Product Assessment Report

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

INSECT ECRAN FAMILLE

COOPERATION PHARMACEUTIQUE FRANCAISE

December 2013

Internal registration:	PB-12-00195
Registration no:	2012/3525/533/FR/APP/1571
Authorisation n°	FR-2014-0183
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
92 055 La Défense cedex – FRANCE
autorisation-biocide@developpement-durable.gouv.fr

Authority in charge of the efficacy and risk assessment:
Anses – French agency for food, environmental and occupational health and safety
Regulated Products Directorate
253 Avenue du Général Leclerc
94 701 Maisons-Alfort Cedex - FRANCE
biocides@anses.fr

Contents

1 GENERAL INFORMATION ABOUT THE PRODUCT APPLICATION

1.1 Applicant

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

1.1.1 Person authorised for communication on behalf of the applicant

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

1.2 Current authorisation holder[1]

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

[1] Applies only to existing authorisations

for the applicant to represent the authorisation holder provided (yes/no):	

1.3 Proposed authorisation holder

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

1.4 Information about the product application

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

1.5 Information about the biocidal product

1.5.1 General information

Trade name:	Insect Ecran Famille
Manufacturer's development code number(s), if appropriate:	IE-DEET-F25
Product type:	PT19
Composition of the product (identity and content of active substance(s) and substances of concern; full composition see confidential annex):	See Confidential annex.
Formulation type:	AL
Ready to use product (yes/no):	Yes
Is the product the very same (identity and content) to another product already authorised under the regime of directive 98/8/EC (yes/no); If yes: authorisation/registration no. and product name:	No

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):	

1.5.2 Information on the intended use(s)

Overall use pattern (manner and area of use):	The product IE-DEET-F25 is presented as a ready-for-use product to be applied on uncovered human skin to repel mosquitoes, sand flies and ticks for consumer use.
Target organisms:	*Aedes aegypti* *Anopheles gambiae* *Aedes albopictus* *Culex pipiens* *Phlebotomus duboscqi* *Ixodes ricinus*
Category of users:	Public
Directions for use including minimum and maximum application rates, application rates per time unit (e.g. number of treatments per day), typical size of application area:	The recommended dose of application of IE-DEET-F25 is 0.6 mg/cm² of skin. The product can be used on children from 6-years old and adults. The number of sprayings recommended to cover face, neck, ¾ arms, hands and ½ legs is from 19 to 40 sprayings depending on the age range (see label) once a day.
Potential for release into the environment (yes/no):	No
Potential for contamination of food/feedingstuff (yes/no)	No
Proposed Label:	See Document III-B9, Annex 2, label
Use Restrictions:	The proposed label contains detailed instructions for use. The product must not be used for children under 6-years. The product can be used for pregnant women in case of risk of disease transmission. The product must not be applied on eyes, mucous membranes and injured skin. Number of applications is one per day. Resistance of the product to water has not been demonstrated.

1.5.3 Information on active substance(s)[2]

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

[2] Please insert additional columns as necessary

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[3]

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 former and the current composition of biocidal product INSECT ECRAN FAMILLE were provided by the applicant.

Efficacy data

- An arm-in-cage study conducted with ten human volunteers with the product **INSECT ECRAN ZONES FAMILLE** (25 % w/w DEET) on four mosquito species *(**Aedes aegypti, Anopheles gambiae, Aedes albopictus** and **Culex pipiens**)* and one sand fly specie *(**Phlebotomus duboscqi**).*

- An arm-in-cage study conducted with ten human volunteers with the product **INSECT ECRAN FAMILLE** (25 % w/w DEET) diluted at 15% w/w on two mosquito species *(**Aedes aegypti*** and ***Anopheles gambiae**).*

- A laboratory study conducted with ten human volunteers with the product **INSECT ECRAN FAMILLE** (25 % w/w DEET) on one tick specie *(**Ixodes ricinus**).*

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

Toxicology data

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

Ecotoxicology data

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

DOC-III A	Type of data	Date	Guideline	GPL	Reference

[3] Please insert additional columns as necessary

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

1.6.2 Access to documentation

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

2 Summary of the product assessment

2.1 Identity related issues

The sources of the active substance used in the biocidal product INSECT ECRAN FAMILLE are one of the sources used for annex I inclusion.
There is no substance of concern in the biocidal product.
The formulation of the biocidal product INSECT ECRAN FAMILLE 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

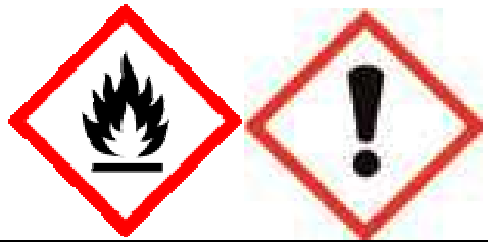
The applicant considers that ecotoxicity properties of INSECT ECRAN FAMILLE can be extrapolated from the data obtained with another formulation INSECT ECRAN ZONES INFESTEES containing 50% of DEET. The composition of these two products differs by four co-formulants which represent 35 % of the preparation contents. Consequently, extrapolation proposals from data obtained with INSECT ECRAN ZONES INFESTEES are not acceptable and the classification proposed for INSECT ECRAN FAMILLE is based only on calculation

Classification - Directive 99/45/EEC	
Class of danger	None
R phrases	R10: Flammable R52/53- Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
S phrases (proposed by the RMS)	S2: Keep out of the reach of children. S46: If swallowed, seek medical advice immediately and show this container or label S61- Avoid release to the environment. Refer to special instructions/Safety data sheets.

Classification - Regulation (EC) 1272/2008	
Hazard statement	Flam. Liq. 3 - H226 : Flammable liquid and vapour Eye Irrit Cat 2 - H319: Cause serious eye irritation Aquatic chronic 3 - H412 : Harmful to aquatic life with long lasting effects.
Precautionary statements (proposed by the RMS)	P273 : Avoid release to the environment.

2.2.3 Labelling of the biocidal product

Labelling - Directive 67/548/EEC	
Symbols:	
Indications of danger:	
Risk phrases:	R10: Flammable. R52/53- Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
Safety phrases:	S2: Keep out of the reach of children. S46: If swallowed, seek medical advice immediately and show this container or label S61- Avoid release to the environment. Refer to special instructions/Safety data sheets.

Labelling - Regulation (EC) 1272/2008	
Pictograms:	
Signal words:	Flam. Liq. 3 ; Warning
Hazard statements:	Flam. Liq. 3 H226 : Flammable liquid and vapour Eye Irrit Cat 2 H319: Cause serious eye irritation Aquatic chronic 3 - H412 : Harmful to aquatic life with long lasting effects.

2.2.4 Packaging of the biocidal product

The product IE-DEET-F25 is packaged in a opaque polypropylene flask with spray pump (POM, PP and PE[4]). The volumes of the flask are 125 mL and 250 mL, filled with respectively 100 mL and 200 mL of product.

2.3 Physical/chemical properties and analytical methods

2.3.1 Active ingredient

2.3.1.1 Identity, origin of active ingredient

The sources of the active substance used in the biocidal product INSECT ECRAN FAMILLE are 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 substance have already been evaluated at EU level and are presented in the CAR of the active substance DEET (2009). The notifier of the product INSECT ECRAN FAMILLE 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 INSECT ECRAN FAMILLE is not the same as the formulation of the representative biocidal product assessed for the inclusion of the active substance in annex I of directive 98/8/EC.

Trade name: Insect Ecran Famille
Code number: IE-DEET-F25

[4] [4] Polypropylene (PP)/ Polyetylene (PE)/ polyoxymethylene (POM)

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

The product INSECT ECRAN FAMILLE is packaged in a opaque polypropylene flask with spray pump (POM, PP and PE). The volumes of the flask are 125 mL and 250 mL, filled with respectively 100 mL and 200 mL of product.

2.3.2.2 Physico-chemical properties

Studies have been performed on former or current composition of biocidal product INSECT ECRAN FAMILLE.

Former and actual compositions are considered to be similar (0.1% w/w difference) for physicochemical properties.

