation (OECD 404)	Non irritant
Eye irritation (OECD 405)	Severely irritant
Skin sensitisation (OECD 406; GPMT)	Not sensitizing

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

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

Annex 6 : Safety for professional operators

<RAMC>

Exposure assessment

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

Primary exposure of professionals: not relevant

Risk assessment: not relevant

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

<RAMC>

General information	
Formulation Type	AL
Active substance(s) (incl. content)	30% DEET
Category	
Authorisation number	

DEET

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

Exposure scenarios for intended uses (Annex IIIB, point 6.6)	
Primary exposure	Spraying + amount applied on skin
Secondary exposure, acute	Oral exposure by hand-to-mouth transfer
Secondary exposure, chronic	Not relevant

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

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

Application on skin

application rate	1.1	mg/cm²

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

Application on clothes

application rate	1,67	mg/cm²

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

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

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

Test substance	Test organisms	Test system / Concentrations applied / exposure time	Test conditions	Test results: effects, mode of action, resistance	Reference	RI
RAMC (less than one year old), DEET 300 g/l	*Culex pipiens* *Aedes albopictus* *Aedes aegypti* *Anopheles gambiae* For each test organism, 200 ± 10 females (5 to 7 days old) for each replicate.	The average duration of efficacy was 8 hours for the 4 species of mosquitoes. Laboratory test. Arm-in-cage study. 3 volunteers (2 men and 1 woman). 3 replicates per volunteer Product applied on one forearm of each volunteer, the other untreated one being used as a control. Dose of product 1.67 g / 600 cm² (± 3%), *i.e.* 3 sprays, a forearm corresponding to an average area of 600 cm². The trial began 30 minutes after the product had been applied. The control forearm was inserted into the cage for 30 seconds, and after validation of this control (10 landings of test organism), the treated forearm was inserted into the cage for 3 minutes (exposure time) The same procedure was repeated every hour until 9 hours or inefficacy. Landings and bites were counted during each exposure time.	200 ± 10 insects in each cage. Ambient conditions in testing chamber were maintained during the period of testing at a temperature of 25 ± 2°C, a relative humidity of 65 ± 5% and with smooth ventilation (30 m^3/h). Throughout the duration of the trial, the cages were maintained at a temperature of 27 ± 2°C, a relative humidity of 65 ± 10%, with a light intensity of 700 lux.	The study demonstrates in laboratory condition, the reppelent efficacy of the product RAMC (liquid, DEET 300 g/l) at the application rate of 1 g / 600 cm² (equivalent to 1.67 mg product/ cm²; 0.5 mg DEET /cm²) against the four mosquitoes tested. The duration of protection was: - 8 hours for *Culex pipiens* - 8.1 hours for *Aedes albopictus* - 7.9 hours for *Aedes aegypti* - 8.1 hours for *Anopheles gambiae* Based on the less sensitive species, the protection duration of the product is 8 hours when the product is applied on skin in laboratory conditions. Note that this application rate has not been claimed by the applicant and has not been taken into account	Serrano B. (2012) B5.10/01	2

Test substance	Test organisms	Test system / Concentrations applied / exposure time	Test conditions	Test results: effects, mode of action, resistance	Reference	RI
RAMC (less than one year old), DEET 300 g/L	*Culex pipiens* *Aedes albopictus* *Aedes aegypti* *Anopheles gambiae* For each test organism, 200 ± 10 females (5 to 7 days old) for each replicate.	The average duration of efficacy was 4 hours for the 4 species of mosquitoes. Laboratory test. Arm-in-cage study. 3 volunteers (2 men and 1 woman). 3 replicates per volunteer Product applied on one forearm of each volunteer, the other untreated one being used as a control. Dose of product 1 g / 600 cm² (± 3%), *i.e.* 3 sprays, a forearm corresponding to an average area of 600 cm². The trial began 30 minutes after the product had been applied. The control forearm was inserted into the cage for 30 seconds, and after validation of this control (10 landings of test organism), the treated forearm was inserted into the cage for 3 minutes (exposure time). The same procedure was repeated every hour until 9 hours or inefficacy. Landings and bites were counted during each exposure time.	200 ± 10 insects in each cage. Ambient conditions in testing chamber were maintained during the period of testing at a temperature of 25 ± 2°C, a relative humidity of 65 ± 5% and with smooth ventilation (30 m^3/h). Throughout the duration of the trial, the cages were maintained at a temperature of 27 ± 2°C, a relative humidity of 65 ± 10%, with a light intensity of 700 lux.	The study demonstrates in laboratory condition, the reppelent efficacy of the product RAMC (liquid, DEET 300 g/l) at the application rate of 0.66 g / 600 cm² (equivalent to 1.1 mg product/ cm²; 0.33 mg DEET /cm²) against the four mosquitoes tested. The duration of protection was: - 4.1 hours for *Culex pipiens* - 3.9 hours for *Aedes albopictus* - 3.9 hours for *Aedes aegypti* - 4.1 hours for *Anopheles gambiae* Based on the less sensitive species, the protection duration of the product is 4 hours when the product is applied on skin in laboratory conditions.	Serrano B. (2013) B5.10/02	2

Test substance	Test organisms	Test system / Concentrations applied / exposure time	Test conditions	Test results: effects, mode of action, resistance	Reference	RI
RAMC (less than one year old), DEET 300 g/L	*Culex pipiens* *Aedes albopictus* *Aedes aegypti* *Anopheles gambiae* For each test organism, 200 ± 10 females (5 to 7 days old) for each replicate.	The average duration of efficacy was 4 hours for the 4 species of mosquitoes. Laboratory test. Arm-in-cage study. 3 volunteers (2 men and 1 woman). 3 replicates per volunteer Product applied on one forearm of each volunteer, the other untreated one being used as a control. Dose of product 1 g / 600 cm² (± 3%), *i.e.* 3 sprays, a forearm corresponding to an average area of 600 cm². The trial began 30 minutes after the product had been applied. The product was sprayed on cotton fabric that was used to cover one forearm volunteer. The control forearm was covered with an untreated cotton and was inserted in the cage, and after validation of this control, the treated foream was inserted into the cage for 3 minutes (exposure time). The same procedure was repeated every hour until 9 hours or inefficacy. Landings and bites were counted during each.	200 ± 10 insects in each cage. Ambient conditions in testing chamber were maintained during the period of testing at a temperature of 25 ± 2°C, a relative humidity of 65 ± 5% and with smooth ventilation (30 m^3/h). Throughout the duration of the trial, the cages were maintained at a temperature of 27 ± 2°C, a relative humidity of 65 ± 10%, with a light intensity of 700 lux.	The study demonstrates in laboratory condition, the reppelent efficacy of the product RAMC (liquid, DEET 300 g/l) at the application rate of 1 g / 600 cm² (equivalent to 1.67 mg product/ cm²; 0.5 mg DEET /cm²) against the four mosquitoes tested. The duration of protection was: - 7.9 hours for *Culex pipiens* - 8.0 hours for *Aedes albopictus* - 8.2 hours for *Aedes aegypti* - 8.1 hours for *Anopheles gambiae* Based on the less sensitive species, the protection duration of the product is 8 hours when the product is applied on fabric (cotton) in laboratory conditions.	Serrano B. (2013) B5.10/03	2