HET COLLEGE VOOR DE TOELATING VAN GEWASBESCHERMINGSMIDDELEN EN BIOCIDEN

August 2016

Following an application for a major change, including a minor change and an administrative change the following amendments were made in the PAR sections referring to the product Mosquito Milk spray 20% DEET:

- The formulation of the product was changed
- New packaging sizes were added
- A new manufacturer of the active substance was added

For the evaluation concerning the major change, we refer to the document 'Annex 10 of PAR Mosquito Milk Products' which can be found in the asset of this product (NL-0003044-0000).
The conclusions of the assessment have not changed.

March 2015

Following applications for minor changes, the authorisations of Mosquito Milk Spray 9,5% DEET, Mosquito Milk Roll On 20% DEET and Mosquito Milk Stick 20% DEET were changed with respect to

- shelf life
- packaging types.

In addition, the composition of Mosquito Milk Roll On 20% DEET has changed.

We refer to the file: 'Addendum to PAR March 2015'

May 2014

The following amendments were made in the PAR sections on risk assessment for the human health and risk assessment for the environment:

- The calculations are based on the pure active substance percentages:

Product name	Old percentages	New percentages used
Mosquito Milk Spray 9.5%	9.5%	9.8%
Mosquito Milk Spray 20%	20%	19.4%
Mosquito Milk Roll On 20%	20%	20.7%
Mosquito Milk Lotion 20%	20%	19.4%
Mosquito Milk Stick 20%	20%	19.4%

- In the environmental risk assessment the Elocal calculated according to the DE swimming scenario is recalculated.

The conclusions of the assessments have not changed.

Product Assessment Report

Mosquito Milk DEET Products

Including:

Mosquito Milk Spray 9.5% DEET

Mosquito Milk Spray 20% DEET

Mosquito Milk Roll On 20% DEET

~~**Mosquito Milk Lotion 20% DEET**~~

Mosquito Milk Stick 20% DEET

November 2013

Product name	**Authorisation no:**
Mosquito Milk Spray 9.5% DEET	NL-0003042-0000
Mosquito Milk Spray 20% DEET	NL-0003044-0000
Mosquito Milk Roll On 20% DEET	NL-0003055-0000
Mosquito Milk Lotion 20% DEET	Withdrawn on request applicant 15/6/2015
Mosquito Milk Stick 20% DEET	NL-0003058-0000
Granting date/entry into force of	01-11-2013
Expiry date of authorisation/	01-11-2023
Active ingredient:	DEET
Product type:	19

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

Contents

1 General information about the product applications

1.1 Applicant

Company Name:	Jaico RDP nv
Address:	Nijverheidslaan 1545
City:	Opglabbeek
Postal Code:	3660
Country:	Belgium
Telephone:	+32 89 85 77 67
Fax:	+32 89 85 23 64
E-mail address:	bert@jaico.be

1.1.1 Person authorised for communication on behalf of the applicant

Name:	Bert LAMBIE
Function:	Regulatory Affairs Manager
Address:	Nijverheidslaan 1545
City:	Opglabbeek
Postal Code:	3660
Country:	Belgium
Telephone:	+32 89 85 77 67
Fax:	+32 89 85 23 64
E-mail address:	bert@jaico.be

1.2 Current authorisation holder

Not applicable

1.3 Proposed authorisation holder

Company Name:	Jaico RDP nv
Address:	Nijverheidslaan 1545
City:	Opglabbeek
Postal Code:	3660
Country:	Belgium
Telephone:	+32 89 85 77 67
Fax:	+32 89 85 23 64
E-mail address:	bert@jaico.be
Letter of appointment for the applicant to represent the authorisation holder	n.a.

provided (yes/no):	

1.4 Information about the product application

Application received:	10-1-2012
Application reported complete:	15-3-2013
Type of application:	Application for first authorisation

1.5 Information about the biocidal products

1.5.1 General information

Product type:	19
Composition of the product (identity and content of active substance(s) and substances of concern; full composition see confidential annex):	See below for specific information on each product.
Formulation type:	See below for specific information on each product.
Ready to use product (yes/no):	All products are ready to use.
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):	Topical application on exposed body parts. Area of use: indoors in well ventilated areas and outdoors.
Target organisms:	*Mosquitoes (Culicidae)* *Culex* spp. *Anopheles* spp. *Aedes* spp.
Category of users:	Non-professional
Directions for use including minimum and maximum application	Apply sparingly on the uncovered parts of the body. Spread equally. Do not apply near eyes,

rates, application rates per time unit (e.g. number of treatments per day), typical size of application area:	lips and damaged skin. Repeat application once if necessary and when allowed (see label instructions). Use ca. 1 ml per 600 cm^2 of skin (corresponds with 1 ml per adult male arm) For use on face, spray into palm of hand before applying. Frequency: 1-2 times a day, if necessary and when allowed (see label instructions).
Potential for release into the environment (yes/no):	Yes
Potential for contamination of food/feedingstuff (yes/no)	No
Proposed Label:	Translation of the Dutch label, see annex 9.
Use Restrictions:	**All Mosquito Milk DEET products:** • Do not breathe spray • Use only outdoors or in a well-ventilated area **Mosquito Milk Spray 9.5% DEET:** • Do not use on children less than two years old, and restrict the use on children between two and twelve years old. **Mosquito Milk Spray 20% DEET,** **Mosquito Milk Lotion 20% DEET,** **Mosquito Roll On 20% DEET,** **Mosquito Milk Stick 20% DEET:** • Not for use on children under 13 years