Subsection (Annex Point IIB. 3/TNsG)	**Method**	**Purity/ Specification**	**Results**	**Reference**
3.1 Appearance (IIB3.1/Pt. I-B3.1) **3.1.1 Physical state and nature** **3.1.2 Colour** **3.1.3 Odour**	Visual	Former composition	limpid liquid	N. COLOMBIES 2012
	Visual	Former composition	Colourless	N. COLOMBIES 2012
3.2 Explosive properties (IIB3.2/Pt. I-B3.2)	DSC	Former composition	During both heating phases, neither endothermic nor exothermic peak was observed up to 500°C under the experimental conditions used. The test item shall not be classified as explosive. Not explosive	ASC report 11/35-2
3.3 Oxidising properties (IIB3.3/Pt. I-B3.3)	Statement	-	Based on structural considerations, INSECT ECRAN FAMILLE is not expected to have oxidising properties. Not oxidizing	ASC report 11/35-2
3.4 Flash-point and other indications of flammability or spontaneous ignition (IIB3.4/Pt. I-B3.4)				
Flammability	EC A.9	Former composition	Flash point: 34°C Classified as R10	B. DEMANGEL 2012
Self ignition temperature of solids	Statement	-	Based on composition, INSECT ECRAN FAMILLE is expected to have auto-flammability point higher than 350 °C.	ASC report 11/35-2
3.5 Acidity/Alkalinity (IIB3.5/Pt. I-B3.5)			Alkalinity of biocidal product is equivalent to 0.1 mL of NaOH	Laurent E. 2013
3.5 pH pure material	CIPAC MT 75.3	Former composition	pH of pure test item at 21°C: 6.19 Due to the high difference between measurements, applicant explained that pH is not representative for this biocidal product	N. COLOMBIES 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></td><td></td><td>due to low content of water in biocidal product and low solubility of DEET in water.</td><td></td></tr>
<tr><td></td><td>pH meter</td><td>Former composition</td><td>pH of pure test item is 10.
Due to the high difference between measurements, applicant explained that pH is not representative for this biocidal product due to low content of water in biocidal product and low solubility of DEET in water.</td><td>B3.7</td></tr>
<tr><td>3.6 Relative density (IIB3.6/Pt. I-B3.6)</td><td>EC A.3
OECD 109</td><td>Former composition</td><td>Relative density at 20°C : 1.019</td><td>B. DEMANGEL 2012</td></tr>
<tr><td>3.7 Storage stability - (IIB3.7/Pt. I-B3.7)</td><td>2 weeks at 54 °C</td><td>Former composition</td><td>After 14 days at 54°C in White plastic spray of 100 mL with green plastic stopper:
<table><tr><td></td><td>T0</td><td>14 d 54 °C</td></tr><tr><td>Appearance</td><td colspan="2">As initial</td></tr><tr><td>Packaging</td><td colspan="2">As initial</td></tr><tr><td>Content of DEET</td><td>25.4%</td><td>25.3%</td></tr><tr><td></td><td>variation</td><td>-0.3%</td></tr><tr><td>pH value (CIPAC MT)</td><td>6.19</td><td>6.01</td></tr></table>
Biocidal product is stable 14 days at 54 °C in commercial packaging.</td><td>N. COLOMBIES 2012</td></tr>
<tr><td></td><td>high temperature (40°C)
Test performed until 6 months</td><td>Former composition</td><td>After 6 months at 40°C in commercial packaging:
<table><tr><td></td><td>T0</td><td>6 M 40°C</td></tr><tr><td>Appearance</td><td colspan="2">As initial</td></tr><tr><td>Packaging</td><td colspan="2">As initial</td></tr><tr><td>Content of DEET</td><td>24.97 %</td><td>25.10 %</td></tr><tr><td>pH value</td><td>10.0</td><td>8.4</td></tr></table></td><td>Laurent E. 2012</td></tr>
</table>

<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></td><td></td><td>
<table>
<tr><td>Density</td><td>1.017</td><td>1.017</td></tr>
</table>

As this study was conducted on former composition, a new shelf life study was started on actual composition.

Considering the decrease value of pH over time, it was agreed with the applicant that pH is not representative of biocidal product. Alkalinity is followed in new shelf life study.</td><td></td></tr>
<tr><td></td><td>high temperature (40°C) Test performed until 6 months</td><td>current composition</td><td>After 6 months at 40°C in commercial packaging:

<table>
<tr><td></td><td>T0</td><td>6 M 40°C</td></tr>
<tr><td>Appearance</td><td colspan="2">As initial</td></tr>
<tr><td>Packaging</td><td colspan="2">As initial</td></tr>
<tr><td>Content of DEET</td><td>25.46 %</td><td>25.14%</td></tr>
<tr><td></td><td>variation</td><td>-1.1%</td></tr>
<tr><td>Alcalinity as NaOH 0.1 M</td><td>0.1 mL</td><td>0.1mL</td></tr>
<tr><td>Density</td><td>1.017</td><td>1.016</td></tr>
</table>

Biocidal product was demonstrated stable 6 months at 40°C.</td><td>Laurent E. 2013</td></tr>
<tr><td></td><td>3 years at ambient temperature (stopped study)</td><td>Former composition</td><td>After 1 year at 25°C in commercial packaging:

<table>
<tr><td></td><td>T0</td><td>1Y 25°C</td></tr>
<tr><td>Appearance</td><td colspan="2">As initial</td></tr>
<tr><td>Packaging</td><td colspan="2">As initial</td></tr>
<tr><td>Volume delivered by pump</td><td>0.11 mL</td><td>0.11 mL</td></tr>
<tr><td>Content of DEET</td><td>24.97 %</td><td>25.05 %</td></tr>
<tr><td></td><td>variation</td><td>+0.3%</td></tr>
</table>
</td><td>Laurent E. 2012</td></tr>
</table>

<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></td><td></td><td>
<table>
<tr><td>pH value (pHmeter)</td><td>10.0</td><td>7.6</td></tr>
<tr><td>density</td><td>1.017</td><td>1.016</td></tr>
<tr><td colspan="3">Microbial contamination</td></tr>
<tr><td>BTLM</td><td><100 UFC /mL</td><td><100 UFC /mL</td></tr>
<tr><td>DMLT</td><td><10 UFC /mL</td><td><10 UFC /mL</td></tr>
<tr><td>Pseudomonas aeruginosa</td><td>Not detected</td><td>Not detected</td></tr>
<tr><td>Staphylococcus aureus</td><td>Not detected</td><td>Not detected</td></tr>
</table>
Content of Microbial contamination are submitted are reported here but are not evaluated in biocidal product dossier.
As this study was conducted on former composition, a new shelf life study was started on actual composition.

Considering the decrease value of pH over time, it was agreed with the applicant that pH is not representative of biocidal product. Alkalinity is followed in new shelf life study.
</td><td></td></tr>
<tr><td></td><td>3 years at ambient temperature (on going study)</td><td>current composition</td><td>
After 6 months at 25°C in commercial packaging:
<table>
<tr><td></td><td>T0</td><td>6M 25°C</td></tr>
<tr><td>Appearance</td><td colspan="2">As initial</td></tr>
<tr><td>Packaging</td><td colspan="2">As initial</td></tr>
<tr><td>Volume delivered by pump</td><td>Not performed</td><td>Not performed</td></tr>
<tr><td>Content of DEET</td><td>25.46 %</td><td>25.23%</td></tr>
<tr><td>Alkalinity as NaOH 0.01M</td><td>0.1 mL</td><td>0.1 mL</td></tr>
<tr><td>density</td><td>1.016</td><td>1.016</td></tr>
<tr><td colspan="3">Microbial contamination</td></tr>
</table>
</td><td>Laurent E. 2013</td></tr>
</table>

<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></td><td></td><td>
<table>
<tr><td>BTLM</td><td><100 UFC /mL</td><td><100 UFC /mL</td></tr>
<tr><td>DMLT</td><td><10 UFC /mL</td><td><10 UFC /mL</td></tr>
<tr><td>Pseudomonas aeruginosa</td><td>Not detected</td><td>Not detected</td></tr>
<tr><td>Staphylococcus aureus</td><td>Not detected</td><td>Not detected</td></tr>
</table>
Content of Microbial contamination are submitted are reported here but are not evaluated in biocidal product dossier.
Biocidal product is stable 6 months at 25 °C
Final study including data on volume delivered by pump is required in post registration.</td><td></td></tr>
<tr><td>Effect of low temperature</td><td>CIPAC MT 39.3</td><td></td><td>Study not provided.
According to the results obtained in low temperature stability of product IE-DEET-A50 (two phases were observed after the undisturbed period and inverting the cones), applicant request a recommendation on biocidal product : “Shake before use”.
RMS agreed with this recommendation</td><td></td></tr>
<tr><td>Effects of light</td><td></td><td></td><td>Not relevant as the product is not in contact with light</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>
<tr><td>Dustiness</td><td></td><td></td><td>Data not required as the product is a ready to use spray</td><td></td></tr>
<tr><td>Attrition/friability of granules; integrity of tablets</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
Emulsifiability / Emulsion stability / Re-emulsifiability			Data not required as the product is a ready to use spray	
Stability of dilute emulsions			Data not required as the product is a ready to use spray	
Flowability			Data not required as the product is a ready to use spray	
Pourability (including rinsed residue)			Data not required as the product is a ready to use spray	
3.9 Compatibility with other products (IIB3.9/Pt. I-B3.9)			Data not required as the product is a ready to use spray	
3.10 Surface tension (Pt. I-B3.10)	OECD 115	Former composition	Surface tension of pure test item at 20°C: 33.6 mN/m Test item is surface active	B. DEMANGEL 2012
3.11 Viscosity (Pt. I-B3.10)	OECD 114	Former composition	Dynamic viscosity of pure test item: 11.89 mPa*s at 20°C 5.62 mPa*s at 40°C the test item was considered to have newtonian properties in the experimental conditions used	B. DEMANGEL 2012
3.12 Particle size distribution (Pt. I-B3.11)	CIPAC MT 187	Former composition	Particle size distribution of droplet when sprayed: Dv (1%) ≤ 18 µm Dv (10%) = 35 µm Dv (50%) = 61 µm. Dv (90%) = 102 µm	N. Rodriguez 2012
Other		Former composition	Volume delivered by pump = 0.11mL	B3.7

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

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

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

Reference: C. Chauvet 2011; DEET determination in “insecte ecran peau famille” ; report Nb1251.

