Product Assessment Report

GOIBI ANTIMOSQUITOS XTREME AEROSOL

May 2016

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Amended sections: 1.5.2; 1.5.4; 2.6.2; 2.7.1.2; 2.7.2; 2.7.2.2; 2.7.3; 2.7.3.2; 2.9; 3; 8; Annex 1 sections 4.1; 5.1; Annex 7.

February 2024

Updated document (February 2024): Amended sections NA-ADC: BC-DG089615-37:
1.5.3 - Information on active substance(s)
1.6.2 Access to documentation

Internal registration/file no:	
Authorisation/Registration no:	ES/APP(NA)-2016-19-00364
Granting date/entry into force of authorisation/ registration:	
Expiry date of authorisation/ registration:	31 July 2022
Active ingredient:	DEET
Product type:	19

Biocidal product assessment report related to product authorisation under Directive 98/8/EC

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1 General information about the product application

1.1 Applicant

Company Name:	Laboratorios Cinfa, S.A.
Address:	Olaz-Chipi, nº 10
City:	Huarte – Pamplona
Postal Code:	31620
Country:	Spain
Telephone:	+34 948 335005
Fax:	+34 948 333774
E-mail address:	cinfa@cinfa.com

1.1.1 Person authorised for communication on behalf of the applicant

Name:	Mrs. Ana Berta Arrieta Azpilicueta
Function:	Regulatory Affairs Manager
Address:	Olaz-Chipi, nº 10
City:	Huarte – Pamplona
Postal Code:	31620
Country:	Spain
Telephone:	+34 948 335005
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1.2 Current authorisation holder[1]

Company Name:	Laboratorios Cinfa, S.A.
Address:	Olaz-Chipi, nº 10
City:	Huarte – Pamplona
Postal Code:	31620
Country:	Spain
Telephone:	+34 948 335005
Fax:	+34 948 333774
E-mail address:	cinfa@cinfa.com
Letter of appointment for the applicant to represent the authorisation holder provided (yes/no):	

1.3 Proposed authorisation holder

Company Name:	Laboratorios Cinfa, S.A.
Address:	Olaz-Chipi, nº 10
City:	Huarte – Pamplona
Postal Code:	31620

[1] Applies only to existing authorisations

Country:	Spain
Telephone:	+34 948 335005
Fax:	+34 948 333774
E-mail address:	cinfa@cinfa.com
Letter of appointment for the applicant to represent the authorisation holder provided (yes/no):	

1.4 Information about the product application

Application received:	05/10/2012
Application reported complete:	-
Type of application:	authorisation
Further information:	ES has not GOIBI ANTIMOSQUITOS XTREME AEROSOL currently authorised under national legislation for use as repellent (PT19). The current application is for PT19 use and that will be assessed and authorised under 98/8/EC.

1.5 Information about the biocidal product

1.5.1 General information

Trade name:	GOIBI ANTIMOSQUITOS XTREME AEROSOL
Manufacturer's development code number(s), if appropriate:	-
Product type:	19
Composition of the product (identity and content of active substance(s) and substances of concern; full composition see confidential annex):	27% DEET (N,N-diethyl-m-toluamide)
Formulation type:	Aerosol
Ready to use product (yes/no):	Yes
Is the product the very same (identity and content) to another product already authorised under the regime of directive 98/8/EC (yes/no); **If yes: authorisation/registration no. and product name:** **or** **Has the product the same identity and composition like the product evaluated in connection with the approval for listing of active substance(s) on to Annex I to directive 98/8/EC (yes/no):**	No

1.5.2 Information on the intended use(s)

Overall use pattern (manner and area of use):	Apply the product sparingly and carefully to parts of the body that are not covered. Do not apply on clothes; divide the product evenly over the skin. The biocidal product is to be applied only once a day for adults and children over 2 years of age. The biocidal product is not for use on children under 2 years of age.
Target organisms:	Mosquitoes: *Anopheles spp.* and *Aedes spp*. Ticks: *Ixodes ricinus*.
Category of users:	Non-professional user (general 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:	
Potential for release into the environment (yes/no):	
Potential for contamination of food/feedingstuff (yes/no)	No
Proposed Label:	See the authorisation
Use Restrictions:	See the authorisation

1.5.3 Information on active substance(s)[2]

Active substance chemical name:	DEET (N,N-diethyl-m-toluamide)
CAS No:	134-62-3
EC No:	205-149-7
Purity (minimum, g/kg or g/l):	970 g/kg
Inclusion directive:	Directive 2010/51/EU
Date of inclusion:	1 August 2012
Is the active substance equivalent to the active substance listed in Annex I to 98/8/EC (yes/no):	Yes
Manufacturer of active substance(s) used in the biocidal product:	Vertellus Performance Materials Inc. (formerly Morflex, Inc.)
Company Name:	Vertellus Performance Materials Inc.
Address:	2110 High Point Road
City:	Greensboro (NC)
Postal Code:	NC 27403
Country:	USA
Telephone:	336 292 1781
Fax:	336 854 4058
E-mail address:	www.vertellus.com
Manufacturer of active substance(s) used in the biocidal product:	Clariant Produkte (Deutschland) GmbH (Acting for Clariant Corporation (United States))

[2] Please insert additional columns as necessary

Company Name:	Clariant Corporation 500 East Morehead St., Charlotte, NC 28202, USA
Manufacturer location site:	625 East Catawba Avenue, Mt. Holly, NC 28120,USA
Manufacturer of active substance(s) used in the biocidal product:	Clariant Produkte (Deutschland) GmbH (Acting for Clariant Corporation (United States))
Company Name:	Clariant Corporation 500 East Morehead St., Charlotte, NC 28202, USA
Manufacturer location site:	Cangzhou Panoxi Chemical Co. Ltd., Chemical 1 Road, Lingang Economic Development Zone, Bohai New Zone, Cangzhou City, Hebei Province, China

1.5.4 Information on the substance(s) of concern[3]

Substance chemical name	Isobutane/propane (petroleum gas)	Ethanol
CAS No:	68512-91-4	64-17-5
EC No :	270-990-9	200-578-6
Purity (minimum, g/kg or g/l):	-	-
Typical concentration (minimum and maximum, g/kg, or g/l):	Please, see information in the confidential annex of this document about the composition of the biocidal product	Please, see information in the confidential annex of this document about the composition of the biocidal product
Relevant toxicological/ecotoxicological information:	-	-
Original ingredient (trade name):	-	-

Based on the legal classification as provided in the safety data sheet submitted by the applicant and the concentration in the biocidal product above 0.1 %, the components listed above (Isobutane/propane, ethanol) was identified as substances of concern according to the Biocidal Products Directive 98/8/EC (BPD) and the current drafts on guidance for SoC. Ethanol has flammability properties but it is covered by petroleum gas. Isobutane/propane is classified with the hazard statement H222.

In addition, isobutane/propane contains 1,3-butadiene as impurity, which is classified as a germ cell mutagen and a human carcinogen at concentration higher than 0.1%. Nevertheless, the contents of 1,3-butadiene is less than 0.1% according to the data sheet.

Ethanol was notified as active substance for the product types 1, 2 and 4 according to the biocides review programme, although the function in this product is as solvent.

On the other hand, C&L inventory database of ECHA contains classification and labelling information on notified and registered substances received from manufacturers and importers. Ethanol is included by some notifiers with the hazard statement H319 (Causes serious eye irritation).

Anyway, since the prevention of the risk of eye irritation is addressed in the labelling of the product and taken into account that exposure by inhalation is considered negligible, the potential risks towards ethanol during application of GOIBI ANTIMOSQUITOS XTREME AEROSOL are sufficiently

[3] Please insert additional columns as necessary

controlled by classification and labelling of the product. For this reason a quantitative risk characterization is not required for this substance of concern.

1.6 Documentation

1.6.1 Data submitted in relation to product application

The applicant has not sent new data about the active substance regarding physico/chemical properties, analytical methods and human health in order to support the product authorisation.

According to the applicant, the formulation of GOIBI ANTIMOSQUITOS XTREME AEROSOL has no impact on the route or rate of degradation of the active substance DEET in the environment. So, it was concluded that no additional studies involving the formulated product are required. There is no substance of concern in the formulated product except the active ingredient DEET: the biocidal product contains various compounds different from the active substance (27% DEET) classifying as dangerous for the environment (denatonium benzoate, D-limonene and citral), but it should not be considered of concern due to the low percentage in which it is present in the biocidal product. Therefore environmental effects of the product can be extrapolated from the environmental effect studies on DEET.

The biocidal product is an aerosol to dermal use ready to use.

1.6.2 Access to documentation

The applicant has submitted the following letter of access:

- a letter of access from Vertellus Performance Materials Inc. (formerly Morflex, Inc.) to all the documents about the active substance DEET associated to the Annex I listing. Vertellus has access to the data used and submitted for the inclusion of DEET into Annex I of Directive 98/8/EC.

  Vertellus Performance Materials Inc. (formerly Morflex, Inc.) was considered as a new source and the technical equivalence was carried out by SE. The RMS considered that the DEET material manufactured by the different sources to be equivalent and it was hence acceptable for the manufacturers to join one task-force.

  - a letter of access from Clariant Produkte (Deutschland) GmbH to all the documents about the active substance DEET associated to two new source from technical equivalence:

  - Asset num. EU-0014131-0000 – Case num. BC-MC023610-64 - Communication number: TAP-D-1267519-19-00/F and

  - Asset num. EU-0026031-0000 – Case num. BC-KJ064508-30 - Communication number: TAP-C-1541678-17-00/F

  These two new sources was carried out by ECHA and were considered that the DEET material manufactured by the different sources to be equivalents.

All substances data sheets are included in the dossier.

2 Summary of the product assessment

2.1 Identity related issues

The active substance DEET (N, N-diethyl-meta-toluamide) was included in the Annex I of Directive 98/8/EC (Commission Directive 2010/51/EC of 11 August 2010).

The formulation includes several components. The biocidal product contains some substances of concern according to the Technical Notes for Guidance on data requirements about toxicological aspects (please, see section 1.5.4). Information on the full composition of the product and assessment are detailed in additional confidential annex of this document.

According to article 19(9) of Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the making available on the market and use of biocidal products, the non-active substances of the biocidal product are included pursuant to Regulation (EC) No 1223/2009 (Commission Decision of 9 February 2006 amending Decision 96/335/EC establishing an inventory and a common nomenclature of ingredients employed in cosmetic products).

In addition, the biocidal product is an aerosol. This means that the labelling of the product has to be taking into account the Commission Directive 2008/47/EC of 8 April 2008 amending, for the purposes of adapting to technical progress, Council Directive 75/324/EEC on the approximation of the laws of the Member States relating to aerosol dispensers (In Spain, Royal Decree 1381/2009).

2.2 Classification, labelling and packaging

2.2.1 Harmonised classification and labelling of the biocidal product

According to Regulation 1272/2008 (Until 1 June 2015, mixtures shall be classified, labelled and packaged in accordance with Directive 1999/45/EC):

GHS Pictograms		
Signal Word	Warning	
Classification	Hazard class and category: Hazard statement	Aerosol. 2 Eye irrit. 2 Aquatic Chronic 3 H223: Flammable aerosol H229: Pressurised container: May burst if heated H319: Causes serious eye irritation H412: Harmful to aquatic life with long lasting effects. EUH 208: "Contains D- and L-Limonene, Citral and Hydroxyisohexyl 3- cyclohexene carboxaldehyde. May produce an allergic reaction"
General precautionary statement	P102: Keep out of reach of children P103: Read label before use	
Prevention precautionary statement	P210: Keep away from heat/sparks/open flames/hot surfaces. No smoking P211: Do not spray on an open flame or other ignition source P251: Pressurized container: Do not pierce or burn, even after use P264: Wash … thoroughly after handling P273: Avoid release to the environment.	

Response precautionary statements	
Storage precautionary statements	P410+P412: Protect from sunlight. Do not expose to temperatures exceeding 50 ºC/122ºF.
Disposal precautionary statements	P501: Dispose of content and / or its container as hazardous waste according to the regulations in force.lations in force.

2.2.2 Packaging of the biocidal product

The biocidal product is packaged in an aluminium aerosol of 150 ml net.

The packaging of the product placed on the market has to be limited to a maximum size of 200ml.

The packaging of the biocidal product shall be fitted with a tactile warning of danger.

2.3 Physico/chemical properties and analytical methods

2.3.1 Physico-chemical properties

Regarding the active substance DEET the table has not been filled in because the letters of access have been submitted.

Regarding the biocidal product, these are the physico-chemical properties:

Table 1: Physico-chemical properties of the biocidal product:

	Method	**Purity/Specification**	**Results**	**Reference**
Physical state and nature	Visual	27%	Liquid	B.3.1.1
Colour			Yellowish	B.3.1.2
Odour			Characteristic	B.3.1.3
Explosive properties			None of the components are classified as explosive	B.3.2
Oxidizing properties			None of the components are classified as oxidant	B.3.3
Flash point			n.a	
Autoflammability			n.a.	
Other indications of flammability				
Acidity / Alkalinity			n.a.	
Relative density / bulk density			0.898 g/ml	B.3.6
Storage stability – stability and shelf life			Stable for 3 months at 25ºC and 60% H.R.	B.3.7
Effects of temperature			Any change is observed in the product during the storage at next conditions:25ºC/60%HR, 40ºC/75%HR and 4ºC for 3 months	B.3.7
Effects of light				
Reactivity towards container material				
Technical characteristics in dependence of the formulation type			The product is ready to use	B.3.9
Compatibility with other products			The product is ready to use	B.3.9

	Method	Purity/Specification	Results	Reference
Surface tension			n.a	
Viscosity			n.a	
Particle size distribution			n.a	

2.3.2 Analytical methods

	Principle of method
Technical active substance as manufactured:	GC-FID y GC-MS
Impurities in technical active substance:	GC-FID y GC-MS
Active substance in the formulation:	HPLC - UV at 275 nm

2.4 Risk assessment for Physico-chemical properties

The active substance DEET is not highly flammable, auto-flammable, explosive or oxidizing and should thus not be classified based on its physic-chemical properties.

The biocidal product GOIBI ANTIMOSQUITOS XTREME AEROSOL contains 27% DEET and it is ready to use.

The first authorisation was conditioned to the submission of a new long term stability test. Applicant submitted in June 2018 a new test but the information included is related to the packaging and no to the variation in the concentration of the active substance. This information was sent with other biocidal product with less concentration of the active substance. In addition, a long term stability test was submitted by other biocidal product in the first authorisation (GOIBI ANTIMOSQUITOS FAMILIA SPRAY) which complied the variation of the active substance concentration. For this, ES CA thinks that a new test should be submitted in the renewal of the product and the shelf life will be 3 months.

2.5 Effectiveness against target organisms

2.5.1 Dose / mode of action / known limitations / resistance

GOIBI ANTIMOSQUITOS XTREME AEROSOL is an insect repellent (PT19) based on 45% DEET.

GOIBI ANTIMOSQUITOS XTREME AEROSOL is used to repel ticks and mosquitoes, in particular Lyme Disease (*Ixodes*) and, Malaria, mosquitoes. This product is an insect repellent for outdoor use, or indoor use in well ventilated areas, that should be applied to the skin of exposed body parts with the purpose to protect the uncovered skin of humans against biting ticks and mosquitoes.

DEET (N,N-Diethyl-m-toluamide) repels mosquitoes without time delay. The mechanism of action of the active ingredient is not revealed yet; however, its effectiveness is determined experimentally. Protection time provided by DEET is proportional to logarithmic dose concentrations, with increased duration of efficacy at higher concentrations; however, increase of duration of efficacy tends to plateau at a concentration of approximately 50% active substance.

New laboratory studies have been provided with the mosquitoes *Anopheles gambiae* and *Aedes albopictus* and the tick *Ixodes ricinus*. The results are summarized in Table below.