1.5.3 Information on active substance

Active substance chemical name:	IUPAC name: *N,N*-diethyl-*m*-toluamide Common name (non-ISO): DEET
CAS No:	134-62-3
EC No:	205-149-7 (EINECS)
Purity (minimum, g/kg or g/l):	970g/kg
Inclusion 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: same source as evaluated for approval of the substance.
Manufacturer of active substance(s) used in the biocidal product:	Please refer to the confidential section of the SPC.

1.5.4 Information on the substance of concern

Substance chemical name	Ethanol
CAS No:	64-17-5

EC No :	200-578-6 (EINECS)
Purity (minimum, g/kg or g/l):	~99.9%, denaturated with 0.1% *tert*-butyl alcohol and 10ppm (0.001%) bitrex
Typical concentration (minimum and maximum, g/kg, or g/l):	335 – 369g/kg Stick 20% DEET: no ethanol
Relevant toxicological/ecotoxicological information:	See paragraph 2.7.1.2 (human tox) and paragraph 1.6.1 (environmental tox)
Original ingredient (trade name):	Ethyl alcohol absolute

Other co-formulants in the formulations were not considered substances of concern, as they are present at concentrations below the cut-off criterion of 0.1% for human hazard assessment and 1% or (0.1/M)% for environmental hazard assessment and/or are covered by the classification and labelling of the products.

1.6 Documentation

1.6.1 Data submitted in relation to product application

New studies concerning the product have been submitted with respect to physical-chemical properties of the product, analytical methods, toxicity and efficacy. The studies are listed in Annex 2.

No new studies concerning the Mosquito Milk DEET products have been submitted with respect to the environmental aspect. According to the applicant the Mosquito Milk DEET products contain only one active substance (DEET and no substances of concern for the environment). Therefore environmental effects of the products can be extrapolated from the environmental effect studies on DEET.

1.6.2 Access to documentation

The applicant has submitted a letter of access of the owner of the data on the active substance DEET submitted for the inclusion of DEET into Annex I of Directive 98/8/EC.

2 Summary of the product assessment

2.1 Identity related issues

General information

This assessment report contains the evaluation of five products based on the active substance DEET (*N,N*-diethyl-*m*-toluamide). DEET was evaluated and included in Annex I of Directive 98/8/EC for PT19 as part of the review programme for existing substances. The manufacturing site of DEET was evaluated as part of the EU review.

Product specific information

Product name	DEET content (%w/w)*		Substance of concern
	TGAI	PAI	
Mosquito Milk Spray 9.5% DEET	10.1	9.8	Ethanol
Mosquito Milk Spray 20% DEET	20**	19.4**	Ethanol
Mosquito Milk Roll On 20% DEET	21.3	20.7	Ethanol
Mosquito Milk Lotion 20% DEET	20.0	19.4	Ethanol
Mosquito Milk Stick 20% DEET	20	19.4	None

** TGAI = technical active ingredient with a minimum purity of 97%; PAI = pure active ingredient. Values rounded to a maximum of three significant digits.*

***April 2016: see Annex 10 for major change of composition*

2.2 Classification, labelling and packaging

2.2.1 Proposed classification based on Directive 1999/45/EC

See Annex 5 for classification according to Directive 1999/45/EC.

2.2.2 Proposed classification based on Regulation EC 1272/2008

Based on the profile of the substances the provided toxicology of the preparations, the characteristics of the co-formulants, the method of application and the risk assessment for the operator, the following labeling of the preparations is proposed:

Mosquito Milk Spray 9.5% DEET

The identity of all substances in the mixture that contribute to the classification of the mixture *:			
-			
Pictogram:	GHS02	Signal word:	Warning
	GHS07		
H-statements:	H226	Flammable liquid and vapour.	
	H319	Causes serious eye irritation.	
P-statements:	P102	Keep out of reach of children	
	P210	Keep away from heat/sparks/open flames/hot surfaces. – No smoking.	
	P260	Do not breathe dust/fume/gas/mist/vapours/spray.	
	P270	Do not eat, drink or smoke when using this product.	
	P271	Use only outdoors or in a well-ventilated area.	
	P305+351+338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and	

		easy to do. Continue rinsing.
Supplemental Hazard information:	EUH208	Contains citronellal. May produce an allergic reaction.
Child-resistant fastening obligatory?		No
Tactile warning of danger obligatory?		No

* according to Reg. (EC) 1272/2008, Title III, article 18, 3 (b)

Mosquito Milk Spray 20% DEET

April 2016: see document 'Annex 10 of PAR Mosquito Milk Products'.