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

Validation data

Linearity	Repeatability	Recovery rate (%)	Specificity
Range : 80-120% of nominal concentration n=5x3 r> 0.998	6 samples injected one time by 2 operators RSD= 0.19% and 0.36%	5 fortification levels tested 3 times in the range 80-120% of nominal value. Mean recovery (%) = 100.5% RSD= 0.22%	Chromatograms data (Dilution solvent and placebo) demonstrate that method is specific

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

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

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

Conclusion: method described in study Nb 1332 is applicable to determine DEET in INSECT ECRAN PEAU FAMILLE

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

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

2.4 Risk assessment for Physico-chemical properties

INSECT ECRAN FAMILLE 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, 6 months at 40°C and 6 months at ambient temperature in commercial packaging. A shelf life of 2 years is granted.
As no study at low temperature was submitted and, according to behaviour of another DEET biocidal product at low temperature, the following restriction is required on the label : the product must be shaken before use .

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

Risk mitigation measures linked to assessment of physico-chemical properties

The product must be shaken before use

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

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

2.5 Effectiveness against target organisms

2.5.1 Function

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

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

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

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

The application rate recommended by the applicant is the following: 0.60 mg/cm^2 of skin

It has to be noted that most of the tested arthropods are present in France and in the overseas territories:
- *Aedes aegypti (stegomya aegypti)*: this species occurs in the Reunion, Mayotte, Guadeloupe, Martinique islands and in Guyane. This species is a vector of Dengue and Chikungunya notably in the French Antilles.
- *Aedes albopictus*: this species occurs in the Indian Ocean, including Reunion island, and Southern Europe, including France. This species is a vector of Dengue and Chikungunya notably in the French Antilles.
- *Anopheles gambiae*: this species is a vector of malaria (paludism), in tropical areas.
- *Culex pipiens*: mosquitoes of the Culex genus are the most present in France. It is a vector of diseases, such as Japanese encephalitis, meningitis, and West Nile fever.
- *Phlebotomus duboscqi*: This species is found in Sub-Saharan Africa. It is not present in France or in overseas territories. However, the species *P. papatasi*, very close to P*. duboscqi*, and convey the same cutaneous leishmaniasis, is present in France, from the Mediterranean to the Cevennes.
- *Ixodes ricinus*: this tick species is present in Central Europe and in the North-East of France. It is a vector of Lyme disease in France.

2.5.3 Effects on target organisms and efficacy

The applicant submitted following studies:

For the use against mosquitoes and sand flies:

- An arm-in-cage study conducted with ten human volunteers with the product **INSECT ECRAN FAMILLE** (25 % w/w DEET) on four mosquito species ***(Aedes aegypti, Anopheles gambiae, Aedes albopictus*** *and* ***Culex pipiens)*** and one sand fly specie ***(Phlebotomus duboscqi)****.*

The duration of efficacy of the product INSECT ECRAN FAMILLE (liquid, DEET 25 % w/w) was tested under laboratory conditions against 4 mosquito species: *Culex pipiens, Aedes albopictus, Aedes aegypti and Anopheles gambiae,* and one sand fly specie: *Phlebotomus duboscqi*.
The product was sprayed at the dose of 0.6 mg/cm² i.e. 0.15 mg/cm² of deet on the forearm. The trial began 30 minutes after the product had been applied. The control forearm was inserted into the cage, and after validation of this control (10 landings), the treated forearm was inserted into the cage for 3 min every hour until 5 hours then every 30 minutes until 6.5 hours or inefficacy considered as the first bite followed by a second one within 30 min.
The time of protection is up to on average 5 hours for the 4 mosquito species and for the sand fly specie.

- An arm-in-cage study conducted with ten human volunteers with the product **INSECT ECRAN FAMILLE** (25 % w/w DEET) diluted at 15 % w/w, on two mosquito species ***(Aedes aegypti*** and ***Anopheles gambiae)****.*

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

The product was sprayed at the dose of 0.60 mg/cm² i.e. 0.09 mg/cm² of DEET on the forearm. The trial began 30 minutes after the product had been applied. The control forearm was inserted into the cage, and after validation of this control (10 landings), the treated forearm was inserted into the cage for 3 min every ½ hour until 1.5 hours or inefficacy considered as the first bite followed by a second one within 30 min.
As concluded by the applicant, the product containing 15 % w/w DEET hasn't provided any protection (0.1 hour protection for both species).

Based on these laboratory efficacy data, the time of protection of the product INSECT ECRAN FAMILLE when used at a dose of 0.60 mg/cm^2 of skin is up to 5 hours for the 4 mosquito species: *Culex pipiens, Aedes albopictus, Aedes aegypti* and *Anopheles gambiae,* and the sand fly: *Phlebotomus duboscqi*.

Furthermore, no field studies have been submitted in support of this authorisation. As under field conditions, many factors can influence and even decrease the protection observed in the laboratory: over sweat due to high temperature, aggressiveness of wild mosquitoes compare to laboratory colonies; this kind of tests should have been performed especially to prove the effectiveness of this product in the French overseas regions.
Moreover, the TNsG on product evaluation (PT18 and 19) and the WHO guidelines require field trials to confirm the effectiveness of repellents in real in use-conditions.
To confirm this approach, FR CA has launched a European consultation. Most of the consulted member States think that field tests are not mandatory. Given the available literature on the active substance DEET and for reasons of standardization of testing and ethics, new field trials would not be justified. Based on the results of this consultation, FR CA agrees to consider the data presented as sufficient to demonstrate the efficacy of the product INSECT ECRAN FAMILLE (25 % w/w DEET).

In addition, the applicant has also provided a scientific review about efficacy of a similar product with 50 % w/w DEET concentration performed at a dose of 0.11 mg of DEET/cm^2 in field conditions on Anopheles in Cameroun. This product provided 86 % protection against *Anopheles gambiae* during 5 hours.

For the use against ticks:

- A laboratory study conducted with ten human volunteers with the product **INSECT ECRAN FAMILLE** (25 % m/m DEET) on one tick specie ***(Ixodes ricinus)***.

The repellent efficacy of the product INSECT ECRAN FAMILLE (DEET 25 % w/w) was tested against nymphs of *Ixodes ricinus* ticks by 10 volunteers. The product was applied with a pipette and spread on one forearm of each volunteer, except on the lowest 5 cm near the wrist. The arm was held vertically (with the fingertips or palm placed on a horizontal surface. Ticks were placed on this untreated area, 3 cm below the treated area, and observed for a maximum of 3 minutes. The test lasted for 8 hours post application, with 10 ticks tested per hour and per volunteer (5 ticks every 30 minutes).
According to the applicant, all ticks crawling onto the treated area, crossing the second mark in direction to the elbow (3 cm above the border), and spending at least 60 seconds onto the treated zone were considered "not repelled". All other ticks were considered "repelled".

Criteria of the TNsG on product evaluation (PT18 and 19) are not very precise concerning whether or not a tick is repelled. Indeed, according to the TNsG, a tick is considered as non-repelled if it crosses the line 3 cm above the wrist or a tick is considered repelled when it drops down from the arm. The laboratory followed the criteria mentioned in the EPA guideline. But this guideline says that:
- a tick is considered as repelled if:
    - it not crosses into the treated area
    - it crawls into the treated area but immediately turns back or falls off
- a tick is considered as not repelled if it crosses the boundary line at least 3 cm into the treated area within 3 minutes, and remains in the treated area for at least one minute.

This guideline doesn't mention for example how to consider a tick that crosses the boundary line but not at least 3 cm into the treated area within 3 minutes, and remains in the treated area for at least one minute. The laboratory proposes to include this case in the "repelled ticks", but we could consider that if a tick stays for at least one minute in a treated area, this tick could be considered as not repelled.
FR CA decided to follow the recommendation of the EPA guideline and so considers that a tick is repelled only if it not crosses into the treated area or it crawls into the treated area but immediately turns back or falls off.
This approach doesn't modify much the laboratory's results.

The product INSECT ECRAN FAMILLE (DEET 25 % w/w) when used at a dose of 0.42 mg/cm^2 of skin provides up to 4 hours protection time against *Ixodes ricinus* (instead of 5 hours concluded by the laboratory).