Table: The following table shows the efficacy of the active substance from its use in the biocidal product - GOIBI ANTIMOSQUITOS XTREME AEROSOL

Test substance	Test organism(s)	Test system/concentrations applied/exposure time	Test results: effects, mode of	Reference

			action, resistance*	
Goibi antimosquitos xtreme Aerosol	*Anopheles gambiae*	Arm-in-test cage: The study was repeated 5 times in the volunteer's forearm treated and untreated. Applying a product on the forearm repellent with an amount of 1.00 grams per 600 cm^2. Test cages containing 50 female adults of *Anopheles gambiae*, 6 days old and show a trophic activity was tested. Aspire females of breeding cages and then are introduced into test cages 30 minutes before each repetition. Before each repetition of the study, the activity of mosquito bites on the forearm was assessed untreated. The arm of the volunteer without treatment was introduced into the box and after 1 minute are beginning to assess the number of attempts to bite, considered valid if there were at least 10 attempts to nibble in 30 seconds The trial began five minutes after treating the forearm voluntary testing and finished 8 hours after treatment. During that time, the test was performed at intervals of one hour. The exposure time of the forearms of volunteers was 3 minutes per interval. The number of pits and the number of landings is recorded. The test ended when the volunteer had two bite attempts within a test interval or within two subsequent testing intervals. Test method: Product performances test guidelines according to the EPA guideline OPPTS 810.3700 and WHO7HTM/NTD/WHOPES/2009.4	The Collected data show Long Product Efficacy tests providing complete protection against *Anopheles gambiae* 5.8 hours	s-2013-02018-2 INC
Goibi antimosquitos xtreme aerosol	*Aedes albopictus*	Arm-in-test cage: Each test consists of 5 repetitions with different persons of the two sexes in a ratio of 2:3. The study was repeated 5 times in the volunteer's forearm treated and untreated. Applying a product on the forearm repellent with an amount of 1.15 gr/600 cm^2. Test cages containing 50 female adults of *Aedes albopictus* 5 days old and show a trophic activity was tested. Aspire females of breeding cages and then are introduced into test cages 30 minutes before each repetition. Before each repetition of the study, the activity of mosquito bites on the forearm was assessed untreated. The arm of the volunteer without treatment was introduced into the box and after 1 minute are beginning to assess the number of attempts to bite, considered valid if there were at least 10 attempts to nibble in 30 seconds The trial began five minutes after treating the forearm voluntary testing and finished 8 hours after treatment. During that time, the test was performed at intervals of 3 minutes each 30 minutes during 8 hours. The number of pits and the number of landings is recorded. . Each repetition is considered finished when the protection percentage drops under 95%. The parameter evaluating is PROBING, this them indicates a mosquito´s attempt to bite.	The average of the protection percentage stay 100% up to 8 hours	

		A probing is counted when the insect has alighted or "landed" on one´s arm, when it assumes the typical posture and "tastes" the skin with its mouth apparatus. As Tiger's mosquitos is very aggressive specie which bite as soon is landed, for this species probing and landing can be assumed as same meaning. The protection percentage of the test formulation is calculated according to the following formula: % PROT= 100 – (Σ probing on the treated arm x 100 : Σ probing on the untreated arm). Test method: Product performances test guidelines according to the EPA guideline OPPTS 810.3700 and WHO7HTM/NTD/WHOPES/2009.4, TNsG CA- DEC 12 – Doc.6.2.a		
Goibi antimosquitos xtrem aerosol	*Ixodes ricinus*	The forearm of each volunteer was treated with repellent product, approx. 1.15 gr / 600 cm^2, from the elbow to the wrist, except a round area of approximately 16 cm^2 which is allowed untreated. To stop monitoring the untreated area is covered with a plastic cover secured with a rubber band until the product has evaporated. The amount of product has been applied is evaluated by measuring the weight of the product packages before and after application. In order to avoid contamination of the forearm control voluntary gets a mono-use sleeve. In the midst of experiments, based on the control arm is left forearm while the treaty is uncovered in order not to hinder the natural process of evaporation of repellent product. The forearm of volunteer stays in a vertical position with the palm of the hand and fingers on the table. Ticks are placed one by one in the untreated area. Ticks that move the treated area for at least 60 seconds are considered as repelled. Ticks do not move to the treated area, which they return to the untreated area within 60 seconds, or those who are dropped from the skin are considered to be repelled. All ticks both repelled as renewed repelled and collected in each experiment: Each tick is used only for one test. The test provides the evaluation of 5 ticks after 30 minutes from when the product is applied and subsequently every hour. Each test consists of 5 repetitions with different people. Time protection is considered as the time until the first intersection confirmed within a trial period of 60 minutes is observed. A cross is defined as a movement of tick's untreated skin to the treated area and quantified with a stay in the treated area for 60 seconds. A cross is a cross confirmed by a second crossing another tick observations within 30 minutes. The test is terminated if 5 ticks within a probationary period are not repelled by 1 hr. Otherwise; the test is repeated until a total of eight hours.	The average of the protection percentage doesn´t goes below 95% for 8 hour. None of the ticks crossed the second mark on the treated skin during 4 hours, resulting in a mean PT of at least 4 hours.	

		Test method: USA guidelines and EPA guidelines for the evaluation of skin repellent products for human use in a open environment, OPPTS 810.3700, EPA draft guidelines for the evaluation of insects skin repellent products for use on human, Sept, 23, 2008		

These tests show the efficacy of **GOIBI ANTIMOSQUITOS XTREME AEROSOL** against mosquitoes in simulated-use tests (arm-in-cage) and against ticks in a laboratory test. The results of the arm-in-cage studies show that GOIBI ANTIMOSQUITOS XTREME AEROSOL repels *Anopheles spp*. and *Aedes spp*. for on average 5 and 8 hours respectively. The laboratory test with *Ixodes ricinus* shows that ticks are repelled for at least 8 hours.

2.5.1.1 Dose

The active substance is incorporated into a ready to use spray at a concentration of 45% and is used by the general public (non-professional users). The product is used as an application on the skin and exposed areas must be used every 8 hours. The exposure time in areas with mosquitoes, it is expected that the product is applied only once daily. If the exposure time in areas with mosquitoes or ticks is greater than 8 hours, the product must be reapplied. Nevertheless, according to the exposure assessment only once per day can be applied.

2.5.1.2 Mode of action

DEET repels biting and sucking insects without time delay. The mechanism of action of the active ingredients in insect repellents is not revealed yet; however, their effectiveness is determined experimentally.

2.5.1.3 Known limitations

Product must be reapplied after swimming, showering or when the efficiency decreases. Nevertheless, according to the exposure assessment only once per day can be applied.

2.5.1.4 Resistance

There is no known instance of target insects developing resistance to DEET. It is unlikely that resistance will occur for DEET, since there is only low selection pressure because the insects that are repelled do not die, and there are many other food sources available for these insects. Therefore, it is considered unnecessary to take actions to prevent development of resistance by target organisms.

2.6 Exposure assessment

2.6.1 Description of the intended use(s)

The biocidal product GOIBI ANTIMOSQUITOS XTREME AEROSOL is an ready-to-use aerosol for non-professional / general public use which contains 27% DEET (N,N-diethyl-m-toluamide). The biocidal product is applied as an aerosol on the body areas to be protected.

MG/PT	**Field of intended use**	**Likely concentration at which a.s. will be used**
MG03/PT19	Non-professional users (consumers), direct application onto the skin.	27%

2.6.2 Assessment of exposure to humans and the environment

Regarding humans health, no new exposure studies have been submitted.

Regarding environment, please, see the section 2.8.

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

2.7.1.2 Toxicology of the substance(s) of concern

Substance chemical name	Isobutane/propane (petroleum gas)	Ethanol
CAS No:	68512-91-4	64-17-5
EC No :	270-990-9	200-578-6
Purity (minimum, g/kg or g/l):	-	-
Typical concentration (minimum and maximum, g/kg, or g/l):	Please, see information in the confidential annex of this document about the composition of the biocidal product	Please, see information in the confidential annex of this document about the composition of the biocidal product
Relevant toxicological/ecotoxicological information:	-	-
Original ingredient (trade name):	-	-

Based on the legal classification as provided in the safety data sheet submitted by the applicant and the concentration in the biocidal product above 0.1 %, the components listed above (Isobutane/propane, ethanol) was identified as substances of concern according to the Biocidal Products Directive 98/8/EC (BPD) and the current drafts on guidance for SoC. Ethanol has flammability properties but it is covered by petroleum gas. Isobutane/propane is classified with the hazard statement H222..

In addition, isobutane/propane contains 1,3-butadiene as impurity, which is classified as a germ cell mutagen and a human carcinogen at concentration higher than 0.1%. Nevertheless, the contents of 1,3-butadiene is less than 0.1% according to the data sheet.

Ethanol was notified as active substance for the product types 1, 2 and 4 according to the biocides review programme, although the function in this product is as solvent.

On the other hand, C&L inventory database of ECHA contains classification and labelling information on notified and registered substances received from manufacturers and importers. Ethanol is included by some notifiers with the hazard statement H319 (Causes serious eye irritation).

Anyway, since the prevention of the risk of eye irritation is addressed in the labelling of the product and taken into account that exposure by inhalation is considered negligible, the potential risks towards ethanol during application of GOIBI ANTIMOSQUITOS XTREME AEROSOL are sufficiently controlled by classification and labelling of the product. For this reason a quantitative risk characterization is not required for this substance of concern.

2.7.1.3 Toxicology of the biocidal product

The toxicology of the biocidal product GOIBI ANTIMOSQUITOS XTREME AEROSOL 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. Justification for non-submission of data has been submitted for acute oral, dermal and inhalation toxicity. In addition, the information derived from existing data on the active substance DEET and co-formulants has been used, in order to minimise animal testing.

Dermal Absorption:

No study was submitted with the biocidal product. Read across with a biocidal product applied by spray (GOIBI ANTIMOSQUITOS XTREME SPRAY) was submitted to assess its potential to permeate human skin. This study was carried out according to OECD 428 (*in vitro* study) and the mean total absorption was found to be 11%. GOIBI ANTIMOSQUITOS XTREME SPRAY has a content of DEET of 45% and GOIBI ANTIMOSQUITOS XTREME AEROSOL has a content of DEET of 27%. Dermal absorption was expressed as a percentage of the total amount recovered. Skin was treated for 8h with the test item followed by further sampling up to 24h. Most of the applied dose (in mean more than 86%) was found remaining on the skin surface and was detected in the skin wash. In the total absorption the amount of test item of strips ≥3, skin, gauze, receptor fluid and chamber wash RF is included. The amount of test item in strip 1 and 2 only was excluded from absorption, since less than 75% of the absorption occurs within half the duration of the study according to EFSA Guidance on Dermal Absorption. The mean total absorption was found to be 11%, values for the single replicates ranging from 8% to 15%. Please, see table below:

Sample	**Mean (%)**	**SD (%)**
Skin wash 8h	84	5
Skin wash 24h	2	2
Chamber wash	0.8	0.9
Strips 1+2	2	2
Strips ≥3	1	1
Skin	0.9	0.3
Receptor Fluid	8	2
Gauze	0.6	0.3
Chamber wash RF	0.4	0.2
Total absorption	**11**	**3**
Recovery	87	3
Absorption after 12h	58	6
Absorption after 12h >75%*	no	

* when absorption after 12h is >75%, strips ≥3 can be excluded from the total absorption

The liquid contents of both biocidal products are the same. The difference is with the inclusion of propellant. In addition, the final formulation ("in-use" concentration) of the biocidal product was tested. Both biocidal products are applied by spray on skin. For these reasons, read across was accepted by the Spanish Competent Authority and an absorption dermal value of **11**% was used in the exposure assessment.

Acute toxicity:

No studies were submitted for the biocidal product. Justification for non-submission of data has been submitted for acute oral, dermal and inhalation toxicity. The Spanish CA accepts the applicant's justification and the data package.

The active substance DEET is classified as dangerous substances by oral acute toxicity and it exists in concentration that contributes to the classification of the product. On the other hand, according to CLP Regulation, where the mixture itself has not been tested to determine its acute toxicity, but there are sufficient data on the individual ingredients and similar tested mixtures to adequately characterise the hazards of the mixture, these data shall be used in accordance with the bridging rules. The acute toxicity estimate (ATE) of the mixture is determined by calculation from the ATE values for all relevant ingredients according to the following formula for oral, dermal or inhalation toxicity:

$$\frac{100}{ATE_{mix}} = \sum_{n} \frac{C_i}{ATE_i}$$

where:

Ci = concentration of ingredient i (% w/w or % v/v)
i = the individual ingredient from 1 to n
n = the number of ingredients
ATEi = Acute Toxicity Estimate of ingredient i

Considering the LD_{50} (oral) value and concentration of DEET, the ATE_{mix} is 7142 mg/kg and the biocidal product is not classified by oral acute toxicity according to CLP Regulation, table 3.1.1.

In addition, the biocidal product GOIBI ANTIMOSQUITOS XTREME AEROSOL does not contain any dangerous substance classified by dermal and inhalation acute toxicity. The study of acute inhalation toxicity was waived because the inhalation route is excluded due to the use outdoor, and because the use indoor only takes place in summer, in situations where there is a high ventilation rate. Furthermore, as reported in the CAR of DEET, the active substance is a low volatile compound that has not and high distribution in air compartment.

Irritation and corrosivity:

Skin irritation

The active susbtance was considered to be skin irritant. In addition, there is a study performed with the biocidal product without the propellant. There are no indications from the published literature that petroleum gases/propellant cause skin corrosion/irritation. For these reasons, considering the study, the biocidal product is not classified as irritant to skin and *read across* is accepted. A summary of the study is given below:

Species	**Method**	**Average score (24, 48, 72h)**		**Result**	**Remark**	**Reference**
		Erythema	Oedema			
Rabbit	OECD 404 GLP	0 (0-0-0)	0 (0-0-0)	Completely reversible	Not irritating	B6.2(1)

Eye irritation

No study was submitted. The active substance DEET was classified in the CAR as irritant to eyes according to CLP Regulation, Annex VI. Considering the concentration of the active substance, the biocidal product GOIBI ANTIMOSQUITOS XTREME AEROSOL is classified as Eye irrit. 2 and the hazard statement H319 according to CLP Regulation (the concentration is higher than 10%).

Taking into account the proposal of some notifiers about irritating properties to eyes of ethanol, the classification of labelling of the biocidal product will be the same with the hazard statement H319.

Sensitization:

No study was submitted with the biocidal product. Read across with a biocidal product applied by spray (GOIBI ANTIMOSQUITOS XTREME SPRAY) was submitted to assess the skin sensitization potential in mice. The method was carried out according to the guidelines of OECD N° 429 (skin sensitisation: Local lymph node assay, LLNA method). The purpose of this local lymph node assay was to identify the contact allergenic potential of GOIBI ANTIMOSQUITOS XTREME SPRAY when administered to the dorsum of both ear lobes of mice at concentrations of 25%, 50% (each diluted with acetone/olive oil 4:1 v/v) and 100%. On basis of the results, at the daily clinical observation the animals did not show any visible clinical symptoms and no case of mortality was observed. None of the three tested concentrations of the test item reached the simulation index of 3.

- The stimulation index at a concentration of 25% was 1.2.
- The stimulation index at a concentration of 25% was 2.0.
- The stimulation index at a concentration of 25% was 1.4.

Consequently, according to OECD 429 the biocidal product GOIBI ANTIMOSQUITOS XTREME SPRAY is expected to have no sensitising properties and therefore should not be regarded as a dermal sensitiser.

Read across was accepted by the Spanish Competent Authority because the liquid composition are the same. GOIBI ANTIMOSQUITOS XTREME SPRAY is a spray formulation and GOIBI ANTIMOSQUITOS XTREME AEROSOL is an aerosol product. The only difference is the incorporation of propellant in the aerosol biocidal product. In addition, the propellant has not sensitising properties. Therefore, GOIBI ANTIMOSQUITOS XTREME AEROSOL has not sensitising properties.

Nevertheless, some substances included in the biocidal product could produce an allergic reaction. These substances (fragrances) are not present in the biocidal product at sufficient concentration(s) to trigger a human health classification but, according to the Regulation 286/2011 of 10 March 2011 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (section 2.8, Annex II), the label on the packaging of mixtures not classified as sensitising but containing at least one substance classified as sensitising and present in a concentration equal to or greater than that specified in Table 3.4.6 of Annex I, of this regulation, shall bear the statement:

EUH208 — "Contains (name of sensitising substance). May produce an allergic reaction".

For this reason, the label of GOIBI ANTIMOSQUITOS XTREME AEROSOL will include the statement: EUH 208: "Contains D- and L-Limonene, Citral and Hydroxyisohexyl 3- cyclohexene carboxaldehyde. May produce an allergic reaction" according to CLP Regulation.

Other information about substances of concern

Isobutane/propane contains 1,3-butadiene as impurity, which is classified as a germ cell mutagen and a human carcinogen at concentration higher than 0.1%. Nevertheless, the contents of 1,3-butadiene is less than 0.1% according to the data sheet.

2.7.2 Exposure

The exposure of the biocidal products containing DEET has been re-assessed in line with the Commission implementing Decision (EU) 2018/1477 of 2 October 2018 on the terms and conditions of the authorisations of biocidal products containing ethyl butylacetylaminopropionate applicable to DEET.

There is a discrepancy between the application rate obtained from the efficacy studies and the application rate used in the exposure assessment. The application rate proven efficacious should be considered to assess the exposure (Article 19(1)(b)(i) of Regulation (EU) No 528/2012), even though it is acknowledged that it may lead to an unacceptable risk for human health with regard to a number of the intended uses (Article 19(1)(b)(iii)).