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

All efficacy studies are presented in annex 3.

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*.[5] show that deet is not simply a behaviour-modifying chemical but that it also inhibits cholinesterase activity, in both insect and mammalian neuronal preparations. DEET is commonly used in combination with insecticides and Corbel *et al* show that DEET has the capacity to strengthen the toxicity of carbamates, a class of insecticides known to block acetylcholinesterase.
In 2011, Lavialle-Defaix *et al*.[6] 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.*[7] wrote an article on a laboratory evaluation of toxicity of sixteen commercial insect repellents (6 botanical and l0 synthetic organic products) in aerosol sprays to adult mosquitoes. These repellents (including 8 insect repellent products containing 6.65 to 38% of DEET) were evaluated in the laboratory for adult knockdown (KD) and mortality of laboratory-reared female *Aedes aegypti*, *Aedes albopictus*, and *Anopheles quadrimaculatus*. All tested formulations except 2 botanical repellent products caused 100% 24-h mortality of *Ae. aegypti* and all but 1 caused 100% 24-h mortality of *Ae. albopictus* and *An. quadrimaculatus*.
In 2006, Licciardi *et al.*[8] 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).

[5] V.Corbel, M. Stankiewicz, C. Pennetier, D. Fournier, J. Stojan, E. Girard, M. Dimitrov, J. Molgó, J-M. Hougard, B. Lapied, *Evidence for inhibition of cholinesterases in insect and mammalian nervous systems by the insect repellent deet*, *BMC Biology* 2009, **7**:47.
[6] C. Lavialle-Defaix, V.Apaire-Marchais, C. Legros, C. Pennetier, A. Mohamed, P. Licznar, V. Corbel, B.Lapied, *Anopheles gambiae mosquito isolated neurons: A new biological model for optimizing insecticide/repellent efficacy*, Journal of Neuroscience Methods, 200 (2011) 68-73
[7] 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
[8] 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

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*[9]*.* 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 INSECT ECRAN FAMILLE (DEET 25 % w/w) provides a protection time up to 5 hours when used on skin at the application rate of 0.60 mg/cm² against four representative species of mosquitoes (*Culex pipiens, Aedes albopictus, Aedes aegypti and Anopheles gambiae*) and one sand fly (*Phlebotomus duboscqi*) and, up to 4 hours when used on skin at an application rate of 0.42 mg/cm², against the tick *Ixodes ricinus*.

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

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

The application rates validated are the following:

Mosquitoes (*Aedes*, A*nopheles* and *Culex* genus) and sand flies (*Phlebotomus* genus): 0.60 mg/cm^2 of skin
Ticks (*Ixodes* genus): 0.42 mg/cm^2 of skin

2.5.7 Conclusion of the efficacy assessment

The product INSECT ECRAN FAMILLE 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

[9] 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.

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[10].
- 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*	0.60 mg/cm^2 of skin, protection up to 5 hours
	Repellent against sand flies *Phlebotomus duboscqi*	
	Repellent against ticks *Ixodes ricinus*	0.42 mg/cm^2 of skin, protection up to 4 hours

Method of application

[10] 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.

The product INSECT ECRAN FAMILLE is an insect repellent lotion containing 25 % w/w DEET as active substance and intended to be applied on human skin to repel mosquitoes, sand flies and ticks.
The product is sprayed in the hand and then spread on the exposed area of the skin (*i.e.* face, neck, three quarter arms, hands and half-legs) to protect people .
Since the product is formulated as a ready-for-use product, no dilution or other preparation is necessary.

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*", INSECT ECRAN FAMILLE 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 product was not a dummy product in the EU- review program for inclusion of the active substance in Annex I of Directive 98/8/EC.

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

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

2.7.1.3.1 Percutaneous absorption

The dermal absorption of DEET formulated in INSECT ECRAN FAMILLE (old formulation containing analyzed 24.05-25.71% w/w DEET) was investigated using human skin *in vitro*. A concentration of 25.71% was used to calculate absorption of DEET through the skin. The average percentage of potentially absorbed DEET (total % at dose site without tape strips 1&2 + total % directly absorbed (receptor fluid + receptor fluid terminal + receptor chamber)) was 44±10% and the total recovery of DEET was 102±4.6% when skin discs were exposed for 24 hours to 6.4 µL of INSECT ECRAN FAMILLE corresponding to 2.4-2.5 mg a.s/cm^2.

2.7.1.3.2 Acute toxicity

ORAL ROUTE:

Route	**Method Guideline**	**Test material**	**Species, Strain Sex, no/group**	**dose levels**	**Value LD_{50}**	**Reference**
Oral	OECD 423	IE-DEET-F25 (old formulation)	Sprague Dawley 6 Females	2000mg/kg bw	> 2000mg/kg bw	Richeux. F. 2012
No mortality occurred during the study. It was noted a decrease in spontaneous activity (3/6), myosis (3/6) and noisy breathing (1/6) during the first hours of the test. No clinical signs related to the administration of the test item were observed from 24 hours post dose.						
Acceptable: Yes						

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

DERMAL ROUTE:

Route	**Method Guideline**	**Test material**	**Species, Strain Sex, no/group**	**dose levels**	**Value LD_{50}**	**Reference**
Dermal	OECD 402	IE-DEET-F25 (old formulation)	Sprague Dawley 5 males/5 females	2000mg/kg bw	> 2000mg/kg bw	Richeux. F. 2012
No mortality occurred during the study. Neither cutaneous reactions nor systemic clinical signs related to the administration of the test item were observed. An erythema was noted only in one animal at 48 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.						
Acceptable: Yes						

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

INHALATION ROUTE:

No study was performed on the product. Considering the intended use and that only 1% of particles were inferior to 18 µm, exposure via inhalation route is considered negligible compared to dermal exposure to INSECT ECRAN FAMILLE.

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

2.7.1.3.3 Irritation and corrosivity

SKIN IRRITATION:

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

Species	**Method**	**Test material**	**Result**	**Reference**
Adult human volunteers 8 females, 15 males (18-32 years, phototype III/IV)	Patch-test 48 hours, semi-occlusive	INSECT ECRAN FAMILLE SANS CONSERVATEUR (old formulation) 60 µl pure spray	IICM (mean cumulative irritation index) = 0.01 Not irritant	Ben Ammar F. 2010
Acceptable : yes.				

Considering the results above, no classification is proposed for this endpoint for INSECT ECRAN FAMILLE.

EYE IRRITATION TEST:

The first test performed with the old formulation of INSECT ECRAN FAMILLE results in irreversible ocular lesions. Reversible eye irritation was observed when the test was performed with the current formulation of INSECT ECRAN FAMILLE.

Species	**Method**	**Test material**	**Average Score (24h, 48h, 72h)**				**Result**	**Reversibility yes/no**	**Reference**
			Cornea	Iris	Redness Conjunctiva	Chemosis			
Albino NZW rabbit 3 females	OECD 405	IE-DEET-F25 (old formulation)	2	0.6	2.7	2.3	Irreversible irritation	Opacity remaining on D21 in one animal. Corneal neovascularisation in one animal on D21.	Richeux. F. 2012
Albino NZW rabbit 3 females	OECD 405	IE-DEET-F25-NF (current formulation)	1.2	0	1.1	1.4	Irritant	7 days after instillation, no ocular reaction persisted in any animal.	Gitton. I. 2012
Acceptable: Yes									

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

2.7.1.3.4 Sensitisation

Species	**Method**	**Number of animals sensitized/total**	**Result**	**Reference**

		number of animals		
Dunkin, Hartley guinea pigs 15 females	OECD 406 (guinea pig maximisation test) IE-DEET-F25 (old formulation) Intradermal injection: 6.25% Epicutaneous induction: 100% Challenge: 100% - 50%	20%, 24 hours after 100% challenge only	Not sensitizing	Richeux. F. 2012
Acceptable: Yes Positive control studies are regularly performed on guinea pigs with α-hexylcinnamaldehyde				

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

2.7.1.3.5 Other studies

An *in vitro* tool for measuring taste (Astree Electronic Tongue) was submitted by the applicant. This assay showed that optimum denatonium benzoate concentrations that can match the taste of INSECT ECRAN FAMILLE (current formulation) spray were estimated at a level greater than 0.020 mg/mL (0.002% - 20 ppm), which could be considered as bitter enough to induce aversion.

2.7.2 Human exposure assessment

INSECT ECRAN FAMILLE is a ready-to-use product containing 25% DEET as active substance and intended to be applied to human skin. The intended use is the dermal spraying on adults and children from 6 year-old. The applicant considers that the product can be used by pregnant women in case of risk of disease transmission. According to the applicant, one application per day must not be exceeded.