Until a consensus on how to generate efficacy for insect repellents data is reached, the human health risk assessment should contemplate the efficacy doses. Therefore the RMS has re-calculated the exposure with the dose that has proven to be efficient. Hence, the dose proven efficacious (1.15 g/600 cm2) has been considered in line with the Commission implementing Decision (EU) 2018/1477.

The product GOIBI ANTIMOSQUITOS XTREME AEROSOL is a ready-to-use aerosol containing DEET at a concentration of 27 %. The biocidal product is packaged in an aluminium aerosol of 150 ml net (see section 2.2.2). It is applied onto the body areas to be protected. The biocidal product will be used by non-professional users. Primary exposure is expected in adults and children over 2 years of age; the use of DEET products is not allowed for children of less than 2 years of age (DEET CAR).

The main paths of human exposure towards this active substance from its use in biocidal product are:

Table 2.7.2- 1 Summary of main paths of human exposure

Exposure route	Industrial use	Professional use	General public	Through the environment
Inhalation	NA	NA	Insignificant	Insignificant
Dermal	NA	NA	Main route	Insignificant
Oral	NA	NA	Significant	Insignificant

The product is intended to be used per dermal route. The exposure assessment is performed assuming a frequency of application of 1 time per day, as described by the applicant. Dermal route is the main path of exposure.

Exposure by inhalation is considered negligible due to the large particle size. Additionally, with respect to insect repellents, the section 5.2 of the "Technical Notes for Guidance - Human Exposure to Biocidal Products - Guidance on Exposure Estimation" (European Commission, 2002, part 2),states: "The inhalation route is excluded due to the use outdoors, and because use indoors takes place in the summer in situations where there is a high ventilation rate. On these grounds, the inhalation exposure to aerosol sprays is also considered to be negligible". This extreme was admitted for the assessment of the active substance (DEET CAR) and the inhalation exposure was not assessed. However, since the inhalation exposure cannot be completely ruled out a recommendation for adequate ventilation has been included on the product label.

Oral exposure by hand-to-mouth transfer is not considered significant route of exposure since due to its smell and taste, the DEET acts as a shelf deterrent. More importantly, all the products of this family contain an ingredient that acts as a strong deterrent for ingestion (Bitrex). However, it should be noticed that Bitrex may not be effective in preventing ingestion in all age groups, in particular children < 12 years old (Technical Meeting Agreement) On this basis, the oral route is considered possible and therefore the calculations for hand to mouth exposure have been included in worst case exposure calculations.

2.7.2.1 Exposure of professional users

The product is not intended for professional use.

2.7.2.2 Exposure of non-professional users and the general public

The exposure calculations are based on the Recommendation 11 Ad hoc Working Group Human Exposure "proposal for harmonizing the assessment of human exposure to repellents (PT19)" as well as on Biocides Human Health Exposure Methodology (ECHA, 2015).

The assessment of the systemic effects has been carried out using the UK proforma approach which is based on the application rates supported by efficacy data. The Proforma method defines a maximun skin area that can be treated safely using a reverse referece scenario. The risk calculations are based on the toxicologically determined AEL for the active substance. Consequently, the potential exposure of the biocidal product is calculated by determining the maximum dose that can be applied onto a person without exceeding the AEL.

The daily exposure has been calculated for adults, children from 12 to < 18 years of age; children from 6 to < 12 years of age; and children from 2 to < 6 years of age. It is agreed that the Recommendation 14 of the Ad hoc working group human exposure does not cover the ages from 12 to 18 years old. In order to simplify the re-assessment, it is assumed that the exposure of adults covers the population of children from 12 to <18 years of age in a worst-case basis.

The default values fo body weight and surface area described at the Recommendation 14 of ad hoc working group human exposure are used for exposure assessment. The biocidal product is applied directly onto the body areas to be protected. For adults and children, the head, arms, legs, trunk and feet could be treated according to US EPA Child-Specific Exposure Factors Handbook, 2002. In addition, since the product can be used in people wearing swimming suits and therefore with the trunk exposed, the trunk has been included as a possible body part to spray on.

The parameters considered to calculate are:

Parameters	Value
DEET $AEL_{repeated}$ (acceptable exposure limit a.s.)	8.2 mg a.s./kg bw/day
Number of applications	One per day (applicant)
Concentration of DEET in the product (AS)	27 %
Dermal absorption for DEET (DA)	11 %
Oral absorption for DEET (AA)	100 % (worst-case approach)
Amount of BP [1]	150 ml net
Efficacy (g DEET/cm^2 skin)	1,15 g/600 cm^2 (0.0019 g/cm^2)
Amount of the product applied that expected to be ingested [2]	
Adults	4 % applied dose (product on fingers)
Children	8 % applied dose (product on hands)
Transfer coefficient[3]	100 %
Area of skin that can be treated (head, trunk, arms, legs, trunk and feet) [4]	
Adults/ Child > 12 years	16600 cm^2
Child 6 to < 12 years	9200 cm^2
Child 2 to < 6 years	6800 cm^2
Body weight [5]	
Adults/ Child > 12 years	60 Kg

Parameters	Value
Child 6 to < 12 years	23.9 Kg
Child 2 to < 6 years	15.6 Kg

[1] (see section 2.2.2)
[2]Amount of product ingested (mg/Kg/day), assuming that a % of the amount deposited is available orally with a transfer coefficient of 100% (Recommendation 11 Ad hoc WGHE);
[3] Recommendation 11 Ad hoc WGHE;
[4, 5] Recommendation 14 ad hoc WGHE.

Both dermal and oral exposures have been considered in a worst-case basis.

According to the Recommendation 11th of the Ad hoc working group on human exposure, adults will ingest the amount applied to fingers. The surface of the fingers is approximately 4% of the treated body surface. The oral exposures for the age group < 12 years is calculated for the whole hands, i.e. approximately 8% of the treated body surface (head, arms, hands, legs and feet according to US EPA Child-Specific Exposure Factors Handbook, 2002), with a 100 % of transfer coefficient.

In this scenario where the biocidal product is applied directly on the body areas, the exposure is expected to happen per dermal and oral route.

The following calculations model a scenario where the biocidal product is lodged onto the skin, leading to both dermal absorption due to direct contact with the skin after spraying; and oral absorption by hand-to-mouth transfer. The RMS acknowledges, that, since both procedures might take place at the same time, the calculation should take into account, out of the total amount of biocide product applied on the skin, that the quantity absorbed per dermal route will not be available to be in-taken per oral route and vice versa.

The amount of active substance absorbed per dermal and oral route has been calculated based on the following formulas:

Internal dermal dose a.s. = External dermal dose product × (content a.s.) × (% dermal absorption)

Internal oral dose a.s. = External oral dose product × (content a.s.) × (% oral absorption)

Total dose a.s. = Internal dermal dose a.s. + Internal oral dose a.s.

Where,

External dermal dose product = amount of applied biocidal product that will be lodged over the skin (mg).
External oral dose product = amount of the biocidal product will be ingested (mg)
Content a.s. = concentration of the active substance (mg/100mg)
% dermal absorption = fraction
% oral absorption = fraction

In line with the reverse scenario proposed by UK Proforma, the amount of product (external dose) that can be applied to a person without exceeding the $AEL_{repeated}$ is:

mg Biocidal product (external dose) = AELa.s. / Total dose a.s. (calculated)

The complexity lies in the fact that the quantity absorbed by the dermal route will not be available to be ingested; and on the contrary.

For **adults**, the ratio *mg active substance/ mg biocidal product* has been calculated assuming i.e. that an adult intakes the entire amount of product rubbed onto their fingers, which assuming a linear relation, is the 4% of total amount. Therefore, a 96% of the product will be left on the skin, available for dermal absorption.

AELrepeted a.s = 96 % dermal route + 4% oral route

If 1 mg of GOIBI ANTIMOSQUITO XTREME AEROSOL is applied, the latter proportion would imply that 0.96 mg of the biocide product will be lodged over the skin, whilst 0.04 mg of the biocide product will be ingested by the adult.

1 mg Biocidal product = 0.96 mg per dermal route + 0.04 mg per oral route

Considering the concentration of DEET is 27 %, a dermal absorption of 11 % and an oral absorption of 100 % the corresponding total internal dose is calculated as follows:

Dermal route

0.96 mg Biocidal product x (27 mg DEET/100 mg Biocidal product) x (11 mg DEET/100 mg DEET) = 0.0285 mg DEET internal

Oral route

0.04 mg Biocidal product x (27 mg DEET/100 mg Biocidal product) x (100 mg DEET/100 mg DEET) = 0.0108 mg DEET internal

Total dose DEET

0.0285 mg internal DEET per dermal route + 0.0108 mg internal DEET per oral route =

0.0393 mg internal DEET / mg GOIBI ANTIMOSQUITO XTREME AEROSOL

For every mg of GOIBI ANTISMOSQUITOS XTREME AEROSOL applied on an adult's skin, considering both oral and dermal exposures (since none of the exposures could occur separately) **0.0393** mg of DEET would be absorbed.

Considering an AEL of 8.2 mg/kg bw/day, the amount of product that can be applied on an adult without exceeding the AEL is:

8.2 mg DEET/kg bw/day x 1 mg Biocidal product/0.0393 mg DEET = 209 mg of Biocidal product/kg bw/day

That implies that **209 mg/Kg bw/day** of GOIBI ANTISMOSQUITOS XTREME AEROSOL can be applied on adult skin before reaching the AEL (limit dose).

For **children**, the ratio *mg active substance/ mg biocidal product* has been calculated assuming i.e. that a child intakes the entire amount of the product rubbed onto their hands, which assuming a linear relation, is the 8% of total amount. Therefore, a 92 % of the product will be left on the skin, available for dermal absorption.

AELrepeated a.s = 92 % dermal route + 8% oral route

For children, If 1 mg of GOIBI ANTIMOSQUITOS XTREME AEROSOL is applied, this proportion would imply that 0.92 mg of the biocide product will be lodged over the skin, whilst 0.08 mg of the biocide product will be ingested by the child.

1 mg Biocidal product = 0.92 mg per dermal route + 0.08 mg per oral route

Dermal route

0.92 mg Biocidal product x (27 mg DEET/100 mg Biocidal product) x (11 mg DEET/100 mg DEET) = 0.0273 mg DEET internal

Oral route

0.08 mg Biocidal product x (27 mg DEET/100 mg Biocidal product) x (100 mg DEET/100 mg DEET) = 0.0216 mg DEET internal

Total dose DEET

0.0273 mg internal DEET per dermal route + 0.0216 mg internal DEET per oral route =

0.0489 mg internal DEET / mg GOIBI ANTIPARASITOS XTREME AEROSOL

For children, for every mg of GOIBI ANTIMOSQUITOS XTREME AEROSOL applied on the skin of a child, considering both oral and dermal exposures (since none of the exposures could occur separately) **0.0489** mg of DEET would be absorbed.

Considering the value of the AEL 8.2 mg/kg bw/day, the amount of product that can be applied on a child in order not to exceed the AEL is:

8.2 mg DEET/kg bw/day x 1 mg Biocidal product/0.0489 mg DEET = 168 mg of Biocidal product/kg bw/day

That implies that **168 mg/Kg bw/day** of GOIBI ANTIMOSQUITOS XTREME AEROSOL can be applied on child skin before reaching the AEL (limit dose).

The number of applications and the maximum area of skin (cm^2) that can be treated in one day with the biocide product ”limit dose” so that the AEL is not exceded has been calculated (Table 2.7.2.2-1). The calculation taking into account the efficacy of the product as is recommended by the implementing decision (EU) 2018/1477. As worst case, the efficacy of product GOIBI ANTIMOSQUITOS XTREME AEROSOL (1.15 g product/600 cm^2 of skin) has been used for calculation.

The surface areas from the Recommendation 14 of the Ad hoc working group human exposure are used for exposure calculations,assuming that the head, trunk, arms, hands, legs and feet are treated. The trunk has been included by the RMS in the worst case exposure calculation, as a possible body part to spray on, since the product can be used person in wearing swimming suits and therefore with the trunk exposed,

In addition, as the product GOIBI ANTIMOSQUITOS XTREME AEROSOL is a ready-to-use aerosol of 150 ml net (see section 2.2.2), the number of applications and the maximum skin area that can be treated in one day (so called ”limit dose”) have been calculated.

Table 2.7.2.2-1. Number of applications, amount product “limit dose” and area of skin treated with product “limit dose

Scenario	Adults/Child > 12 years	Child 6 to < 12 years	Child 2 to < 6 years
nº application/day	1	1	1
Concentration DEET (% w/w)	27	27	27
AELdermal (mg a.s./kg bw/day) = Application rate "safely"	8,2	8,2	8,2
Body weight (kg)	60	23,9	15,6
Dermal absorption (%)	11	11	11
Oral absorption (%)	100	100	100
Amount of PRODUCT applied to reach repeted AEL (mg product /Kg/day)	209	168	168

Scenario	Adults/Child > 12 years	Child 6 to < 12 years	Child 2 to < 6 years
Amount of PRODUCT applied to reach repeted AEL (mg product /day)	12115	4006	2615
Eficacia (1,15 g/600 cm^2)	0.0019	0.0019	0.0019
Area of skin that can be treated with product in one day [cm^2]	6530	2093	1364
Superficie cuerpo (cm^2)	16600	9200	6800
Number of applications / day	0.4	0.2	0.2
% skin that can be treated in a day	39	20	20

2.7.2.3 Exposure to residues in food

Not relevant, as no contamination of food is expected if users follow the label instructions.

2.7.3 Risk Characterisation

GOIBI ANTIMOSQUITOS XTREME AEROSOL is an aerosol containing 27 % DEET. There are no ingredients considered as substances of concern. Therefore, only DEET is included in the risk characterisation.

2.7.3.1 Risk for Professional Users

The product is not intended for professional use.

2.7.3.2 Risk for non-professional users and the general public

The exposure assessment for GOIBI ANTIMOSQUITO XTREME AEROSOL is expressed as the estimated amount product that can be applied without exceeding the AEL (so called "limit dose), as well as the area of skin to be treated and the number of applications and number of aerosols are presented in Table 2.7.3.2-1.

As a worst-case approach, the oral exposure has also assessed, considering potential ingestion of 4% of the total applied product by adults (amount on fingers) and a potential ingestion of 8% of the total applied product by children

Table 2.7.3.2-1. Amount product "limit dose" and area of skin treated with product "limit dose".

Scenarios	**Adults/Child > 12 years**	**Child 6 to < 12 years**	**Child 2 to < 6 years**
Amount product "limit dose" (mg product/kg bw/day)	209	168	168
Amount product "limit dose (mg product/day)	12515	4006	2615
Area of skin treated in one day (cm^2) with "limit dose"	6530	2090	1364
% skin that can be treated	39	23	20
Number of arosolss	83	27	17
Number of applications	0.4	0.2	0.2

The recommended maximum skin area to be treated in one day to reduce exposure is show below. The default values for the body surfaces are based in the Recommendation 14 Ad Hoc working group human exposure.

There are different ways of phrasing the maximum dose recommendation. For clarification purposes, the following wording has been decided:

-An adult can be treated a maximum of 6530 cm^2 of area of skin. Apply in a uniform manner on face, neck, arms, hands, lower legs and feet (6547 cm^2).

-Children of 6 to < 12 years can be treated a maximum of 2090 cm^2 of area of skin. Apply in a uniform manner on face, neck, lower arms and lower legs (2101 cm^2).

-Children of 2 to < 6 years can be treated a maximum of 1364 cm^2 area of skin. Apply in a uniform manner on face, lower arms and lower legs(1382 cm^2)."

The reverse dose calculations for exposure show that the 73 to 56 % of the estimated internal dose per application (8.2 mg product/kg/d) of use for adults and children < 12 years respectively, can be absorbed on skin and the 18 to 30 % can be ingered before an AELrepeated is exceeded.

Although considering the oral exposure represents the worst-case determines that the oral exposure should not be overruled especially for children < 12 years old. However, according to the CAR of DEET, the oral dose is likely to be overestimated given the DEET short half-life after oral exposure in dogs and rats and the rapid achievement of Cmax. The hand to mouth behaviour is more frequent in small children and that taking into account Bitrex may not be sufficiently effective to protect small children, an age limit of 2 years has been proposed together with the recommendation "restrict the use on children between three and twelve years old".

The maximum skin area that can be treated without exceeding the AEL is compared to surface to be treated, in order to show how many applications/day will be acceptable before reaching the AEL (Table 2.7.3.2-2).