MG/PT	Field of uses envisaged	Likely concentrations at which a.s. will be used
Main Group 03; Pest Control PT19: Repellents and attractants	Professional uses	
	No	Not relevant
	Non-professional uses	
	Repellent for use by consumers (non-professional users/adults and children, dermal application) against arthropods' attacks (mosquitoes, ticks and sand flies).	25% (w/w)

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

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

Inhalation exposure:

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

Based on a study, the mass median aerodynamic diameter (MMAD) of the aerosol droplets generated by INSECT ECRAN FAMILLE is 61 µm. Only 10% of particles were < 35 µm and 1% < 18 µm.

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

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

Oral exposure:

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

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

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

Dermal exposure:

Dermal exposure is the primary route of exposure as the product is directly applied to the skin. According to the applicant, the product can be used on children from 6 year-old. In this context, the assessment of the scenario of a person who applies the product on another person is considered as relevant in order to consider a parent applying the product on his/her children.

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

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

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

2.7.2.2.2 Exposure of non-professional users

Primary exposure to INSECT ECRAN FAMILLE consists on the application of the product by spraying.

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

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

Tier	Inhalation exposure – amount of substance mainly swallowed
Without PPE	Systemic dose
	mg a.s. / kg bw /day
Task – time frame:	**Scenario : exposure during application – one application**
Adult woman	4.48×10^{-4}
Adult man	3.70×10^{-4}
9 -14 years-old	5.34×10^{-4}
3 – 9 years-old	6.71×10^{-4}

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

The exposure by dermal route was calculated according to the following equation:

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

where:

ID	Internal dose (mg/kg b.w./day)
AR_p	Average dose of product applied on skin (mg/cm²)
C_{DEET}	Average concentration of substance in product (%)
BS	Body surface exposed to the product (cm²)
DA	Dermal absorption (%)
N	Number of product application per day (/day)
BW	Body weight (kg)

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

The product is not intended to be applied on the total body surface but on the following body segments which correspond to uncovered parts: head + neck + ¾ arms + ½ legs + hands.
According to the applicant, one application per day must not be exceeded.

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

Parameter	Value	Source
Average dose of product applied on skin (mg/cm²)	0.6	Applicant data
Average concentration of substance in product	25 % w/w	Applicant data
Body surface exposed to the	See Table below	RIVM General Fact Sheet

product (cm²)		
Dermal absorption (%)	44	See IIIB6.4
Number of product applications per day (/day)	1	Applicant data
Body weight (%)	See Table below	RIVM General Fact Sheet

Table 2.7.2.2.2-2: Results of exposure by dermal route after application of INSECT ECRAN FAMILLE at 0.6 mg/cm^2

	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 mg/kg
man	7215	74	4329.0	25	1082.3	44	476.2	6.4
woman	6451	61	3870.6	25	967.7	44	425.8	7.0
9-14 years-old	5361	39,3	3216.6	25	804.2	44	353.8	9.0
3-9 years-old (mean 6.5 years-old)	3544	20.6	2126.4	25	531.6	44	233.9	11.4

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 behaviour

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

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

Parameter	Value	Source
Average dose of product applied on skin (mg/cm^2)	0.6	Applicant data
Average concentration of substance in product	25% w/w	Applicant data
Number of application per day	1	Applicant data
Surface of one hand	See Table below	RIVM General Fact Sheet
Oral absorption (%)	100	Assessment Report
Body weight (%)	See Table below	RIVM General Fact Sheet

The results are summarized in the table below.

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

	Surface of one hand (cm^2)	Body weight (kg)	AEL (mg/kg bw/day)	mass of substance active needed to reach the AEL (mg)	mass of product needed to reach the AEL (mg)	Skin surface put in the mouth needed to reach the AEL (cm^2)	Hand surface put in the mouth to reach the AEL (%)
man	468	74	0.75	55.5	222	370	79
woman	411.5	61	0.75	45.8	183	305	74
9-14 years-old (mean 6.5 years-old)	373.4	39.3	0.75	29.5	117.9	197	53
3-9 years-old	231.3	20.6	0.75	15.5	61.8	103	45

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 79% (man) or 74% (woman) of the surface of one hand of an adult. For children, the lowest percentage of hand surface to put in the mouth to reach the AEL is 45% (child 3-9 years old) or 53% (child 9-14 years old) of the surface of one hand.

2.7.2.4 Indirect exposure via residues in food

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

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

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

INSECT ECRAN - FAMILLE = IE-DEET-F25									
TP19									
PB-12-00195									
COOPERATION PHARMACEUTIQUE FRANCAISE									
Product application rate (mg product/cm²) (effective)	0,6								
Concentration (a.s in % w/w in the product)	25								
Applicated active substance (mg a.s/cm²) (effective)	0,150								
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)								70,2	61,7
transfer factor (hand to food) in %								100	
transfer factor (food to mouth) in %								100	
ingested a.s in mg and per application								70,2	61,7
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								0,9	1,0
Proposed restriction : handwash after use (i.e rinsing factor)								3	
% of ARfD (per application)								126	135
% of ARfD (per application) including hand washing								42	45
Exposure (in %) according to proposed statements proposed on the label : - no application on children's hand - washing hands for adults after each application								42	45

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[11]. This dilution factor is not deemed to be an overestimation according to physico-chemical properties of the active substance with water :

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

Resulted acute exposure is below 100% for adults. 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.[12]

U.S. EPA label requirements state that[13] :

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

Consequently

Following assessment based on supported uses for the product INSECT INSECT ECRAN FAMILLE 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

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

The secondary exposure by oral route cannot be combined to exposure by dermal route, considering that it is more appropriate to compare the relevant routes for human exposure to the AELs derived for the corresponding specific routes. Indeed, according to the CAR for DEET and the final minutes of TMII09, the dermal rat study is considered as the most appropriate study to set the $AEL_{repeated}$ since the dermal route is the relevant one for human exposure to DEET. In addition, since child poisoning

[11] 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

[12] 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

[13] 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

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

	Systemic exposure active substance mg/kg	AEL (mg/kg/d)	% AEL (%)	Number of acceptable applications per day
man	6.4	8.2	78	1
woman	7.0	8.2	85	1
9-14 years-old	9.0	8.2	110	<1
3 – 9 years-old (mean 6.5 years-old)	11.4	8.2	138	<1

The results show that the % AEL for adults is below 100 %. The risk is thus acceptable for adult consumers using the product INSECT ECRAN FAMILLE once a day.

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

However, the % AEL for children from 6 years of age (as recommended in the product label) is above 100 %. The risk is thus unacceptable for children from 6 years of age using the product INSECT ECRAN FAMILLE once a day.

In this context, the assessment of the scenario of a person applying the product on another person is considered as non relevant due to the unacceptable risk observed with children from 6 years-old.

2.7.3.2 Risk for indirect exposure

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

Risk for combined exposure

The assessment of the scenario of a person applying the product on another person is considered as non relevant due to the unacceptable risk observed with children from 6 years-old.

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.

2.7.3.3 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 INSECT ECRAN FAMILLE 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 INSECT ECRAN FAMILLE is unlikely to cause a significant dietary risk to the adults.

2.7.3.4 Conclusion of risks assessment for human health

Acceptable risk was identified for male and female adults using the product INSECT ECRAN FAMILLE once a day. Unacceptable risk was identified for children.

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

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

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

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

Denatonium benzoate is used in the biocidal product as bittering agent. This substance is classified as “Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment” in the frame of the Directive 91/414/EEC. Nevertheless at the concentration used in INSECT ECRAN FAMILLE, 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 INSECT ECRAN FAMILLE 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

Refer to section 2.8.2.1.1

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 INSECT ECRAN FAMILLE containing 25% DEET is used in personal insect repellent (PT19) that is applied on uncovered **human skin**. It is sprayed in the hand and then spread on the exposed area of the skin (*i.e.* face, neck, three-quarter arms, hands and half-legs). The recommended application rate is **0.6 mg product.cm^{-2}** of skin, without exceeding one application per day. The resistance of the product to water has not been demonstrated, therefore it is not recommended to use the product before bathing or showering.

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

The direct outdoor emissions to surface water *via* some direct flow of DEET from skin during direct contact with water while swimming can be assumed. The recommendations proposed by the applicant (it is not recommended to use the product before bathing or showering) can not be considered sufficient to waive the evaluation of direct contamination of the water compartement ; this route of direct entry in the aquatic compartment must be assessed.

For both routes (direct and indirect), sediment compartment is not considered as relevant for DEET due to its low adsoprtion potential (log Pow<3).

In the following sections, PEC values for indirect exposure are derived by using the Emission Scenario Document (ESD) for PT01 (Human hygiene products)[14] 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[15]) 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”)

<u>Consumption based approach for PEC STP, surface water, soil</u>

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)

[14] Environmental Emission Scenarios for biocides used as human hygiene biocidal products (Product type 1). European Commission DG ENV/RIVM. January 2004.

[15] 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

Finh	Fraction of inhabitants using an insect repellent (CAR value = 0.37)
F_{water}	Fraction released to wastewater during skin cleaning (adapted CAR value for DEET applied on skin only = 0.865)
$Qform_{inh}$	Consumption per inhabitant per day ($g.day^{-1}$; Nappl * $Qform_{appl}$ * BS)
$Cform_{weight}$	Concentration of the active substance in the product (specific value for INSECT ECRAN FAMILLE = 250 $g.kg^{-1}$)
Fpenetr	Market share for DEET-containing repellent products (CAR value for DEET based products = 0.28)
Nappl	Number of applications (specific value for INSECT ECRAN FAMILLE = $1.day^{-1}$)
$Qform_{appl}$	Consumption per application (specific value for INSECT ECRAN FAMILLE = 0.6 mg $product.cm^{-2}$)
BS	Body surface treated (7215 cm^2; see Human Exposure Section)

According to the survey presented in the CAR regarding the uses of DEET based products (Boomsma and Parathasarathy, 1990), 37% (*Finh* 0.37) of the population use an insect repellent. This value was applied to carry out the risk assessment of the representative product presented to support DEET inclusion. It is therefore considered also applicable to INSECT ECRAN FAMILLE. 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 INSECT ECRAN FAMILLE. The evaporation and the dermal absorption rates reported in the CAR (5% and 9% respectively) are subtracted from the total amount of DEET applied. In fact, since the product INSECT ECRAN FAMILLE is used on skin only, applications on clothes are not considered and the emission reduction due to dermal penetration can be applied on the total quantity of INSECT ECRAN FAMILLE used. 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 INSECT ECRAN FAMILLE (44%; see toxicology section) represents a worst case approach for the environmental exposure assessment.

The applicant supplied a document justifying the use of a market share (Fpenetr) specific to INSECT ECRAN FAMILLE 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 INSECT ECRAN FAMILLE ($Qform_{appl}$ × $Cform_{weight}$ × BS x 10^{-6}= 1.08 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 75^{th} percentile of dermal exposure estimated for subgroups (for instance male adult, female adult, children...), since this value is more relevant in the context of the environmental exposure assessment conducted at the STP scale. However, it was verified that the estimation of emissions using the 75^{th} percentile approach (1.5 g or 1.66 g of DEET per skin application for male adult or children respectively), and 1 application per day as a mean application rate, led to the same conclusions.

Then,

$Elocal_{water}$ = 0.97 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,

$Clocal_{inf}$ = 0.48 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:		**Value**	**Unit**	**Reference**
INPUTS				
$Elocal_{water}$	Emission rate to wastewater	0.97	[$kg.d^{-1}$]	-
$Clocal_{inf}$	Concentration in sewage water to default STP	0.48	[$mg.L^{-1}$]	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
OUTPUTS				
PEC_{STP}	PEC in the treated wastewater	6.11E-02	[$mg.L^{-1}$]	TGD Eq. 33
$PEClocal_{water}$	PEC in water during emission episode	6.11E-03	[$mg.L^{-1}$]	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

Local emission of active substance to soil during episode:		**Value**	**Unit**	**Reference**
INPUTS				
$Elocal_{water}$	Emission rate to wastewater	0.97	$[kg.d^{-1}]$	-
$Fstp_{\ sludge}$	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
OUTPUTS				
Csludge	Concentration in dry sewage sludge	5.56	$[mg.kg^{-1}_{dwt}]$	TGD Eq. 36
PEC local soil	PEC in soil after 10 years of application - Twa over 30 d	5.76E-03	$[mg.kg^{-1}_{wwt}]$	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. Modelling is based on the annual tonnage of DEET placed on the EU market as proposed in the CAR for the active substance inclusion, given that it was verified that the annual tonnage of DEET placed on the French market (representing 3 EU regions) is covered by the EU tonnage considered in the CAR.

A tonnage approach has been favored for groundwater compared to a consumption approach for different reasons. The consumption approach represents a peak of release with worst case assumptions which can be considered realistic in case of daily emission to environmental compartments (surface water downstream the STP for instance). Nevertheless, sludge applied as a soil enrichment product is collected in the STP over weeks or months. This matter is stored and sometimes mixed with other additives (for instance during composting). However, no dilution or degradation can be taken into account in the exposure calculations without validated data. The actual assessment model probably overestimates the concentration of DEET in sludge at the time of land spreading considering the ready biodegradability property of the substance. It was therefore considered more relevant to follow a tonnage approach that allows taking into consideration a mean emission to the sludge which seems more realistic for exposure of groundwater.

The model used, input data and assumptions presented below are chosen according to DE proposals (Klein, 2011[16]). 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 Table 2.8.4.2-5 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

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

[16] 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

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 recreational activities has been proposed by the applicant in the product authorisation dossier, as a harmonized approach does not exist yet for this type of exposure. In the frame of the review program of the active substance, the direct release to surface water during swimming etc. was also not considered on reasons of missing scenario and the issue reported to the authorisation phase. A "swimming scenario" was therefore developed by the German Federal Environment Agency. This scenario is still under discussion after its presentation during the TM II/2011.

The proposed emission calculation is based on equations of EU TGD II (2003) and on the specific scenario developed by DE that simulates the release of active substance into natural and artificial lakes by swimming of people treated with a PT19 biocidal product. Some modifications of the receiving aquatic compartment volume and the number of swimmers are further proposed for the assessment of the product INSECT ECRAN FAMILLE 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 INSECT ECRAN FAMILLE 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[17,18], 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.

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

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

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 INSECT ECRAN FAMILLE 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 INSECT ECRAN FAMILLE = 250 g.kg^{-1})
Nappl	Number of applications (specific value for INSECT ECRAN FAMILLE = 1 day^{-1})
$Qform_{appl}$	Consumption per application (specific value for INSECT ECRAN FAMILLE = 0.6 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,

$$\mathbf{Elocal_{water} = 7.56E\text{-}02\ kg\ DEET.d^{-1}}$$

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,

$$\mathbf{Clocal_{water} = 1.08E\text{-}03\ mg\ DEET.L^{-1}}$$

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,

$$\mathbf{Clocal_{water\_annual} = 1.40E\text{-}03\ mg\ DEET.L^{-1}}$$

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,

$$\mathbf{Total\ Clocal_{water} = 2.48E\text{-}03\ mg\ DEET.L^{-1}}$$

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)		
STP	6.11E-02	[$mg.L^{-1}$]
Surface water	6.11E-03	[$mg.L^{-1}$]
Direct emissions (Swimming scenario)		
Surface water – $Clocal_{water}$ *Short term assessment in the bathing area*	1.08E-03	[$mg.L^{-1}$]
Surface water – $Clocal_{water\_annual}$ *Long term assessment in the lake*	1.40E-03	[$mg.L^{-1}$]
Surface water – Total Clocalwater *Cumulative assessment*	2.48E-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)		
Soil	5.76E-03	[$mg.kg^{-1}_{wwt}$]
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 INSECT ECRAN FAMILLE 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)

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

Table 2.8.5.1-1: Risk characterization in the aquatic compartment

	PEC ($mg.L^{-1}$)	**PEC/PNEC**
Indirect emissions (*via* the STP)		
STP	$PNEC_{STP\ microorganisms}$ = 10 $mg.L^{-1}$	
	6.11E-02	6.11E-03
Surface water	$PNEC_{water}$ = 0.043 mg/L	
	6.11E-03	0.14
Direct emissions (swimming scenario)		
Surface water	$PNEC_{water}$ = 0.043 $mg.L^{-1}$	
Short term assessment in the bathing area	1.08E-03	2.51E-02
Long term assessment in the lake	1.40E-03	3.26E-02
Cumulative assessment	2.48E-03	5.77E-02

The PEC/PNEC ratios are all below the trigger value of 1. Then, risks for aquatic organisms and for STP microorganisms are acceptable for both indirect and direct emissions and after 1 daily skin application of INSECT ECRAN FAMILLE at 0.6 $mg.cm^{-2}$.

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	PEC/PNEC
Indirect emissions (via the STP)		
Soil	$PNEC_{soilEP}$ = 0.0379 $mg.kg^{-1}_{wwt}$	
	5.76E-02	0.15
Groundwater	< 0.1 ($\mu g.L^{-1}$) Threshold value in groundwater	

The PEC/PNEC ratio for soil compartment is below the trigger value of 1. Then, risks for terrestrial organisms are acceptable after 1 daily skin application of INSECT ECRAN FAMILLE at 0.6 $mg.cm^{-2}$.
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 $\mu g.L^{-1}$ (CAR, 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 INSECT ECRAN FAMILLE, risks for aquatic (including waterand STP), soil and groundwater compartments are acceptable.

Considering direct emissions through bathing activities and according to the applicant intended uses for INSECT ECRAN FAMILLE, 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 INSECT ECRAN FAMILLE.

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

Risk assessment for Physico-chemical properties

INSECT ECRAN FAMILLE 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, 6 months at 40°C and 6 months at ambient temperature in commercial packaging. A shelf life of 2 years is granted.