Table 2.7.3.2-2. Risk indicator value

Scenarios	Adults/Child > 12 years	Child 2 to < 6 years	Child 6 to < 12 years
Skin treated in one day (%)	39	23	20
Nº applications/day	0.4	0.2	0.2
Body areas which can be treated	face, neck, arms, hands, lower legs and feet	face, neck, lower arms and lower legs	face, lower arms and lower legs

Therefore, for adults, children < 12 years of age and children > 12 years of age the number of applications/day is 0.4. 0.2 and 0.2 respectivaly. The number of applications per day does not cover the area that needs to be treated for adults, children 2 to <6 years and children 6 to <12 years.

For adults, the number of applications covers the 39 % of the area that could be treated; and for children approximately the 23 % of the area that could be treated.

The CAR of DEET requires the inclusion of a recommendation on maximum skin areas to be treated to reduce exposure.

In summary, the risk characterization performed, considering both dermal and oral routes, concludes that there is risk for each subpopulation (adults, children < 12 years of age, and children > 12 years of age). The product can be used once per day, on adults and children over 2 years of age. Children's hands must not be treated with this product. Children under 2 years must not be treated with this product.

The RMS is in the opinion that not authorizing GOIBI ANTIMOSQUITO XTREME AEROSOL would result in disproportionate negative impacts for society when compared to the risks to human health. It should be taken into account that insect repellents are essential to prevent vector borne diseases. Also, the availability of insect repellents containing different active substances is necessary to minimize the occurrence of resistance in the target harmful organisms. There is an immediate need to maintain a number of insect repellent products containing DEET on the market in order to protect human health.

In consequence, the RMS is in the opinion that GOIBI ANTIMOSQUITO XTREME AEROSOL must be authorized on the grounds of Article 19(5) of Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the market and use of biocidal products.

This authorization is granted under the following conditions:

Once a consensus is reached and the efficacy methods are refined, the applicant commits to provide new efficacy data. At that point, the competent authorities will re-evaluate the human health risk assessment, and will take the appropriate regulatory measures, if necessary. Until then, the existence of risk for human health cannot be overruled.

GOIBI ANTIMOSQUITO XTREME AEROSOL must not be used by children younger than two years old

Children must not handle or apply the product by themselves.

The application for adults and children > 2 years of age must be restricted to one application a day and the area of skin that can be treated safely with the product should be taken into account.

2.7.3.3 Risk for consumers via residues

The acute or chronic exposure to residues in food resulting from the intended uses is unlikely to cause a risk to consumers. Regarding consumer health protection, there are no objections against the intended uses.

2.8 Risk assessment for the environment

The product GOIBI ANTIMOSQUITOS XTREME AEROSOL (DEET 27%) is not considered to contain any substances of concern that require a formal quantitative risk assessment and none has been performed. The risks arising from the product can be adequately determined based on the assessment of the active substance.

2.8.1 Fate and distribution in the environment

The environmental fate and behaviour of the active substance DEET has been fully evaluated during its assessment for Annex I inclusion. A summary of the fate and distribution of DEET is presented in Section 2.2.2.1 of the final Assessment Report (11 March 2010), and the relevant endpoints appear in the EU List of Endpoints.

DEET is considered to be ready biodegradable and no major (>10%) transformation products were formed in studies of hydrolysis and aquatic phototransformation. DEET is extensively metabolised and excreted through the urine in all assessed mammals, and because the parent structure is ready biodegradable, and the metabolite structures found in urine do not differ significantly from the parent structure it is likely that they are also ready biodegradable. It causes only minor inhibitory effects on (STP) microbial activity.

DEET is moderately volatile and absorbs UV in the region 200-250 nm. The substance is predicted to have an atmospheric half-life of 0.63 days (15.2 hours). An extensive accumulation of DEET in air

and long range transport is unlikely. DEET is a liquid at room temperature, and it has a water solubility of 11.2 g/L and its log Pow is 2.4. It is hydrolytically stable under acidic, basic and neutral conditions, and photolytically stable in sterile distilled water.

Based on the calculated BCFs for aquatic and terrestrial organisms, DEET is considered to have very little or no potential to bioaccumulate.

DEET has a Koc of 43.3, suggesting that it is very mobile in soil and therefore could leach to the groundwater. However, DEET will not be directly emitted to soil and exposure is expected to be negligible.

The following statement appeared in Section 3.4 (Requirement for Further Information) of the final Assessment Report (11 March 2010);

"It is considered that the evaluation has shown that sufficient data have been provided to verify the outcome and conclusions, ands permit the proposal for the inclusion of N,N-diethyl-meta-toluamide (DEET) in Annex I to Directive 98/8/EC.

However, further validation data to prove the applicability of the proposed analytical method for the water compartment is considered needed (The applicant has stated that further validation work is underway and the data will be submitted as soon as possible)."

According to verbal information: The CAR request was completed and submitted to the KEMI, who is the CA for DEET. They accepted the method with no questions.

DEET is used in products for repellents (PT19 Scenario, Repellents and attractants). An ESD has been published for repellents (PT19) on June 2015, and ES CA has used it for calculation of releases to the environment. Furthermore, emissions have also been calculated using the ESD for PT1. PT1 includes biocidal products used for human hygiene purposes and DEET is the active ingredient of insect repellents used by the general public. As such, GOIBI ANTIMOSQUITOS XTREME AEROSOL can for exposure modelling purposes be considered as a "leave on" Personal Care Product (PCP) and would thus fit into this scenario.

2.8.2 Effects on environmental organisms

No studies have been conducted with the biocidal product. Reference is made to the active substance data; no effects are expected which cannot be predicted from the acute toxicity of the active substance. In Doc II-A of CAR, section 4.2.1, calculations of PNEC values for surface water are presented. Values are presented below for organisms of three trophic levels.

- LC_{50} fish = 97 mg/L
- LC_{50} invertebrates = 75 mg/L
- ErC_{50} algae = 43 mg/L

No marine species were tested. The applicant argues that these are not necessary based on the presence of studies performed on freshwater species, all suggesting low toxicity. Besides, DEET will not be used or released in marine environments in considerable amounts. The effect of DEET on microbial activity in water was assessed by determining the level of inhibition of respiration of microorganisms present in activated sludge. DEET had only a minor inhibitory effect on aquatic microbial activity (26.8% inhibition at the highest tested concentration, 1000 mg/L).

The PNEC values for the water compartment and microorganisms can be calculated from toxicity data by using recommended assessment factors. Because only three acute aquatic tests were performed, all on freshwater species, the assessment factor for the freshwater compartment will be 1000 and for the marine water compartment 10 000 (assuming a greater species sensitivity distribution and thus greater

uncertainties in extrapolation of data from the freshwater to the marine environment; or lower species diversity resulting in high ecosystem dependency).

For the sediment and soil compartments, there are no toxicity data available. The low Koc value indicates that sorption to sediment and soil is not likely. Nevertheless, PNEC values have been calculated based on equilibrium partitioning theory (Eq.P.) and PNECwater. The formulas used assume uptake from the water phase only. This assumption is accepted for DEET, because of its low log P_{OW} and KOC values. No quantitative estimation of PNECmarine sediment is necessary because the PEC values for the marine sediment compartment will be based on EqP and the same P_{OW} and Koc values. The PEC/PNEC ratios for the marine sediment compartment will therefore be the same as for the corresponding water compartment.

PNECs were not calculated for the air compartment, as there are no data on biotic effects in the atmosphere. Furthermore, 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 and DT50 is less than 2d; cf the TNsG on Annex I inclusion), ozone depletion in the stratosphere (atmospheric lifetime is <<1year, and it does not contain Cl, Br or F substituents) or acidification (the AP, Acidification Potential is low).

The log P_{OW} is 2.4, suggesting a low bioaccumulation potential (BCF estimates range between 3.85 and 63.1), see doc II-A 4.1.4 of the Assessment Report. The risk of secondary poisoning is therefore expected to be low via ingestion of potentially contaminated food (e.g., fish) by birds or mammals. The risk for secondary poisoning via intake of terrestrial organisms such as earthworms is considered unlikely also because exposure to earthworms is expected to be negligible. No avian dietary tests were therefore required. The available avian acute lethality data are not appropriate for extrapolation to chronic dietary uptake conditions (cf TGD II3.8.3.5). PNECs were therefore not calculated for oral uptake from the food chain (to quantify the risk of secondary poisoning).

According to the CAR the effects assessment is summarized in the following table:

Table 2.8.2-1. PNECs for the environmental compartments

Compartment	Available data	Assessment factor/Eq P	Remark	PNEC
Freshwater	LC_{50} daphnia: 75 mg/L LC_{50} fish: 97 mg/L EC_{50} algae: 43 mg/L	**1000**	No chronic data available (except for NOEC algae)	43/1000 = 0.043 mg/L
Saltwater	LC_{50} daphnia: 75 mg/L LC_{50} fish:97 mg/L EC_{50} algae: 43 mg/L	**10.000** (TGD II4.3.1.3)	No chronic data available (except for NOEC algae), and no additional marine data	43/10000 = 0.0043 mg/L
STP microorganisms	EC_{50}: >1000 mg/L NOEC: 300 mg/L	For EC_{50}: 100 For NOEC: 10	At the highest test concentration (1000 mg/L) there was 26.8% inhibition. At NOEC, there was 13% simulation rather than inhibition.	>1000/100 = >10 mg/L

Sediment, freshwater	Measured Koc: 43.3 Default assumptions: RHO_{water}: 1000 kg/m^3 $Fwater_{susp}$: 0.9 $Fsolid_{susp}$:0.1 RHO_{solid}: 2500 kg/m^3 Foc_{susp}: 0.1 (TGD II 2.3.4 table 5)	$PNEC_{sed}$: 1000 * $PNEC_{water}$* ($K_{susp-water}$/RHO_{susp}) (TGD II 3.5.3 eq70) Where: RHO_{susp}: $Fsolid_{susp}$*RHO_{solid}+ $Fwater_{susp}$*RHO_{water} and $K_{susp-water}$: $Fwater_{susp}$ + $Fsolid_{susp}$*RHO_{solid}*(FOC_{susp}*Koc)/1000	RHO_{susp}=0.1*2500+0.9*1000 = 1150 kg/m^3 $K_{susp-water}$= 0.9+0.1*(0.1*43.3*(1.98/1150) = 0.0741 mg/kg ww	1000*0.043*(1.98/1150) = 0.074 mg/kg ww
Soil	Measured Koc: 43.3 Henry´s law constant: 3.93E-03 Pa*m^3/mol Default assumptions: R (gas constant)= 8.314 Pa*m^3/(mol*K) Temp:285 K $Fair_{soil}$:0.2 $Fwater_{soil}$:0.2 $Fsolid_{soil}$: 0.6 Foc_{soil}: 0.02 RHO_{air}: 1.3 kg/m^3 RHO_{solid}: 2500 kg/m^3 RHO_{water}: 1000 kg/m^3 (TGD II 2.3.4. and 2.3.5.2)	$PNEC_{soil}$: 1000 * $PNEC_{water}$ * ($K_{soil-water}$/RHO_{soil}) (TGD II3.6.2.1) where: RHO_{soil}: $Fsolid_{soil}$ * RHO_{solid} + $Fwater_{soil}$ * RHO_{water} + $Fair_{soil}$ * RHO_{air} $K_{soil-water}$: $Fair_{soil}$*$K_{air-water}$ + $Fwater_{soil}$ +$Fsolid_{soil}$ * (Kp_{soil}/1000) * RHO_{solid} and Kp_{soil} = Foc_{soil} * Koc and: $K_{air-water}$ = HENRY/(R*Temp)	RHO_{soil}= 0.6*2500+0.2*1000+0.2*1.3 = 1700 kg/m^3 $K_{air-water}$: 3.93E-03/ (8.314*285) = 1.66E-06 Kp_{soil}: 0.02*43.3 = 0.866 L/Kg $K_{soil-water}$ = 0.2[3.93E-03/ (8.314 *285)]+0.2+0.6* [0.866/1000]* 2500 = 1.499	1000*0.043*(1.499/1700) = 0.0379 mg/kg ww

2.8.3 Environmental exposure assessment

The environmental exposure of the product was assessed by the applicant in accordance with the *"Guideline of Environmental Risk Assessment of Medicinal Products for Human Use"*. Besides the exposure assessment was only done for surface and groundwater. A new version for PT19 was published in May 2015. Therefore, ES CA has recalculated predicted Environmental Concentrations (PEC) in STP, surface water, sediment, soil and groundwater following PT19 Scenario (Repellents and Attractants) and the Guidance on the Biocidal Products Regulation (Volume IV Environment – Part B Risk Assessment (active substances) Version 1, April 2015 (BPR Guidance).

According to Scenario PT19 Emissions to the environment can take place during the application of the product on human skin. A fraction can be released to the floor when repellents are applied indoors or to paved or unpaved ground during outdoor applications. However, according to TM IV/2013, emissions resulting from the stage of application on human skin are of minor importance since they take place non-repeatedly on a very limited area and are therefore not considered within this ESD.

The main emissions to the environment occur during the removal phase of the insect repellent.
Removal of the product from human skin can either take place:

- Through showering or bathing of humans who have used an insect repellent and/or washing of the clothes treated with the repellent formulation. Sewage treatment plants are the primary compartment for emissions whereas surface water bodies (including sediment) as well as the soil compartment (including groundwater) are secondary exposed compartments for remnants via sewage treatment plant effluents and sewage sludge applications, respectively. Major emissions from the application of mosquito and tick repellents result from indoor showering or bathing with emission via the STP to surface water and sediment (waste phase).

- Through direct release to surface water if people with treated skin go swimming in outdoor surface waters (only for human skin repellents).

The water compartment is therefore expected to be exposed to DEET, and because of the physiochemical character of the substance, the emissions will continue to primarily remain in this compartment (supported by level III fugacity modelling). Emission to fresh water is expected to be worst case. Therefore risk for the marine environment is considered covered by the freshwater risk assessment.

2.8.3.1 PEC in surface water, sewage treatment plant, ground water and sediment

In view that an ESD has been published for repellents (PT19) on June 2015, ES CA has used it for calculation of releases to the environment. It can be distinguished between indirect release to surface water, when another environmental compartment (e.g. STP) is exposed before or direct release, when surface water is the first receiving environmental compartment.

PEC sewage treatment plant for indirect emission through showering and bathing of humans

The emission scenario for calculating the release of repellents used on human skin is based on the average consumption. According to the Applicant the percentage of active substance in the product is 27% w/w. The product is applied 1 time per day.

The local scenario was assessed for indirect emission pathway, considering that the product can be applied only on human skin. PECs for the local scenario were calculated by using ESD for PT19 and equations in the BPR guidance.

Elocalwater values for skin (Emission rate to wastewater (standard STP), kg/d), i.e. the inflow of DEET to an STP during an emission episode, can be calculated from the formula below following the Scenario PT19; meanwhile the respective PEC_{STP} values have been obtained following the BPR Guidance.

$$\mathbf{Elocal_{water} = Nlocal \times N_{appl} \times Qform_{appl} \times AREA_{skin/garment} \times Cform_{weight} \times F_{inh} \times F_{water} \times F_{penetr} \times 10^{-9}}$$
eq (3.8) ESD PT19

Table 2.8.3.1-1. Inputs for Elocalwater calculation according to Scenario PT19

		Value	Unit	Origin
INPUTS				
Number inhabitants feeding one sewage treatment plant	Nlocal	10000	cap	D
Active substance in the product	$Cform_{weight}$	270	$g.kg^{-1}$	S
Consumption per application	$Qform_{appl}$	1.9	$mg.cm^{-2}$ skin	D/s
Number of applications per day (skin)	$N_{appl,skin}$	1	d^{-1}	D
Treated area of human skin	$AREA_{skin}$	10660	cm^2	P
Fraction released to air	F_{air}	0	-	D
Fraction dermally absorbed	F_{skin}	0	-	D
Fraction released to wastewater	F_{water}	1	-	D/O
Fraction of inhabitants using a repellent product	F_{inh}	0.2	-	P
Market share of repellent	F_{penetr}	0.5	-	D
Specific density of the product	RHOform	1000	$kg.m^{-3}$	D

Intermediate calculation: $F_{water} = 1 - (F_{air} + F_{skin}) = 1$

Table 2.8.3.1-2. Elocalwater according to Scenario PT19

OUTPUT				
Local emission rate to wastewater (skin)	**$Elocal_{water,skin}$**	5.46	$kg.d^{-1}$	O

PEC value for skin is calculated according to the BPR Guidance. Following calculations done in the DEET CAR $Clocal_{eff}$ is used for PEC_{STP} calculation:

$Clocal_{inf} = Elocal_{water} \times 10^6 / EFFLUENT_{STP}$ eq (32) BPR Guidance

$EFFLUENT_{STP} = CAPACITY_{STP} \times WASTEWinhab = 2000000$ eq (34) BPR Guidance

$PEC_{STP} = Clocal_{eff}$ (Continuous release) = $Clocal_{inf} \times F_{STPwater}$ **eq (33)** BPR Guidance

Table 2.8.3.1-3. Intput and output table for PEC_{STP} calculation

		Value	**Unit**	**Origin**
INPUTS				
Concentration in untreated wastewater (skin)	$Clocal_{inf,skin}$	2.73	$mg.L^{-1}$	eq (32) BPR Guidance
Fraction of emission directed to water by STP	$F_{STPwater}$	0.126	-	EUSES/D TGD
OUTPUT				
$PEC_{STP,skin}$ =	**$Clocal_{eff,skin}$**	0.34	$mg.L^{-1}$	O

<u>PEC in surface water and sediment for indirect emission through showering and bathing of humans</u>

In this section, the local concentration in surface water during emission episode is derived. According to the BPR Guidance:

$PEClocal_{water} = Clocal_{water} = Clocal_{eff} / [(1 + kp_{susp} \times SUSP_{water} \times 10^{-6}) \times DILUTION]$ eq (45) BPR Guidance

Where

$K_{p,susp} = Foc_{susp} \times K_{oc}$ eq. (23) BPR Guidance

Table 2.8.3.1-5. Inputs for $K_{p,susp}$ calculation

Weight fraction organic carbon in suspended matter (Foc_{susp})	0.1	$kg.kg^{-1}$	table 5 BPR Guidance
Part.coef. Carbon-water	43.3	$L.kg^{-1}$	S

Table 2.8.3.1-6. Model inputs and outputs for PEClocal$_{water}$ calculation indirect release

		Value	Unit	Origin
INPUTS				
Concentration of the substance in the STP effluent (skin)	Clocal$_{eff,skin}$	0.344	mg.L^{-1}	eq (33) BPR Guidance
solids-water partitioning coefficient of suspended matter	K$_{p,susp}$	4.33	L.kg^{-1}	eq (23)BPR Guidance
Concentration of suspended matter in the river	SUSPwater	15	mg.L^{-1}	D
Dilution factor	DILUTION	10	-	D
OUTPUT				
PEClocal$_{water,skin}$ =	**Clocal$_{water,skin}$**	0.034	mg.L^{-1}	O

According to EUSES the local PEC in surface water during emission episode is 0.0106 mg/L.

In order to estimate the PEClocal$_{sed}$, equation no. 50 of the BPR Guidance is applied:

PEClocal$_{sed}$ = (K$_{susp-water}$ / RHO$_{susp}$) x PEClocal$_{water}$ x 1000 eq (50) BPR Guidance

Where:

K$_{susp-water}$ = Fwater$_{susp}$ + [Fsolid$_{susp}$ x (Kp$_{susp}$ / 1000) x RHOsolid] eq (24) BPR Guidance

Table 2.8.3.1-7. Input for calculation of Ksusp-water

Fraction water in susp.matter	0.9	m^3.m^{-3}	Table 5 BPR Guidance
Fraction solids in susp.matter	0.1	m^3.m^{-3}	Table 5 BPR Guidance
solids-water part. Coef. of susp	4.33	L.kg^{-1}	eq. (23) BPR Guidance
Density of the solid phase	2500	kg.m^{-3}	D

Table 2.8.3.1-8. Inputs and outputs table for the calculation of PEClocalsediment indirect release

Concentration in surface water during emission episode (skin)	PEClocal$_{water,skin}$	0.034	mg.L^{-1}	eq. (45) BPR Guidance
Suspended matter-water partitioning coefficient	K$_{susp-water}$	1.9825	m^3.m^{-3}	eq. (24) BPR Guidance
Bulk density of suspended matter	RHO$_{susp}$	1150	kg.m^{-3}	eq. (18) BPR Guidance
OUTPUT				
PEClocal$_{sed,skin}$ =		**0.059**	mg.kg^{-1}	O

PEC in surface water and sediment for direct emission through swimming

The estimation of the direct local PECs for the aquatic compartment only includes surface water and sediment for the swimming-pathway because of direct entry of biocidal product in the environment.

According to ESD PT19, the local emission rate to surface water body ($Elocal_{water}$) can be calculated from the formula (Table 3-7 [3.12]):

$Elocal_{water} = N_{swimmer} * N_{appl} * Qforma_{ppl} * AREA_{skin} * Cform_{weight} * F_{swim} * F_{waterbody} * 10^{-9}$

The input values used to estimate $Elocal_{water}$ are summarized in the table below:

Table 2.8.3.1-9. Model inputs and outputs for $Elocal_{water}$ calculation direct release.

parameters (abbrev)		**Value**	**Unit**	**Remarks**
INPUT				
$N_{swimmers}$	Daily number of swimmers	1500	-	Set per default (see Appendix 6.3. ESD PT19).
F_{swim}	Fraction of swimmers using the repellent product	0.1	-	As a best guess it is assumed, that 2% of the swimmers use an insect repellent before entering the surface water body. This value of 0.02 for F_{swim} should be used as default value for active substance approval. However, for product authorisation a higher value (0.1) can be appropriate, to cover areas with higher insect infestation.
N_{appl}	Number of applications per day	1	d^{-1}	According to Schets *et al*. (2011) visits of swimmers at Dutch fresh- and seawater sites lasted 41-79 minutes per occasion in 2007 and 2009. It can be expected that during this time period, treatment with a repellent will take place only once.
$F_{waterbody}$	Fraction released to surface water body	1	-	Set per default.
$Cform_{weight}$	Active substance in the product	270	$g.kg^{-1}$	27% (information submitted by the applicant).
$Qform_{appl}$	Consumption per application	1.9	$mg.cm^{-2}$ skin	D
$AREA_{skin}$	Treated area of human skin	16600	cm^2	D (see Table 3-3 ESD PT19).
RHOform	Specific density of the product	1000	$kg.m^{-3}$	D
OUTPUT				
Local emission rate to surface water	**Elocalwater**	**1.27**	$kg.d^{-1}$	O

The surface water concentrations following swimming of humans having used an insect repellent on their skin are calculated with these equations:

$Clocal_{water,1d} = Elocal_{water} * 10^3 * T_{emission,1d} / V_{waterbody}$ (3.13 ESD PT19)

$Clocal_{water,91d} = Elocal_{water} * 10^3 * T_{emission,91d} / V_{waterbody}$ (3.14 ESD PT19)

$Clocal_{water,91d-ref} = Clocal_{water,1d}[1-(e^{-kdegwater*Temission,1d})^{Nemission,91d} / 1-e^{-kdegwater*Temission,1d}]$ (3.15 ESD PT19)

Table 2.8.3.1-10. Input values used to estimate $PEClocal_{water}$ direct release

Input parameters (abbrev)		Value	Unit	Remarks
INPUT				
$Elocal_{water}$	Local emission rate to surface water	1.27	$kg.d^{-1}$	-
$V_{waterbody}$	Volume of waterbody	435000	m^3	D
$Kdeg_{water}$	1st order rate constant for biodegradation in surface water	0.047	d^{-1}	The rate constant for biodegradation in surface water for readily biodegradable substances can be taken from Table 7 of the Technical Guidance Document (k = 0.047 d^{-1}; EC, 2003).
$T_{emission,1d}$	Number of emission days	1	d	Concentrations of the repellent have to be calculated for emission periods of 1 day and 91 days.
$T_{emission,91d}$	Number of emission days	91	d	Concentrations of the repellent have to be calculated for emission periods of 1 day and 91 days.
$N_{emission,91d}$	Number of emission events	91	-	-

As a first tier approach, the $PEClocal_{water}$ corresponds to $Clocal_{water,91d}$ from equation 3.14 and should be used for the risk assessment, representing the worst-case situation. Therefore, $PEClocal_{water,91d}$ is **0.267mg/L**.

Calculation of $PEClocal_{water}$ according to $Clocal_{water,91d\text{-}ref}$ (equation 3.15) provides a refinement option considering degradation processes in the water body. This approach is based on equations 4, 7 and 8 of the ESD for PT 18 (OECD ESD No. 14 (insecticides for stables and manure storage systems); OECD, 2006). Therefore, $PEClocal_{water,91d\text{-}ref}$ is **0.063 mg/L**.

In order to estimate the $PEClocal_{sed}$, equation no. 50 of the BPR Guidance is applied:

$$\mathbf{PEClocal_{sed} = (K_{susp\text{-}water} \ / \ RHO_{susp}) \ x \ PEClocal_{water} \ x \ 1000}$$ eq (50) BPR Guidance

Table 2.8.3.1-11. Inputs and outputs table for the calculation of PEClocalsediment direct release

		Value	Unit	Origin
INPUTS				
Concentration in surface water during emission episode (1st Tier)	$PEClocal_{water,91d}$	0.267	$mg.L^{-1}$	eq. (3.14) BPR Guidance
Concentration in surface water during emission episode (2nd Tier)	$PEClocal_{water,91d\text{-}ref}$	0.063	$mg.L^{-1}$	eq. (3.15) BPR Guidance
Suspended matter-water partitioning coefficient	$K_{susp\text{-}water}$	1.9825	$m^3.m^{-3}$	eq. (24) BPR Guidance
Bulk density of suspended matter	RHO_{susp}	1150	$kg.m^{-3}$	eq. (18) BPR Guidance
OUTPUT				
$PEClocal_{sed,91d}$ =		**0.46**	$mg.kg^{-1}$	O
$PEClocal_{sed,91d\text{-}ref}$ =		**0.108**	$mg.kg^{-1}$	O

2.8.3.2 PEC in air

DEET has a vapour pressure of 0.23 Pa (25°C) /EU Endpoint List/ and a Henry's law constant of 3.93E-03 Pa*m^3/mol /EU Endpoint List/. The substance is predicted to have an atmospheric half-life of 0.63 days (15.2 hours) /EU Endpoint List/. Thus an accumulation of DEET in air and long range transport is unlikely. As it is unlikely that the substance shows significant long-range transport, it is considered of no concern for ozone depletion. According to the TGD II, in IC5, UC36 (cosmetic odour agents; p 226), 5% of the applied amount (for substances having vapour pressure below 100 Pa) is assumed to be emitted to the air. However the half life is below the trigger value of < 2 days that is used as cut-off value to identify chemicals that could be of potential concern. The PEC of DEET in air is therefore considered to be negligible and the substance will not pose a risk to the atmospheric environment. Therefore no risk assessment is performed for the atmosphere.

2.8.3.3 PEC in soil

PEC in agricultural soils is used for risk characterisation of terrestrial ecosystems. According to the BPR Guidance section 2.3.8.5 it can be distinguished between indirect releases (i.e.: release via sewage sludge application from a STP) or direct releases when soil is the first receiving environmental compartment. However, most relevant direct emissions result from outdoor swimming and bathing after application of the product, important direct emissions to soil are therefore not expected. Besides, scenario PT 19 does not contemplate direct emissions to soil.

Indirect release

Exposure to soil via the sewer system can occur through application of sewage sludge from a STP, which can be used as a fertiliser or soil improver. The concentrations in soil arising from such application of sewage sludge will depend on the concentration of DEET in sludge, the amount of sludge applied to soil, and the volume of soil mixed with the sewage sludge.

In this section the following endpoints and underlying parameters are derived both for skin:

- Local concentration in soil (averaged for a certain time period)
- Local concentration in agricultural soil (averaged over a certain time period)
- Local concentration in grassland (averaged over a certain time period)

The concentration at the regional scale is used as background concentration for the local scale and refers to the concentration in unpolluted soil resulting from deposition only. But as deposition is not considered to be a relevant exposure process the Predicted Environmental Concentration for local soils (PEClocal) is equal to the Clocal for soils.

PEClocalsoil = Clocalsoil = (1/kT) x Csoil 10 (0) x (1 - e^{-kT}) Eq (66) (55) BPR Guidance

Table 2.8.3.3-1. Inputs and outputs table for the calculation of PEClocalsoil indirect release

		Value	Unit	Origin
INPUTS				
Averaging time	T	30	d	Table 11 BPR Guidance
First order rate constant for removal from top soil	k	0.0254	d^{-1}	eq. (56) BPR Guidance
Initial concentration after 10 years (skin)	$C_{soil\ 10,\ skin}$ (0)	0.046	$mg.kg^{-1}$	eq. (63) BPR Guidance
OUTPUTS				
$PEClocal_{soil,skin}$ =	**$Clocal_{soil,skin}$**	**0.032**	$mg.kg^{-1}$	O

For $PEC_{localsoil}$ air emissions are not considered because an extensive accumulation of DEET in air and long range transport is unlikely. A series of equations must be solved before obtaining PEC values.

Constant k is obtained by applying the following formula:

k = kvolat + kleach + kbiosoil eq (56) BPR Guidance

Table 2.8.3.3-2. Calculation of constant k

INPUT			
kvolat	0.0007	d^{-1}	eq. (57) BPR Guidance
kleach	0.0016	d^{-1}	eq. (58) BPR Guidance
kbiosoil	0.0231	d^{-1}	eq. (29) BPR Guidance
OUTPUT			
k	**0.0254**	d^{-1}	Eq (56) BPR Guidance

The rest of the values are obtained following this step-wise procedure. In accordance with BPR Guidance the initial concentration in year 10 is:

C soil10 (0) = Csludgesoil 10 (0) = Csludgesoil 1 (0) x [1 + ∑9n=1Faccn] + Cdepsoil10 eq (6 2/63) BPR Guidance

Table 2.8.3.3-3 Inputs and outputs for C_{soil10} (0) calculation

		Value	Unit	Origin
INPUTS				
Concentration in soil due to sludge in first year at t=0 (skin)	Csludgesoil,skin 1(0)	0.046	$mg.kg^{-1}$	eq. (60) BPR Guidance
Fraction accumulation in one year	Facc	9.516E-05	-	eq. (61) BPR Guidance
OUTPUT				
Csoil 10, skin (10) = Csludgesoil 10 (0)	Csludgesoil,skin 1(0)	**0.046**	$mg.kg^{-1}$	O

Since the fraction of accumulation equals to 0 Csoil 10 (0) = Csludge 1 (0)

The concentration of DEET in soil, just after the first year of sludge application, is estimated in the following way:

$Csludgesoil\ 1(0) = (C_{sludge} * Appl_{sludge}) / (DEPTH_{soil} * RHO_{sludge})$ eq. (60) BPR Guidance

Table 2.8.3.3-4. Inputs and outputs for $Csludge_{soil\ 1}(0)$ calculation

INPUT				
Concentration in dry sewage sludge (skin)	Csludge, skin	31.34	$mg.kg^{-1}$	eq. (36) BPR Guidance
Dry sludge application rate	APPLsludge	0.5	$kg.m^{-2}.yr^{-1}$	Table 11 BPR Guidance
Mixing depth of soil	DEPTHsoil	0.2	m	Table 11 BPR Guidance
Bulk density of soil	RHOsoil	1700	$kg.m^{-3}$	eq. (18) BPR Guidance
OUTPUT				
Csludgesoil,skin 1(0)		**0.046**	$mg.kg^{-1}$	O

Where C_{sludge} (concentration in sewage sludge) is:

Csludge = $(F_{STPsludge} * Elocal_{water} * 10^6) / SLUDGERATE$ eq (36) BPR Guidance

Table 2.8.3.3-5. Inputs and outputs for Csludge calculation

INPUT			
Fraction of emis. to sludge by STP	0.00407	-	EUSES
Local em. rate to water during episode (skin)	5.468	$kg.d^{-1}$	PT-19
Rate of sewage sludge production (SLUDGERATE)	710	$kg.d^{-1}$	eq. (37) BPR Guidance
OUTPUT			
Concentration in dry sewage sludge (skin)	31.34	$mg.kg^{-1}$	eq. (36) BPR Guidance

Where:
SLUDGERATE= 2/3 * SUSPCONCinf * $EFFLUENT_{STP}$ + SURPLUSsludge * $CAPACITY_{STP}$ eq. (37) BPR Giudance

Table 2.8.3.3-6. Inputs and outputs for SLUDGERATE calculation

INPUT			
Concentration of suspended matter in STP influent	0.45	$kg.m^{-3}$	Table 9 BPR Guidance
Effluent discharge rate of STP	2000	$m^3.d^{-1}$	eq. (34) BPR Guidance
Surplus sludge per inhabitant equivalent	0.011	$kg.d^{-1}.eq^{-1}$	Table 9 BPR Guidance
Capacity of the STP	10000	eq	Table 9 BPR Guidance
OUTPUT			
SLUDGERATE	710	$kg.d^{-1}$	eq (37) BPR Guidance

PEC calculations for agriculture and grassland are obtained using the same formulas but varying the depth of soil and average time (see table 11 BPR Guidance)

Agric. Soil: PEClocalagr.soil = Clocalagr.soil = (1/kT) x Cagr.soil 10 (0) x (1 - e^{-kT}) eq (66) (55)

Table 2.8.3.3-7. Inputs and outputs for PEClocal$_{agr.soil}$ calculation indirect release

		Value	**Unit**	**Origin**
INPUTS				
Averaging time	T	180	d	Table 11 BPR Guidance
First order rate constant for removal from top soil	k	0.0254	d^{-1}	eq. (56) BPR Guidance
Initial concentration after 10 years (skin)	Cagr.soil 10, skin (0)	0.046	$mg.kg^{-1}$	eq. (63) BPR Guidance
OUTPUT				
PEClocalagr.soil,skin =	Clocalagr.soil,skin	**0.0099**	$mg.kg^{-1}$	O

Grassland: PEClocalgrassland = Clocalgrassland = (1/kT) x Cgrassland (0) x (1 - e^{-kT}) (66) (55)

Table 2.8.3.3-7. Inputs and outputs for PEClocal$_{grassland}$ calculation indirect release

		Value	**Unit**	**Origin**
INPUTS				
Averaging time	T	180	d	Table 11 BPR Guidance
First order rate constant for removal from top soil	k	0.027	d^{-1}	eq. (56) BPR Guidance
Initial concentration after 10 years (skin)	Cgrassland 10, skin (0)	0.018	$mg.kg^{-1}$	eq. (63) BPR Guidance
OUTPUTS				
PEClocalgrassland,skin =	Clocalgrassland,skin	**0.0037**	$mg.kg^{-1}$	O

2.8.3.4 PEC in groundwater

In order to confirm if the product leaches into groundwater an evaluation was conducted. As an indication for potential groundwater levels, the concentration in porewater of agricultural soil is taken. It should be noted that this is a worst-case assumption, neglecting transformation and dilution in deeper soil layers.