As no study at low temperature was submitted and, according to behaviour of another DEET biocidal product at low temperature, the following restriction is required on the label : the product must be shaken before use .

Summary of efficacy assessment

The product INSECT ECRAN FAMILLE 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

Acceptable risk was identified for male and female adults using the product INSECT ECRAN FAMILLE once a day. Unacceptable risk was identified for children.

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

Based on the reverse scenario calculation and the presence of bittering agent in the product, adults and children with hand-to-mouth behaviour are not at significant risk of poisoning.
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 INSECT ECRAN FAMILLE 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 INSECT ECRAN FAMILLE, risks for aquatic (including water and STP), soil and groundwater are acceptable.

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

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

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

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
- The product must not be stored more than 6 months at 40°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[19].
- 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
- Wash the palm of hands after application

[19] 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.

- 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.

Formulation: INSECT ECRAN FAMILLE		**Name of the product and type of formulation (gel, paste, spray, dust, powder, …)**
I.3.12.1 Culicidae II.1.5 Adults	I.1.1.1 Ixodidae II.1.3 Nymphs II.1.5 Adults	**Target organisms (common species and genus) and development stages (larvae, nymph, adults, female or male…)***
	V.1 Non professional user / consumer	**User category (professional/non professional)***
	VII.2 Health protection (human)	**Application aim (human or animal protection)**
	IV.3 Use on skin	**Area of use (dermal, clothes, indoor or outdoor buildings…)**
	VI.1 Spraying	**Method of application including description of system used**
	0,6 mg/cm² Max 1 application per day	**Application rate (expressed in g/m^3, g/m^2, ml/m^2…)** **Maximum and minimum dosage (if appropriate)**
III.4.2 Residual activity (long time effect)	III.2.6 Repellent	**Mode of action including time delay (repellent or attractant)**
	Not applicable	**Time delay of residual efficacy (hours, days, weeks and months)**
	Not appropriate	**Time delay for human , food and animals reentrance after treatment (if appropriate)**
Number of applications : max 1 per day	Duration of efficacy : 5 hours	**Frequency and duration of application (number of application, time between each application…)**
	Yes	**Package details : Individual packaging (yes/no)****
	Polypropylene bottle	**Primary packaging : type : bulk, individual wrapping…/ nature: bucket, bottle, sachet…/ material: paper, polyethylene…/**
250 mL bottle filled in with 200 mL of product	125 mL bottle filled in with 100 mL of product	**Size of each packaging**
	None	**Secondary packaging**

I.3.12.4
Psychodidae
II.1.5 Adults

Time delay :
none

Annex 0b: Proposed uses for authorisation

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

Users	Field of uses envisaged	Likely doses at which product will be used
Public - Adults only	Repellent against mosquitoes *Aedes aegypti, Anopheles gambiae, Aedes albopictus* and *Culex pipiens*	0.60 mg/cm^2 of skin, protection up to 5 hours Max. one application per day
	Repellent against sand flies *Phlebotomus duboscqi*	
	Repellent against ticks *Ixodes ricinus*	0.42 mg/cm^2 of skin, protection up to 4 hours Max. one application per day

Annex 1: Summary of product characteristics

See separated file.

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 B3.5 B3.7.1	B3.1	Colombies N.	2012	Physico-chemical tests and analyses before and after an accelerated storage procedure for 14 days at 54 ± 2°C on IE-DEET-F25 Défitraces, Report No.12-903055-005	COOPER		**X**	**X**	
B3.2 B3.3 B3.4 B3.6	B3.2	Detrimont H., Ambrosi D.	2012	Literature survey on explosive properties, oxidising properties, auto-flammability of the ingredients of the product IE-DEET-F25 A.S.C. Report No.11/35-2	COOPER		**X**	**X**	
B3.4 B3.10 B3.11	B3.4	Demangel B.	2012	Physico chemical tests on IE-DEET-F25: relative density, surface tension, flash point, viscosity and DSC, Défitraces Report No.12-903055-003	COOPER		**X**	**X**	
B3.7.2	B3.7.2	Laurent E.	2012	Insect Ecran Famille, Etude de stabilité ICH, Cooper, Study No. 1437	COOPER		**X**	**X**	
B3.12	B3.12	Rodriguez N.	2012	Determination of the Particle Size Distribution for IE-DEET-F25 in 100 mL PP bottles with PP Spray Head, Biogenius, Study number Mo4361	COOPER		**X**	**X**	
Method validation						**Yes**	**No**	**Yes**	**No**
B4.1	B4.1/01	Cooper	2011	Insect Ecran, répulsif peau famille (IE-DEET-F25), CCOPER analytical method No. CHM-INS008 Revision No.3 – Revision date 09/01/2012	COOPER		**X**	**X**	
B4.1	B4.1/02	Chauvet C.	2012	DEET determination in "Insect Ecran peau famlle", validation of HPLC analysis technique, Cooper, Report No.1251	COOPER		**X**	**X**	

Efficacy						**Yes**	**No**	**Yes**	**No**
B5.8 B5.11	B5.8/01	Maibach *et al.*	1974	Use of insect repellents for maximum efficacy, Archives of Dermatological Research, Vol. 109, No. 19, pp. 32-35	Public Domain		**X**		**X**
B5.8 B5.11	B5.8/02	Syed and Leal	2008	Mosquitoes smell and avoid the insect repellent DEET, Proceedings of the National Academy of Science (PNAS), Early edition	Public Domain		**X**		**X**
B5.8 B5.11	B5.8/03	Stanczyk *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 Science (PNAS), Vol. 107, No. 19, pp. 8575-8580	Public Domain		**X**		**X**
B5.10	B5.10/01	Serrano B.	2012	Laboratory trial evaluating an arthropod repellent lotion, Laboratoire TEC, Assay No. 1491b/0212	COOPER		**X**	**X**	
B5.10	B5.10/02	Serrano B.	2012	Laboratory trial evaluating an arthropod repellent lotion, Laboratoire TEC, Trial No. 1491e/0212	COOPER		**X**	**X**	
B5.10	B5.10/03	Dautel H.	2012	Evaluation of the efficacy of two sprays, "INSECT ECRAN FAMILLE" (25% DEET), and "INSECT ECRAN ZONES INFESTÉES" (50% DEET), against the European Sheep Tick *Ixodes ricinus* on human volunteers, Insect Services GmbH, Trial No. CP_IR_0111b	COOPER		**X**	**X**	

Toxicity							**Yes**	**No**	**Yes**	**No**
B6.1.1	B6.1.1	Richeux F.	2012	IE-DEET-F25: Evaluation of Acute Oral Toxicity in rats – Acute toxic class method -Phycher Bio Développement, Report number TAO423-PH-11/0671	COOPER			**X**	**X**	
B6.1.2	B6.1.2	Richeux F.	2012	IE-DEET-F25: Evaluation of Acute Dermal Toxicity in rats-Phycher Bio Développement, Report number TAD-PH-11/0671	COOPER			**X**	**X**	
B6.1.3	B6.1.3	Maibach *et al.*	1974	Use of insect repellents for maximum efficacy, Archives of Dermatological Research, Vol. 109, No. 19, pp. 32-35	Public Domain			**X**		**X**
B6.2.1	B6.2.1/01	Ben Ammar F.	2012	Evaluation of the acute cutaneous tolerance of a cosmetic product on adult subjects: single patch test method under dermatological control, Laboratoire DERMSCAN, Report number 10E2418.	COOPER			**X**	**X**	
B6.2.1	B6.2.1/02	Le Roux E.	2012	Certitifcate of Analysis for the product Insect Ecran Famille assessed in the single Patch Test on adult subjects (Ben Ammar F.)	COOPER			**X**	**X**	
B6.2.2	B6.2.2/01	Richeux F.	2012	IE-DEET-F25: Assessment of acute eye irritation, Phycher Bio Développement, Report number IO-OCDE-PH-11/0671	COOPER			**X**	**X**	
B6.2.2	B6.2.2/02	Gitton I.	2012	IE-DEET-F25-NF: Acute eye irritation study in the rabbit OECD 405, Centre de Recherches Biologiques (CERB), Report number 20120114TLC, draft report	COOPER			**X**	**X**	
B6.3	B6.3	Richeux F.	2012	IE-DEET-F25: Assessment of sensitising properties on albino guinea pigs – Maximisation test according to Magnusson and Kligman, Phycher Bio Développement, Report number SMK-PH-11/0671	COOPER			**X**	**X**	
B6.4	B6.4	Meerts I.	2012	Determination of the dermal absorption of N,N-Diethyl-*m* -Toluamide (DEET) in two formulations through human skin *in vitro,* NOTOX B.V., Report number 499729, draft report	COOPER			**X**	**X**	

Doc II							**Yes**	**No**	**Yes**	**No**
IIB IIC	II	Cooper	2012	Benefit / risk analysis	COOPER		**X**	**X**	
IIB IIC	II_Annex 1	Bouchaud O.	2012	Avis d'expert	COOPER		**X**	**X**	
2.4	IIB-2.4/01	Maibach *et al.*	1974	Use of insect repellents for maximum efficacy, Archives of Dermatological Research, Vol. 109, No. 19, pp. 32-35	Public Domain		**X**		**X**
2.4	IIB-2.4/02	Syed and Leal	2008	Mosquitoes smell and avoid the insect repellent DEET, Proceedings of the National Academy of Science (PNAS), Early edition	Public Domain		**X**		**X**
2.4 2.5	IIB-2.4/03	Stanczyk *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 Science (PNAS), Vol. 107, No. 19, pp. 8575-8580	Public Domain		**X**		**X**
3.2	IIB-3.2/01	Ayouni F.	2012	Taste evaluation of mosquito spray "Insect EcranFamille IE-DEET-A25-NF", Alpha-Mos, Report No.1869a	COOPER		**X**	**X**	
3.2	IIB_3.2/02	Brzozowska-Cieloch K.	2012	Consumer test measurement of the dose applied of a biocide product, Report #11E2728, Dermscan Poland	COOPER		**X**	**X**	
3.3	IIB-3.3.1	EUSES	2012	Full report EUSES calculations	COOPER		**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)[20]	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.