Thus, the predicted environmental concentration in groundwater ($PEC_{localgroundwater}$) is equal to the predicted environmental concentration in porewater ($PEC_{localagrsoil,\ porew}$). In order to calculate the concentration of the a.s. in porewater, a number of partition coefficients are derived from the following equations:

$K_{soil\text{-}water}$ = $Fair_{soil}$ x $K_{air\text{-}water}$ + $Fwater_{soil}$ + [$Fsolid_{soil}$ x (Kp_{soil} / 1000) x RHOsolid]
eq (24) BPR Guidance

Table 2.8.3.4-1. Inputs and outputs for $K_{soil\text{-}water}$ calculation

Fraction air in soil	0.2	$m^3.m^{-3}$	Table 5 ECHA
K Air-water partitioning coeff.	1.6586E-06	-	eq. (22)
Fraction water in soil	0.2	$m^3.m^{-3}$	Table 5 ECHA
Fraction solids in soil	0.6	$m^3.m^{-3}$	Table 5 ECHA
K solids-water part. Coef. of soil	0.866	$L.kg^{-1}$	eq. (23)
Density of the solid phase	2500	$kg.m^{-3}$	D
$K_{air\text{-}water}$ = HENRY / R x TEMP			**(22)**
Henry's law constant	0.0039	$Pa.m^3.mol^{-1}$	S
Gas constant	8.314	$Pa.m^3.mol^{-1}.k^{-1}$	D
Temperature air-water interface	285	k	D
$Kp_{soil} = F_{oc,soil}$ x K_{oc}			**(23)**
Weight fraction of org.carbon in soil	0.02	$kg.kg^{-1}$	Table 5
Partition coeff. Org.carbon-water	43.3	$L.kg^{-1}$	S

Solving the equations for PEC_{local} the following results are obtained.

$PEClocal_{grw} = PEClocal_{agr.soil,\ porewater}$ = ($PEClocal_{agr.soil}$ x RHO_{soil}) / ($K_{soil\text{-}water}$ x 1000) eq (68)(67)

Table 2.8.3.4-2. Inputs and outputs for $PEClocal_{agr.soil,\ porewater}$ calculation

		Value	Unit	Origin
INPUTS				
Predicted environmental conc. in soil (skin)	$PEClocal_{agr.soil,skin}$	0.0099	$mg.kg^{-1}$	eq. (66)(55)
Soil-water partitioning coefficient	$K_{soil\text{-}water}$	1.499	$m^3.m^{-3}$	eq. (24)
Bulk density of wet soil	RHO_{soil}	1700	$kg.m^{-3}$	eq. (18)
OUTPUT				
$PEClocal_{grw,skin}$ =	**$PEClocal_{agr.soil,\ porewater,skin}$**	**0.011**	$mg.L^{-1}$	O

$PEClocal_{grw} = PEClocal_{grassland,\ porewater}$ = ($PEClocal_{grassland}$ x RHO_{soil}) / ($K_{soil\text{-}water}$ x 1000) eq (68)(67)

Table 2.8.3.4-3. Inputs and outputs for $PEClocal_{grassland,\ porewater}$ calculation

		Value	Unit	Origin
INPUTS				
Predicted environmental conc. in soil (skin)	$PEClocal_{soil,skin}$	0.0037	$mg.kg^{-1}$	eq. (66)(55)
Soil-water partitioning coefficient	$K_{soil\text{-}water}$	1.499	$m^3.m^{-3}$	eq. (24)
Bulk density of wet soil	RHO_{soil}	1700	$kg.m^{-3}$	eq. (18)
OUTPUT				
$PEClocal_{grw,skin}$ =	**$PEClocal_{grassland,\ porewater,skin}$**	**0.0042**	$mg.L^{-1}$	O

The concentration in groundwater should be <0.1 µg/L for active substance, relevant metabolites or breakdown/reaction products and substances of concern. Since the values obtained are aboved this value PECgw was further refined using the nine FOCUS groundwater scenarios, as developed for plant protection products (see tables 2.8.4.3-3 and 2.8.4.3-4).

2.8.3.5 Non compartment specific exposure relevant to the food chain (secondary poisoning)

DEET log K_{ow} is 2.4, suggesting a low bioaccumulation potential (BCF estimates range between 3.85 and 63.1). The risk of secondary poisoning is therefore expected to be low via ingestion of potentially contaminated food (e.g., fish) by birds or mammals. The risk for secondary poisoning via intake of terrestrial organisms such as earthworms is considered unlikely also because exposure to earthworms is expected to be negligible. No avian dietary tests were therefore required. However, acute avian toxicity was measured by oral intubation and there was a clear dose-response relationship regarding both lethality and sublethal effects. DEET was found to have only slight acute avian toxicity (LD50 1375 mg/kg bw). Sublethal effects (behaviour, appearance and weight loss and reduced feed intake) appeared relatively soon after dosing, but signs of toxicity disappeared with time among the survivors.

2.8.4 Risk characterisation for the environment

The risk characterisation for the environment is the comparison of the exposure estimates to the toxicity of the substance. Both aspects were already discussed in sections 2.8.2 and 2.8.3, respectively, and only the relevant values are summarised below. The environmental risk has been assessed solely for the active substance as the available tests do not indicate formation of metabolites at a level higher than 10% of the active substance. It is thereby assumed that the risk assessment for the active substance also covers risks for the metabolites.

2.8.4.1 Aquatic compartment (incl. sediment)

Even when making worst case assumptions for the local environment none of the PEC/PNEC ratios exceed 1, except for direct emissions to water (when refinement aspects are considered the product has no risk for the aquatic compartment).

Indirect Emissions: Risk assessment for indirect emission via STP through showering and bathing of humans

Two local scenarios were assessed for indirect emission pathway, considering that the product can be applied on human skin. PECs for both local scenarios were calculated by using ESD for PT19 and equations in the BPR Guidance,

Estimated local PECs for microorganism (in STP), fresh surface water and sediment are shown below. None of the PEC/PNEC ratios exceed 1, even if based on worst case local PEC values for skin scenario (Table 2.8.4.1-1).

Note that emission to surface water is expected to be worst case. Therefore risk for the marine environment is considered covered by the surface water risk assessment. Furthermore, no quantitative estimation of $PNEC_{marine\ sediment}$ is necessary because the PEC values for the marine sediment compartment will be based on EqP and the same P_{OW} and K_{oc} values. The PEC/PNEC ratios for the marine sediment compartment will therefore be the same as for the corresponding water compartment.

Table 2.8.4.1-1. PEC/PNEC ratios for the worst case local scenario for the aquatic compartments during an indirect emission episode according to ESD 19.

PEC/ Aquatic Compartment	PEC	PNEC	PEC/PNEC
Microorganisms (STP), skin (mg/L)	0.34	>10	<0.034
Surface Freshwater, skin (mg/L)	0.034	0.043	0.80
Freshwater sediment, skin (mg/kg)	0.059	0.0741	0.80

Direct emission through swimming

In table 2.8.4.1-2 the PEC/PNEC ratios for direct emission to surface water and sediment due to swimming are indicated. The PECs were calculated using ESD PT19. The PEC/PNEC ratios for TIER 1 both in surface water and sediment are > 1 indicating a risk for the environment. However, for TIER 2, once degradation processes in water are taken into account there is no risk.

Table 2.8.4.1-2. PEC/PNEC ratios for the worst case local scenario for the aquatic compartments during a direct emission episode.

Aquatic Compartment	PEC	PNEC	PEC/PNEC
Freshwater,91d (mg/L)	0.267	0.043	6.2
Freshwater,91d-ref (mg/L)	0.063	0.043	1.46
Freshwater sediment, 91d (mg/kg)	0.46	0.0741	6.21
Freshwater sediment, 91d-ref (mg/kg)	0.108	0.0741	1.46

2.8.4.2 Atmosphere

DEET has a vapour pressure of 0.23 Pa (25°C) /EU Endpoint List/ and a Henry's law constant of 3.93E-03 Pa*m^3/mol /EU Endpoint List/. The substance is predicted to have an atmospheric half-life of 0.63 days (15.2 hours) /EU Endpoint List/. Thus an accumulation of DEET in air and long range transport is unlikely. As the substance unlikely shows significant long-range transport, it is considered of no concern for ozone depletion. According to the TGD II, in IC5, UC36 (cosmetic odour agents; p 226), 5% of the applied amount (for substances having vapour pressure below 100 Pa) is assumed to be emitted to the air. However the half life is below the trigger value of < 2 days that is used as cut-off value to identify chemicals that could be of potential concern. The PEC of DEET in air is therefore considered to be negligible and the substance will not pose a risk to the atmospheric environment. Therefore no risk assessment is performed for the atmosphere.

2.8.4.3 Terrestrial compartment

In the scenario for the swimming pathway (direct emission), the terrestrial compartment is not exposed and therefore is not assessed.

Risk assessment for indirect emission via STP through showering and bathing of humans

Exposure to soil via the sewer system can occur through application of sewage sludge from a STP as a fertilizer or soil improver. The local scenarios for human skin were assessed for indirect emission

pathway. PECs for local scenarios were calculated using two different approaches: by using ESD for PT19 and equations in the BPR guidance.

For risk assessment purposes, the **PEC soil** values calculated using ESD for PT19 were selected as worst case scenarios. None of the PEC/PNEC ratios exceed 1 (See Table 2.8.4.3-1).

Table 2.8.4.3-1. PEC/PNEC ratios for the terrestrial compartments during an indirect emission episode (PEC soil values calculated using ESD for PT19).

ESD PT19			
Terrestrial Compartment	**PEC (mg/kg)**	**PNEC (mg/kg)**	**PEC/PNEC**
Soil	0.032	0.0379	0.85
Agricultural soil	0.0099	0.0379	0.26
Grassland	0.003	0.0379	0.099

Concerning the **PECs for groundwater**, estimations on porewater agricultural soil and porewater grassland using ESD for PT19 are shown below (See Table 2.8.4.3-2).

Table 2.8.4.3-2. PECs for groundwater for indirect emission to groundwater

PECporewater agr. Soil (µg/L)	PECporewater grassland (µg/L)
36.6	4.2

Considering that the calculated PECs for porewater exceed the drinking water limit for groundwater of 0.1 µg/L, PEC_{gw} for the nine FOCUS groundwater scenarios, as developed for plant protection products, were calculated. Model used, input data and assumptions are shown in table 2.8.4.3-3, assuming that the only exposure route to groundwater is via the application of sludge from STPs.

Table 2.8.4.3-3. Summary of data used and assumptions made to calculate PEC_{gw} for DEET in FOCUS scenarios.

Parameter	Value
Model used:	FOCUS PEARL ver. 4.4.4.
Years of simulation:	26 (including 6 yrs "warming-up" period)
Application rate:	0.156 kg/ha[a]
Application method:	To the soil surface
Date of application:	1 October annually for 20 years[b]
Molar mass:	191.27 g/mol
Vapour pressure:	0.11 Pa (20°C)
Water solubility:	11200 mg/L (25°C)
Kom:	25.1 L/kg[c]
Freundlich exponent 1/n:	0.9 (FOCUS default)
DT_{50} soil:	30 days (12°C)[d]
Coefficient for uptake in plants:	0 (worst-case assumption)

[a] Calculated from Simple Treat output concentration of DEET in dry sewage sludge of 33 mg/kg (see table 2.8.3.3-4.), and application of 5000 kg dry sludge/ha and year to agricultural land (at a single event as suggested in the BPR Guidance 2.3.8.5).

[b] Autumn application assumed to represent a worst-case situation.

[c] Calculated from Koc as 43.3/1.724.

[d] In accordance with EUSES/TGD, Part II 2.3.6.5., for ready biodegradable substances.

The resulting PEC_{gw} (as FOCUS standard output; 80th percentile annual average PEC_{gw} at 1 m depth) are shown in table 2.8.4.3.-4. These results show that the predicted groundwater concentrations of DEET following the intended use of this substance are > 0.1 µg/L for four FOCUS scenarios.

Table 2.8.4.3-4. 80th percentile annual average PEC of DEET in groundwater (at 1 m depth) calculated for nine FOCUS scenarios, assuming application of sewage sludge from STP to land.

Scenario	PEC_{gw}, µg/L (grass)	PEC_{gw}, µg/L (winter cereal)
Chateaudun	0.02	0.006
Hamburg	0.207	0.234
Jokioinen	0.086	0.05
Kremsmuenster	0.078	0.090
Okehampton	0.21	0.19
Piacenza	0.288	0.229
Porto	0.179	0.165
Sevilla	0.0127	0.0013
Thiva	0.030	0.0035

2.8.4.4 Non compartment specific exposure relevant to food chain (primary and secondary poisoning)

Primary poisoning of birds and mammals due to intake of the product is not expected to be relevant. Considering the low acute toxicity of DEET to birds (LD50 1375 mg/kg bw) and the type of use intake by birds and mammals of the active substance via water is considered as negligible. Although PEC/PNEC ratios could not be calculated, it can be concluded that no risk for secondary poisoning has been identified based on the low BCF value, see section 2.8.3.5.

2.8.4.5 PBT assessment

PBT assessment is summarized in the N,N-diethyl-m-toluamide (DEET) CAR, Doc I section 2.2.2.3. 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.

2.8.4.6 Conclusion

Summary table for the risk assessment of this product.					
	PEC/PNECstp	PEC/PNECwater	PEC/PNECsed	PEC/PNECsoil	PEC/PNECGW
Scenario 1, Indirect release		Acceptable	Acceptable		Acceptable
Scenario 2, Direct release	Acceptable	Acceptable	Acceptable	Acceptable	Unacceptable

Unaceptable risk has been found for groundwate, however ESCA considers that the product should be authorized despite unaceptable risk for groundwater compartment since there is not many products containing active substances with different modes of action available for repelencing of mosquitos. Hence the unauthorisation of the product GOIBI ANTIMOSQUITOS XTREME AEROSOL would have disporporcionate negative consequences for the society against the risk of the groundwater. We consider that the product should be authorized, despite unacceptable risk in groundwater, in applicaction of article 19(5) of the Biocidal product Regulation 528/2012.The following risk

mitigation measures must be followed when using the product, notably to limit risk for the consumers and the environment (section 2.9)

2.9 Measures to protect man, animals and the environment

For the product GOIBI ANTIMOSQUITOS XTREME AEROSOL, no unacceptable risks were identified for the environment but the following risk mitigation measures are required:

Do not throw the product on the ground, into a water course, into the sink or down the drain and into the environment.

Prevent accidental exposure of the product to the environment.

Stop release, if possible without risk. Dike or contain release, if possible, and if immediate response can prevent further damage or danger. Isolate and control access to the release area. Take actions to reduce vapors. Collect substance into drums, etc. via drains, pumps, etc., if appropriate. Absorb with appropriate absorbent. Clean spill area of residues and absorbent.

For non-professional users:

- P501: Dispose of content and / or its container as hazardous waste according to the regulations in force.

Regarding the possibility of destruction or decontamination following release in or on the following: (a) Air, (b) Water, including drinking water, and (c) Soil:

a) The risk of release of the active ingredient or the product to atmosphere is negligible.

b) Leak/spill: Remove all sources of ignition. Use an inert absorbent material, and non-sparking tools. Ventilate area. Prevent from entering a watercourse.

Because of the smell and taste of DEET, it acts as a self deterrent against consumption by humans and animals. The GOIBI ANTIMOSQUITOS XTREME AEROSOL product contains an ingredient that acts as a strong deterrent for ingestion (denatonium benzoate).

For the product GOIBI ANTIMOSQUITOS XTREME AEROSOL, risks were identified for the human health taking into account the following risk mitigation measures are required:

Apply the product sparingly and carefully to parts of the body that are not covered. Do not apply on clothes; divide the product evenly over the skin.

The application for adults and children over 2 years of age must be restricted to one application a day.

Children under 2 years of age must not be treated with this product.

Avoid contact with eyes, mucous membranes, nose, lips and damaged skin. Apply carefully to areas where skin folds normally occur.

Do not apply on young children´s hands. For other users, wash your hands thoroughly with soap and water before eating or drinking.

Do not mix with other chemical substances/mixtures.

When used in combination with sun block lotion, apply sun block first then wait 30 minutes before applying the biocidal product.

Wash the areas of skin that have been treated when protection is no longer needed or if side effects occur.

The biocidal product must not be applied where food, feeding stuffs or drinking water can become contaminated.

Apply hygiene measures: do not eat, drink or smoke during the applying of the product and wash hands after use.

The label of the biocidal product will include the established in the Commission Directive 2008/47/EC, Commission Directive 94/1/EC and Commission Directive 2013/10/EU relating to aerosol dispensers.

Use only outdoors or in a well-ventilated area.

Do not inhale the product.

Keep this product away from children.

Avoid contact with plastics, synthetic-/leather clothing and painted surfaces.

Do not throw the product on the ground, into a water course, into the sink or down the drain.

Specific treatment in case of an accident, e.g. first aid measures, antidotes, medical treatment if available.

Poisoning may cause:

- Irritation of the eyes, skin, mucous membranes, respiratory and gastrointestinal tract.
- Allergic skin reaction (including anaphylaxis).
- Overuse and/or multiples dermal applications may cause neuronal disorders (behavioural disorders, ataxia, hypertonia, seizures, encephalopathy and coma).

Basic first aid procedures

- Move the person away from the contaminated area and remove contaminated or spattered clothing
- If contact in eyes, rinse with plenty of water for 15 minutes. Do **NOT** forget to remove the contact lenses.
- If contact on skin, wash with soap and plenty of water, without rubbing. Remove the product from skin folds and from under fingernails.
- If swallowed, do **NOT** induce vomiting unless told to do so by poison control or a health care professional. Call immediately to a poison control center and if necessary take the person to a hospital and show the label or packaging whenever possible.
- Keep the patient at rest and maintain the body temperature.
- If the person in unconscious, turn the patient sideways with the head at lower than the rest of the body and the knees bended.
- If necessary take the person to a hospital and show the label or packaging whenever possible.

DO NOT LEAVE THE POISENED PERSON ALONE UNDER ANY CIRCUMSTANCE

Medical advice for doctors and sanitary staff

- Gastrointestinal decontamination is not recommended.
- Contraindication: Syrup of Ipecac
- Symptomatic and supportive treatment.

IF MEDICAL ADVICE IS NEEDED, HAVE THE PRODUCT CONTAINER OR LABEL AT HAND AND CONTACT THE POISON CONTROL CENTER

3 Proposal for decision

GOIBI ANTIMOSQUITOS XTREME AEROSOL is an aerosol (ready-to-use) for non-professional / general public use for the purpose of applying on the body areas to be protected that contains 27% (w/w) DEET (N, N-diethyl-meta-toluamide).

The physico-chemical properties have been evaluated and there are no hazards associated with the product under normal conditions of use.

Tests show the efficacy of GOIBI ANTIMOSQUITOS XTREME AEROSOL against mosquitoes in simulated-use tests (arm-in-cage) and against ticks in a laboratory test. The results of the arm-in-cage studies show that GOIBI ANTIMOSQUITOS XTREME AEROSOL repels *Anopheles spp*. and *Aedes spp*. for on average 5 and 8 hours respectively. The laboratory test with *Ixodes ricinus* shows that ticks are repelled for at least 8 hours.

Regarding the risk for human health of non-professional users it can be concluded that there is risk for each subpopulation (adults, children younger than 12 years old, and children older than 12 years old). The product can be used once per day on adults and children over 2 years. Children's hands must not be treated with this product. Children under 2 years must not be treated with this product. For reasons of public health, GOIBI ANTIMOSQUITO XTREME AEROSOL must be authorized on the grounds of Article 19(5) of Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2019 concerning the market and use of biocidal product.

The risk for the environment for the use of GOIBI ANTIMOSQUITOS XTREME AEROSOL has been evaluated when applied directly on uncovered human skin, on an application frequency of 1 time per day. The product, containing 27% (270 g/kg) DEET will be used to repel biting mosquitoes, ticks and other arthropods (flies, horse flies). The overall conclusion is that the intended uses of GOIBI ANTIMOSQUITOS XTREME AEROSOL do not pose an unacceptable risk to the sewage treatment plant, soil, air, surface water, sediment compartments, however an unacceptable risk has been found for groundwater compartment..

Although unaceptable risk has been found for groundwate, ESCA considers that the product should be authorized since there is not many products containing active substances with different modes of action available for repelencing of mosquitos. Hence the unauthorisation of the product KILMOS REPELLENT AEROSOL would have disporporcionate negative consequences for the society against the risk of the groundwater. We consider that the product should be authorized, despite unacceptable risk in groundwater, in applicaction of article 19(5) of the Biocidal product Regulation 528/2012.The following risk mitigation measures must be followed when using the product, notably to limit risk for the consumers and the environment (section 2.9).

The Spanish CA authorises the biocidal product GOIBI ANTIMOSQUITOS XTREME AEROSOL as a repellent (PT19) for dermal use, against mosquito, tiger mosquito, ticks by applying on the body areas to be protected by non-professional users.

Particular Conditions

The biocidal product under PT19 (Repellent) GOIBI ANTIMOSQUITOS XTREME AEROSOL contains 27% (w/w) DEET (N, N-diethyl-meta-toluamide).

The active substances as manufactured shall have the following minimum purities:
DEET (N, N-diethyl-meta-toluamide): 970 g/kg

Read attached instructions before use.

Only ready-to-use GOIBI ANTIMOSQUITOS XTREME AEROSOL product is authorised.

The biocidal product acts against vector-borne topical diseases as for example malaria, yellow fever, zika virus, dengue fever or chikungunya, etc.

Apply only in areas where there is significant risk of infection by vector-borne diseases.

The product is authorised only for use against *Anopheles spp*. and *Aedes spp*. for on average 6 and 8 hours. The laboratory test with *Ixodes ricinus* shows that ticks are repelled for at least 8 hours. Authorisation of this product does not allow use against non-target organisms.

Apply the product sparingly and carefully to parts of the body that are not covered. Do not apply on clothes; divide the product evenly over the skin.

The application for adults and children over 2 years of age must be restricted to one application a day.

Children under 2 years of age must not be treated with this product.

Keep the spray bottle at least 15 cm from the skin; do not spray directly on the face. To protect the face from insect bites, first spray or spread a small quantity of the product onto the palm of the hand and then spread on the face.

Avoid contact with eyes, mucous membranes, nose, lips and damaged skin. Apply carefully to areas where skin folds normally occur.

Do not apply on young children´s hands. For other users, wash your hands thoroughly with soap and water before eating or drinking.

The product contains an aversive or bittering agent.

Do not mix with other chemical substances/mixtures.

When used in combination with sun block lotion, apply sun block first then wait 30 minutes before applying the biocidal product.

Wash the areas of skin that have been treated when protection is no longer needed or if side effects occur.

The biocidal product must not be applied where food, feeding stuffs or drinking water can become contaminated.

Apply hygiene measures: do not eat, drink or smoke during the applying of the product and wash hands after use.

The label of the biocidal product will include the established in the Commission Directive 2008/47/EC, Commission Directive 94/1/EC and Commission Directive 2013/10/EU relating to aerosol dispensers.

Use only outdoors or in a well-ventilated area.

Do not inhale the product.

Keep this product away from children.

Avoid contact with plastics, synthetic-/leather clothing and painted surfaces.

The packaging of the product placed on the market has to be limited to a maximum size of 200ml.

The packaging of the biocidal product shall be fitted with a tactile warning of danger.

Do not throw the product on the ground, into a water course, into the sink or down the drain.

Expiry Date of the Authorisation:

The authorisation of the product GOIBI ANTIMOSQUITOS XTREME AEROSOL expires on 31 July 2022, which is the expiry date of Annex I listing of the active substance DEET (N, N-diethyl-meta-toluamide).

Nevertheless, the authorisation of the biocidal product GOIBI ANTIMOSQUITOS XTREME AEROSOL is conditioned to the submission a storage stability long term study at ambient temperature (2 years) in June 2018.

Annex:

1. **Summary of product characteristics**
2. **List of studies reviewed**
3. **Analytical methods residues – active substance**
4. **Toxicology and metabolism –active substance**
5. **Toxicology – biocidal product**
6. **Safety for professional operators**
7. **Safety for non-professional operators and the general public**
8. **Residue behaviour**

Summary of product characteristics for a biocidal product

GOIBI ANTIMOSQUITOS XTREME AEROSOL

Product type(s) [19]

ES/APP(NA)-2016-19-00364

ES-0008808-0000

1. Administrative information

1.1. Trade name(s) of the product

Trade name(s)[4]	GOIBI ANTIMOSQUITOS XTREME AEROSOL

1.2. Authorisation holder

Name and address of the authorisation holder	**Name**	Laboratorios Cinfa, S.A.
	Address	Olaz-Chipi, nº 10 31620 - Huarte (Pamplona)
Authorisation number	ES/APP(NA)-2016-19-00364	
Suffixes to the authorisation number linked to trade names[5]		
R4BP asset reference number	ES-0008808-0000	
Date of the authorisation	19/05/2016	
Expiry date of the authorisation	31 July 2022	

1.3. Manufacturer(s) of the product

Name of manufacturer 1	Laboratorios Cosméticos Feltor, S.A. (bulk product manufacture)
Address of manufacturer	Pol. Ind. "Molí de les Planes" C/ Roques Blanques, 3-5 08470 San Celoni (Barcelona) Spain
Location of manufacturing sites	Pol. Ind. "Molí de les Planes" C/ Roques Blanques, 3-5 08470 San Celoni (Barcelona) Spain

Name of manufacturer 2	IGEPAK, S.A. (bulk product packing)
Address of manufacturer	C/ Legarda, 2 20170 - Usurbil (Guipuzkoa) Spain
Location of manufacturing sites	C/ Legarda, 2 20170 - Usurbil (Guipuzkoa) Spain

1.4. Manufacturer(s) of the active substance(s)

Active substance	DEET (N,N-diethyl-m-toluamide)
Name of manufacturer	Vertellus Performance Materials Inc. (formerly Morflex, Inc.)
Address of manufacturer	Vertellus Performance Materials Inc. 2110 High Point Road

[4] In case the product would have more than one name, all names can be provided in this field.

[5] Where relevant for the Member State delivering a national authorisation. Insert rows as necessary.

	Greensboro (NC) NC 27403 (USA)
Location of manufacturing sites	Vertellus Performance Materials Inc. 2110 High Point Road Greensboro (NC) NC 27403 (USA)

Active substance	DEET (N,N-diethyl-m-toluamide)
Name of manufacturer	Clariant Produkte (Deutschland) GmbH (Acting for Clariant Corporation (United States))
Address of manufacturer	Clariant Corporation 500 East Morehead St., Charlotte, NC 28202, USA
Location of manufacturing sites	625 East Catawba Avenue, Mt. Holly, NC 28120, USA

Active substance	DEET (N,N-diethyl-m-toluamide)
Name of manufacturer	Clariant Produkte (Deutschland) GmbH (Acting for Clariant Corporation (United States))
Address of manufacturer	Cangzhou Panoxi Chemical Co. Ltd Chemical 1 Road, Lingang Economic Development Zone, Bohai New Zone, Cangzhou City, Hebei Province, China
Location of manufacturing sites	Cangzhou Panoxi Chemical Co. Ltd., Chemical 1 Road, Lingang Economic Development Zone, Bohai New Zone, Cangzhou City, Hebei Province, China

2. Product composition and formulation

2.1. Qualitative and quantitative information on the composition of the product

Common name	IUPAC name	Function	CAS number	EC number	Content (%)
DEET	N, N-diethyl-m-toluamide	Active substance	134-62-3	205-149-7	27
Ethanol		Solvent	64-17-5	200-578-6	29.9999964
Propellant	Hydrocarbons, C3-4-rich, petroleum distillate (Petroleum gas)	Propellant	68512-91-4	270-990-9	40
		Non active substance			

2.2. Type of formulation

Aerosol

3. Hazard and precautionary statements[6]

Hazard statements	H223: Flammable aerosol H229: Pressurised container: May burst if heated H319: Causes serious eye irritation H412: Harmful to aquatic life with long lasting effects. EUH208: "Contains D- and L-Limonene, Citral and Hydroxyisohexyl 3- cyclohexene carboxaldehyde. May produce an allergic reaction"
Precautionary statements	P102: Keep out of reach of children P103: Read label before use P210: Keep away from heat/sparks/open flames/hot surfaces. No smoking P211: Do not spray on an open flame or other ignition source P251: Pressurized container: Do not pierce or burn, even after use P264: Wash … thoroughly after handling P273: Avoid release to the environment. P410+P412: Protect from sunlight. Do not expose to temperatures exceeding 50 ºC/122ºF. P501: Dispose of the content and / or its container as hazardous waste according to the regulations in force.

4. Authorised use(s)

4.1. Use description[7]

Table 1. Use # 1 – Repellent – Mosquitoes and ticks– Non-professional user (general public) – Adultx and children over 2 years of age - Aerosol – Indoor and Outdoor use

Product Type	PT19, repellent
Where relevant, an exact description of the authorised use	Repellent against mosquitoes and ticks for human hygiene
Target organism(s) (including development stage)	Mosquitoes: *Aedes albopictus* and *Anopheles gambiae* Ticks: *Ixodes ricinus*
Field(s) of use	Outdoor and indoor in a well-ventilated area
Application method(s)	Topical application in human skin by aerosol
Application rate(s) and frequency	The biocidal product is to be applied only **once** a day, for adults and children over 2 years of age. The maximum time protection is between 6 and 8 hours for mosquitoes and until 8 hours for ticks.
Category(ies) of users	Non professional user (general public)
Pack sizes and packaging material	The biocidal product is packaged in an aluminium aerosol of 150 ml net.

[6] According to Regulation (EC) 1272/2008, or where relevant, Directive 1999/45/EC. This section shall only include precautionary statements triggered by the CLP legislation. In accordance with paragraph 8 of document CA-May13-Doc.5.4, a precautionary statement that has been proven unnecessary in the risk assessment because of the intended use of the product should be left out of the SPC and of the label. For micro-organisms based products: indication on the need for the biocidal product to carry the biohazard sign specified in Annex II to Directive 2000/54/EC (Biological Agents at Work).

[7] Copy this section as many times as necessary (one table per use, together with any instructions for use, risk mitigation measures and other directions for use that are use-specific. It has to be noted that in accordance with Document CA-May14-Doc.5.6 – Final, the SPC of a single biocidal product presents the authorised uses as a number of pre-defined uses to which the product label shall have full correspondence.

4.1.1. Use-specific instructions for use[8]

See section 5.1

4.1.2 Use-specific risk mitigation measures

See section 5.2

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

See section 5.3

4.1.4 Where specific to the use, the instructions for safe disposal of the product and its packaging

See section 5.4

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

See section 5.5

5. General directions for use[9]

5.1. Instructions for use[6]

Read attached instructions before use.

The biocidal product acts against vector-borne topical diseases as for example malaria, yellow fever, zika virus, dengue fever or chikungunya.

Apply the product sparingly and carefully to parts of the body that are not covered. Do not apply on clothes; divide the product evenly over the skin.

Keep the spray bottle at least 15 cm from the skin; do not spray directly on the face. To protect the face from insect bites, first spray or spread a small quantity of the product onto the palm of the hand and then spread on the face.

The application for adults and children over 2 years of age must be restricted to one application a day.

Children under 2 years must not be treated with this product.

Do not throw the product on the ground, into a water course, into the sink or down the drain.

[8] Describe the necessary instructions for use like for example: period of time needed for the biocidal effect; the interval to be observed between applications of the biocidal product or between application and the next use of the product treated, or the next access by humans or animals to the area where the biocidal product has been used, including particulars concerning decontamination means and measures and duration of necessary ventilation of treated areas; particulars for adequate cleaning of equipment; particulars concerning precautionary measures during transport; precautions to be taken to avoid the development of resistance.