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

Annex 5 : Toxicology – biocidal product

<INSECT ECRAN FAMILLE>

General information

Formulation Type	Spray
Active substance(s) (incl. content)	DEET (25%)
Category	PT19

Acute toxicity, irritancy and skin sensitisation of the preparation (Annex IIIB, point 6.1, 6.2, 6.3)	
Rat LD50 oral (OECD 423)	> 2000 mg/kg bw/day
Rat LD50 dermal (OECD 402)	> 2000 mg/kg bw/day
Rat LC50 inhalation (OECD 403)	Justification for non submission
Skin irritation (patch test on volunteers)	Not irritating to skin
Eye irritation (OECD 405)	Irritant
Skin sensitisation (OECD 406)	Non sensitizing

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

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

Annex 6 : Safety for professional operators

<INSECT ECRAN FAMILLE>

Exposure assessment

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

Primary exposure of professionals: not relevant

Risk assessment: not relevant

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

<INSECT ECRAN FAMILLE>

General information	
Formulation Type	Spray
Active substance(s) (incl. content)	DEET (25%)
Category	PT19
Authorisation number	

<DEET>

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

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

Conclusion:

Primary exposure:
Dermal exposure of adults to the biocidal product containing DEET as active substance induce acceptable risk, if the biocidal product is used as intended and all safety advices are followed.

Exposure of children above 6 years old to the biocidal product containing DEET as active substance is considered unacceptable.

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

Details for the exposure estimates – Direct exposure

	Component	**CAS**	**Dermal Exposure [mg/kg/d]**	**Inhalation Exposure [mg/kg/d]**
Man	DEET	134-62-3	6.4	3.7×10^{-4}
Woman	DEET	134-62-3	7.0	4.5×10^{-4}
9-14 y-o	DEET	134-62-3	9.0	5.3×10^{-4}
3-9 y-o	DEET	134-62-3	11.4	6.7×10^{-4}

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

Risk assessment – Direct dermal exposure

	Component	CAS	AEL [mg/kg/d]	Absorption [%]	Total syst exposure [mg/kg bw/d]	% AEL	Risk
				dermal			
Man	DEET	134-62-3	8.2	44	6.4	78	Acceptable
Woman	DEET	134-62-3	8.2	44	7.0	85	Acceptable
9-14 y-o	DEET	134-62-3	8.2	44	9.0	110	Unacceptable
3-9 y-o	DEET	134-62-3	8.2	44	11.4	138	Unacceptable

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

Test substance	Test organisms	Test system / Concentrations applied / exposure time	Test conditions	Test results: effects, mode of action, resistance	Reference	RI
INSECT ECRAN FAMILLE (less than one year old), DEET 25 % w/w	*Aedes aegypti* *Anopheles gambiae* *Aedes albopictus* *Culex pipiens* *Phlebotomus duboscqi* For each test organism, 200 ± 10 females (5 to 7 days old) for each replicate.	Laboratory test. Arm-in-cage study. 10 volunteers (5 men and 5 women). Product applied on one forearm of each volunteer, the other untreated one being used as a control. Dose of product 0.60 mg/cm² (± 0.01), *i.e.* 3 sprays for a forearm which corresponds to an average area of 600 cm². The trial began 30 minutes after the product had been applied. The control forearm was inserted into the cage for 30 seconds, and after validation of this control (10 landings of test organism), the treated forearm was inserted into the cage for 3 minutes (exposure time). The same procedure was repeated every hour until 5 hours and then every 30 minutes, until inefficacy. Landings and bites were counted during each exposure time.	200 ± 10 insects in each cage, 10 volunteers for each test organism. Ambient conditions in testing chamber were maintained during the period of testing at a temperature of 25 ± 2°C, a relative humidity of 65 ± 5% and with smooth ventilation (30 m^3/h). Throughout the duration of the trial, the cages were maintained at a temperature of 27 ± 2°C, a relative humidity of 70 ± 10%, with a light intensity of 700 lux.	Repellent efficacy = the ability to offer a subject total protection (100%) against the bites of arthropods. Duration of the repellent efficacy = time between application of the product and the first bite, followed by a second one. The average duration of efficacy was 5 hours for 2 species of mosquitoes and 5.5 hours for the 2 others, and 5.10 hours for the sand fly tested.	Serrano B. (2012) B5.10/01	1

Test substance	Test organisms	Test system / Concentrations applied / exposure time	Test conditions	Test results: effects, mode of action, resistance	Reference	RI
DEET 15 % w/w, dilution of INSECT ECRAN FAMILLE 25 % w/w	*Aedes aegypti.* *Anopheles gambiae.* For each test organism, 200 ± 10 females (5 to 7 days old) for each replicate.	Laboratory test. Arm-in-cage study. 10 volunteers (5 men and 5 women). Product applied on one forearm of each volunteer, the other untreated one being used as a control. Dose of product 0.60 mg/cm² (± 0.02), *i.e.* 3 sprays for a forearm which corresponds to an average area of 600 cm². The trial began 30 minutes after the product had been applied. The control forearm was inserted into the cage for 30 seconds, and after validation of this control (10 landings of test organism), the treated forearm was inserted into the cage for 3 minutes (exposure time). The same procedure was repeated every 30 minutes until inefficacy. Landings and bites were counted during each exposure time.	200 ± 10 insects in each cage, 10 volunteers for each test organism. Ambient conditions in testing chamber were maintained during the period of testing at a temperature of 25 ± 2°C, a relative humidity of 65 ± 5% and with smooth ventilation (30 m^3/h). Throughout the duration of the trial, the cages were maintained at a temperature of 27 ± 2°C, a relative humidity of 70 ± 10%, with a light intensity of 700 lux.	Repellent efficacy = the ability to offer a subject total protection (100%) against the bites of arthropods vectors. Duration of the repellent efficacy = time between application of the product and the first bite, followed by a second one. The average duration of repellency was 0.3 hours for the 2 species of mosquitoes. No relevant protection against mosquitoes demonstrated.	Serrano B. (2012) 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
INSECT ECRAN FAMILLE (less than one year old), DEET 25 % w/w	*Ixodes ricinus* (sheep tick) 80 nymphs for each replicate.	Laboratory test. Simulated-use test: run test. 10 volunteers (5 men and 5 women). Dose of product 0.417 mg/cm² (± 0.029). Product applied on one forearm of each volunteer, leaving the lowest 5 cm near the wrist untreated. 3 marks on the forearm: at the border between treated and untreated zone, 3 cm below and 3 cm within the treated area. The arm was held vertically (with the fingertips or palm placed on a horizontal surface) and a tick was placed on the first mark, 3 cm below the treated area. Each test run lasted a maximum of 3 minutes. The test lasted for 8 hours post application, with 10 ticks tested per hour and per volunteer (5 ticks every 30 minutes). Between the 30-min test periods, ticks to be tested were screened for activity on the untreated control arm of the same volunteer. Only ticks that walked up and crossed the second mark (limit of the treated area on the treated arm) within the given time period of 3 minutes were further used on the treated arm.	10 ticks * 10 volunteers Temperature and relative humidity continuously recorded, and ambient conditions maintained during the period of testing at an average temperature of 22.1 ± 0.7°C, relative humidity 41.8 ± 4.1% in the test room.	The effect investigated was the repellency of the product. A tick is considered as repelled if it not crosses into the treated area, or if it crawls into the treated area but immediately turns back or falls off. Efficacy period: the period after application during which ≥90% of the ticks were repelled. The product INSECT ECRAN FAMILLE showed an efficacy period of 4 hours.	Dautel H. (2012) B5.10/03	1