[9] Instructions for use, risk mitigation measures and other directions for use under this section are valid for any authorised uses.

5.2. Risk mitigation measures

Apply only in areas where there is significant risk of infection by vector-borne diseases.

Avoid contact with eyes, mucous membranes, nose, lips and damaged skin. Apply carefully to areas where skin folds normally occur.

Do not apply on young children´s hands. For other users, wash your hands thoroughly with soap and water before eating or drinking.

The product contains an aversive or bittering agent.

Do not mix with other chemical substances/mixtures.

When used in combination with sun block lotion, apply sun block first then wait 30 minutes before applying the biocidal product.

Wash the areas of skin that have been treated when protection is no longer needed or if side effects occur.

The biocidal product must not be applied where food, feeding stuffs or drinking water can become contaminated.

Apply hygiene measures: do not eat, drink or smoke during the applying of the product and wash hands after use.

Use only outdoors or in a well-ventilated area.

Do not inhale the product.

Keep this product away from children.

Avoid contact with plastics, synthetic-/leather clothing and painted surfaces.

The packaging of the product placed on the market has to be limited to a maximum size of 200ml.

The label of the biocidal product will include the established in the Commission Directive 2008/47/EC, Commission Directive 94/1/EC and Commission Directive 2013/10/EU relating to aerosol dispensers.

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

Poisoning may cause:

- Irritation of the eyes, skin, mucous membranes, respiratory and gastrointestinal tract.
- Allergic skin reaction (including anaphylaxis).
- Overuse and/or multiples dermal applications may cause neuronal disorders (behavioural disorders, ataxia, hypertonia, seizures, encephalopathy and coma).

Basic first aid procedures

- Move the person away from the contaminated area and remove contaminated or spattered clothing
- If contact in eyes, rinse with plenty of water for 15 minutes. Do **NOT** forget to remove the contact lenses.
- If contact on skin, wash with soap and plenty of water, without rubbing. Remove the product from skin folds and from under fingernails.
- If swallowed, do **NOT** induce vomiting unless told to do so by poison control or a health care professional. Call immediately to a poison control center and if necessary take the person to a hospital and show the label or packaging whenever possible.
- Keep the patient at rest and maintain the body temperature.
- If the person in unconscious, turn the patient sideways with the head at lower than the rest of the body and the knees bended.
- If necessary take the person to a hospital and show the label or packaging whenever possible.

DO NOT LEAVE THE POISENED PERSON ALONE UNDER ANY CIRCUMSTANCE

Medical advice for doctors and sanitary staff

- Gastrointestinal decontamination is not recommended.
- Contraindication: Syrup of Ipecac
- Symptomatic and supportive treatment.

IF MEDICAL ADVICE IS NEEDED, HAVE THE PRODUCT CONTAINER OR LABEL AT HAND AND CONTACT THE POISON CONTROL CENTER.

5.4. Instructions for safe disposal of the product and its packaging

Dispose of the content and / or its container as hazardous waste according to the regulations in force.

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

The product is stable to three months

6. Other information

The packaging of the biocidal product shall be fitted with a tactile warning of danger.

Definition of non-professional users (general public): users who are not professionals and that apply the biocidal product is in his private life.

Annex 2: List of studies reviewed

List of <u>new data</u>[10] submitted in support of the evaluation of the active substance

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
						Yes	No	Yes	No
						☐	☐	☐	☐
Add rows as necessary									

List of <u>new data</u> 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	
						Yes	No	Yes	No
B3.7	EET 5061/12-1 F6176	Laboratorios Cinfa, S.A.	2012	Estudio de estabilidad del producto Goibi Xtreme Aerosol en 3 meses	Laboratorios Cinfa, S.A.		X	X	
B 4	Ref.51 UDA	Ane de la Maza	2007	Informe de Validación del Método de determinación de N,N-Dietil-m-Toluamida en materia prima	Laboratorios Cinfa, S.A.		X	X	
B 4	Ref.52 UDA	Ane de la Maza	2006	Informe de Validación del Método de valoración de N,N-Dietil-m-Toluamida en Repelente de Insectos Tropical	Laboratorios Cinfa, S.A.		X	X	

10 Data which have not been already submitted for the purpose of the Annex I inclusion.

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
						Yes	No	Yes	No
B6.2(1)	2012/1089/AMi	Vicenzo Freli	2012	Acute dermal irritation test on REPELENTE DE MOSQUITOS AEROSOL	Laboratorios Cinfa, S.A.		X	X	
B6.2(2)	CD06/10096T	Silvia López	2006	Test de tolerancia cutánea a las aplicaciones repetidas durante dos semanas, en conejo	Laboratorios Cinfa, S.A.		X	X	
B6.3	134814	Katharina Weidmann	2013	Test for sensitisation (Local Lymph Node Assay – LLNA) with GOIBI ANTIMOSQUITOS XTREME SPRAY	Laboratorios Cinfa, S.A.		X	X	
B6.4	134813	Dipl.-Ing. (FH) Kristin Rödig	2014	Percutaneous Absorption of GOIBI ANTIMOSQUITOS XTREME SPRAY – in vitro method	Laboratorios Cinfa, S.A.		X	X	
Add rows as necessary									

Annex 3: Analytical methods residues – active substance

DEET

Matrix, action levels, relevant residue and reference

matrix	limit	relevant residue	reference or comment
plant products			
food of animal origin			
soil			
drinking water			
surface water			
air			
body fluids / tissues			

Methods suitable for the determination of residues (monitoring methods)

Methods for products of plant origin

reference	matrix	LOQ (mg/kg)	principle	comment	owner

Methods for foodstuffs of animal origin

reference	matrix	LOQ (mg/kg)	principle	comment	owner

Methods for soil

reference	LOQ (mg/kg)	principle	comment	owner

Methods for drinking water and surface water

reference	matrix	LOQ (µg/l)	principle	comment	owner

Methods for air

reference	LOQ (µg/m3)	principle	comment	owner

Methods for body fluids/tissue

reference	matrix	LOQ (mg/kg)	principle	comment	owner

Annex 4: Toxicology and metabolism –active substance

DEET

This information can be consulted in the Assessment Reports of the active substance DEET (N,N-diethyl-m-toluamide)

Annex 5: Toxicology – biocidal product

GOIBI ANTIMOSQUITOS XTREME AEROSOL

General information

Formulation Type	Aerosol (ready to use)
Active substance(s) (incl. content)	27% DEET
Category	

Acute toxicity, irritancy and skin sensitisation of the preparation (Annex IIIB, point 6.1, 6.2, 6.3)	
Rat LD50 oral (OECD 420)	Justification for non submission of data*
Rat LD50 dermal (OECD 402)	Justification for non submission of data*
Rat LC50 inhalation (OECD 403)	Justification for non submission of data*
Skin irritation (OECD 404)	No irritant
Eye irritation (OECD 405)	Justification for non submission of data*
Skin sensitisation (OECD 429; LLNA)	

*****No study was submitted about acute toxicity. Justification for non-submission of data has been submitted for acute oral, dermal and inhalation toxicity. The Spanish CA accepts the applicant's justification and the data package.

The active substance DEET is classified as dangerous substances by oral acute toxicity and it exists in concentration that contributes to the classification of the product. On the other hand, according to CLP Regulation, where the mixture itself has not been tested to determine its acute toxicity, but there are sufficient data on the individual ingredients and similar tested mixtures to adequately characterise the hazards of the mixture, these data shall be used in accordance with the bridging rules. The acute toxicity estimate (ATE) of the mixture is determined by calculation from the ATE values for all relevant ingredients according to the following formula for oral, dermal or inhalation toxicity:

$$\frac{100}{ATE_{mix}} = \sum_{n} \frac{C_i}{ATE_i}$$

where:

Ci = concentration of ingredient i (% w/w or % v/v)
i = the individual ingredient from 1 to n
n = the number of ingredients
ATEi = Acute Toxicity Estimate of ingredient i

Considering the LD_{50} (oral) value and concentration of DEET, the ATE_{mix} is 7142 mg/kg and the biocidal product is not classified by oral acute toxicity according to CLP Regulation, table 3.1.1.

In addition, the biocidal product GOIBI ANTIMOSQUITOS XTREME AEROSOL does not contain any dangerous substance classified by dermal and inhalation acute toxicity. The study of acute inhalation toxicity was waived because the inhalation route is excluded due to the use outdoor, and because the use indoor only takes place in summer, in situations where there is a high ventilation rate. Furthermore, as reported in the CAR of DEET, the active substance is a low volatile compound that has not and high distribution in air compartment.

The active susbtance was considered to be skin irritant. In addition, there is a study performed with the biocidal product without the propellant. There are no indications from the published literature that petroleum gases/propellant cause skin corrosion/irritation. For these reasons, considering the study, the

biocidal product is not classified as irritant to skin and *read across* is accepted. A summary of the study is given below:

Species	Method	Average score (24, 48, 72h)		Result	Remark	Reference
		Erythema	Oedema			
Rabbit	OECD 404 GLP	0 (0-0-0)	0 (0-0-0)	Completely reversible	Not irritating	B6.2(1)

No study was submitted about eye irritation. The active substance DEET was classified in the CAR as irritant to eyes according to Directive 1999/45/EC and according to CLP Regulation, Annex VI. Considering the concentration of the active substance, the biocidal product GOIBI ANTIMOSQUITOS XTREME AEROSOL is classified as as Eye irrit. 2 and the hazard statement H319 according to CLP Regulation (the concentration is higher than 10%).

No study was submitted with the biocidal product about skin sensitization. Read across with a biocidal product applied by spray (GOIBI ANTIMOSQUITOS XTREME SPRAY) was submitted to assess the skin sensitization potential in mice. The method was carried out according to the guidelines of OECD N° 429 (skin sensitisation: Local lymph node assay, LLNA method). The purpose of this local lymph node assay was to identify the contact allergenic potential of GOIBI ANTIMOSQUITOS XTREME SPRAY when administered to the dorsum of both ear lobes of mice at concentrations of 25%, 50% (each diluted with acetone/olive oil 4:1 v/v) and 100%. On basis of the results, at the daily clinical observation the animals did not show any visible clinical symptoms and no case of mortality was observed. None of the three tested concentrations of the test item reached the simulation index of 3.

- The stimulation index at a concentration of 25% was 1.2.
- The stimulation index at a concentration of 25% was 2.0.
- The stimulation index at a concentration of 25% was 1.4.

Consequently, according to OECD 429 the biocidal product GOIBI ANTIMOSQUITOS XTREME SPRAY is expected to have no sensitising properties and therefore should not be regarded as a dermal sensitiser.

Read across was accepted by the Spanish Competent Authority because the liquid composition are the same. GOIBI ANTIMOSQUITOS XTREME SPRAY is a spray formulation and GOIBI ANTIMOSQUITOS XTREME AEROSOL is an aerosol product. The only difference is the incorporation of propellant in the aerosol biocidal product. In addition, the propellant has not sensitising properties. Therefore, GOIBI ANTIMOSQUITOS XTREME AEROSOL has not sensitising properties.

Nevertheless, some active substances included in the biocidal product could produce an allergic reaction. These substances (fragrances) are not present in the biocidal product at sufficient concentration(s) to trigger a human health classification but, according to the Regulation 286/2011 of 10 March 2011 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (section 2.8, Annex II), the label on the packaging of mixtures not classified as sensitising but containing at least one substance classified as sensitising and present in a concentration equal to or greater than that specified in Table 3.4.6 of Annex I, of this regulation, shall bear the statement:

EUH208 — "Contains (name of sensitising substance). May produce an allergic reaction".

For this reason, the label of GOIBI ANTIMOSQUITOS XTREME AEROSOL will include the statement: EUH 208: "Contains D- and L-Limonene, Citral and Hydroxyisohexyl 3- cyclohexene carboxaldehyde. May produce an allergic reaction" according to CLP Regulation.

Additional toxicological information (e.g. Annex IIIB, point 6.5, 6.7)	
Short-term toxicity studies Toxicological data on active substance(s) (not tested with the preparation)	
Toxicological data on non-active substance(s) (not tested with the preparation)	The propellant, sobutane/propane contains 1,3-butadiene as impurity, which is classified as a germ cell mutagen and a human carcinogen at concentration higher than 0.1%. Nevertheless, the contents of 1,3-butadiene is less than 0.1% according to the data sheet.
Further toxicological information	

Classification and labelling proposed for the preparation with regard to toxicological properties (Annex IIIB, point 9)	
Regulation 1272/2008/EC	Eye irrit. 2 H319: Causes serious eye irritation EUH 208: "Contains D- and L-Limonene, Citral and Hydroxyisohexyl 3- cyclohexene carboxaldehyde. May produce an allergic reaction"

Annex 6: Safety for professional operators

GOIBI ANTIMOSQUITOS FAMILIA SPRAY

Exposure assessment

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

GOIBI ANTIMOSQUITOS XTREME AEROSOL is not intended for professional use.

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

DEET

General information	
Formulation Type	Spray (ready to use)
Active substance(s) (incl. content)	27% DEET
Category	
Authorisation number	ES/APP(NA)-2016-19-00364

DEET (N,N-diethyl-m-toluamide)

Data base for exposure estimation	
according to	Appendix: Toxicology and metabolism – active substance/CAR and UK Proforma (reverse scenario

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

Conclusion:

Regarding the risk for human health of non-professional users it can be concluded that there is risk for each subpopulation (adults, children < 12 years old, and children > 12 years old): the product can be used once per day on adults, children < 12 years and children > 12 years. Children's hands must not be treated with this product. Children under 2 years must not be treated with this product.

For reasons of public health, GOIBI ANTIMOSQUITO XTREME AEROSOL must be authorized on the grounds of Article 19(5) of Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2019 concerning the market and use of biocidal product.

Details for the exposure estimates:

Internal dermal dose a.s. = (Number of applications) × External dermal dose product × (content a.s.) × (% dermal absorption)

Internal oral dose a.s. = (Number of applications) × External oral dose product × (content a.s.) × (% ingested amount)

Total dose a.s.= Internal dermal dose a.s + Internal oral dose a.s

External dose (x mg/kg/d product) = AELrepeted / Internal dose (x mg/kg/d a.s.)

Number of sprays = External dose (x mg/kg/d product) /Amount of spray in a single spray spot (mg)

Area of skin (limit dose) = External dose (x mg/kg/d product) / Efficacy

Number of applications = Area of skin (limit dose)/Area could be treated

GOIBI XTREME AEROSOL			
Scenario	**Adult**	**Children 6 to >12**	**Children 2 to > 6**

potential Dermal (applied)			
nº application/day	1	1	1
Concentration DEET (% w/w)	27	27	27
AELdermal (mg a.s./kg bw/day) = Application rate "saferty"	8,2	8,2	8,2
Body weight (kg)	60	23,9	15,6
Dermal absorption (%)	11	11	11
Oral absorption (%)	100	100	100
Dermal (0,96 mg product/Kg/day) / (1 mg product/Kg/day)	**0,96**	**0,92**	**0,92**
Oral (0,04 mg product/Kg/day) / (1 mg product/Kg/day)	**0,04**	**0,08**	**0,08**
Amount of a.s. (mg) per mg product (Dermal) = (mg a.s/Kg/day) / (mg product/Kg/day)	**0,0285**	**0,0273**	**0,0273**
Amount of a.s. (mg) per mg product (Oral) = (mg a.s/Kg/day) / (mg product/Kg/day)	**0,0108**	**0,0216**	**0,0216**
Amount of a.s. (mg) per mg product (dermal + oral) = (mg a.s/Kg/day) / (mg product/Kg/day)	**0,0393**	**0,0489**	**0,0489**
Amount of PRODUCT applied to reach repeated AEL (mg product /Kg/day)	**209**	**168**	**168**
Amount of PRODUCT applied to reach repeated AEL (mg product /day)	**12515**	**4006**	**2615**
Efficacy (1,15 g/600 cm2)	0,0019	0,0019	0,0019
Area of skin that can be treated with product in one day [cm2]	**6530**	**2090**	**1364**
Body surface (cm2) 64%	16600	9200	6800
Number of applications	**0,4**	**0,2**	**0,2**
% skin that can be treated	**39**	**23**	**20**

Annex 8: Residue behaviour

DEET

Intended Use (critical application)
Active substance(s): 27% DEET
Formulation of biocidal product: spray (ready to use)
Place of treatment: Apply the aerosol on the body areas to be protected

The intended use descriptions of the DEET containing biocidal products for which authorisation is sought indicate that these uses are not relevant in terms of residues in food and feed. No further data are required concerning the residue behaviour.

The acute or chronic exposure to residues in food resulting from the intended uses is unlikely to cause a risk to consumers. Regarding consumer health protection, there are no objections against the intended uses.