~~The identity of all substances in the mixture that contribute to the classification of the mixture *:~~			
~~-~~			
~~Pictogram:~~	~~GHS02~~	~~Signal word:~~	~~Danger~~
	~~GHS05~~		
~~H-statements:~~	~~H226~~	~~Flammable liquid and vapour.~~	
	~~H318~~	~~Causes serious eye damage.~~	
~~P-statements:~~	~~P102~~	~~Keep out of reach of children.~~	
	~~P210~~	~~Keep away from heat/sparks/open flames/hot surfaces. – No smoking.~~	
	~~P260~~	~~Do not breathe dust/fume/gas/mist/vapours/spray.~~	
	~~P270~~	~~Do no eat, drink or smoke when using this product.~~	
	~~P271~~	~~Use only outdoors or in a well-ventilated area.~~	
	~~P305+P351+P338+P310~~	~~IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER or doctor/physician.~~	
~~Supplemental Hazard information:~~	~~EUH208~~	~~Contains geraniol. May produce an allergic reaction.~~	
~~Child-resistant fastening obligatory?~~			~~No~~
~~Tactile warning of danger obligatory?~~			~~No~~

~~* according to Reg. (EC) 1272/2008, Title III, article 18, 3 (b)~~

Mosquito Milk Roll On 20% DEET

The identity of all substances in the mixture that contribute to the classification of the mixture *:			
-			
Pictogram:	GHS02	Signal word:	Danger
	GHS05		
H-statements:	H226	Flammable liquid and vapour.	
	H318	Causes serious eye damage	
P-statements:	P101	If medical advice is needed, have product container or label at hand.	
	P102	Keep out of reach of children.	
	P210	Keep away from heat/sparks/open flames/hot surfaces. – No smoking.	
	P270	Do not eat, drink or smoke when using this product.	
	P305+351+338+310.	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if	

		present and easy to do. Continue rinsing. Immediately call a POISON CENTER or doctor/physician.	
Supplemental Hazard information:	-	-	
Child-resistant fastening obligatory?			No
Tactile warning of danger obligatory?			No

* according to Reg. (EC) 1272/2008, Title III, article 18, 3 (b)

Mosquito Milk Lotion 20% DEET

The identity of all substances in the mixture that contribute to the classification of the mixture *:			
-			
Pictogram:	GHS02	Signal word:	Danger
	GHS05		
H-statements:	H226	Flammable liquid and vapour.	
	H318	Causes serious eye damage	
P-statements:	P101	If medical advice is needed, have product container or label at hand.	
	P102	Keep out of reach of children	
	P210	Keep away from heat/sparks/open flames/hot surfaces. – No smoking.	
	P270	Do not eat, drink or smoke when using this product	
	P305+P351+P338+P310	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER or doctor/physician.	
Supplemental Hazard information:	EUH208	Contains geraniol and citronellal. May produce an allergic reaction.	
Child-resistant fastening obligatory?			No
Tactile warning of danger obligatory?			No

* according to Reg. (EC) 1272/2008, Title III, article 18, 3 (b)

Mosquito Milk Stick 20% DEET

The identity of all substances in the mixture that contribute to the classification of the mixture *:			
-			
Pictogram:	-	Signal word:	-
H-statements:	-	-	
P-statements:	P102	Keep out of reach of children	
	P103	Read label before use	
Supplemental Hazard information:	-	-	
Child-resistant fastening obligatory?			No
Tactile warning of danger obligatory?			No

* according to Reg. (EC) 1272/2008, Title III, article 18, 3 (b)

2.2.3 Packaging of the biocidal products

Product specific information concerning packaging

Product	Container	Opening	Closure
Mosquito Milk Spray 9.5% DEET	75 mL PP flask.	13 mm	PP cap and PP/PE/steel/alu spray pump.
Mosquito Milk Spray 20% DEET New packaging sizes were added by a major change application in April 2016, see document 'Annex 10 of PAR Mosquito Milk Products'.	75 mL PP flask.	13 mm	PP cap and PP/PE/steel/alu spray pump.
Mosquito Milk Roll On 20% DEET	50 mL glass roll-on flask.	30 mm	PP cap and PE fitment with PP ball.
Mosquito Milk Lotion 20% DEET	200 mL HDPE flask.	33 mm	PP cap
Mosquito Milk Stick 20% DEET	50 mL PP cartridge.	Oval 49 mm x 29 mm	PP cap

The shelf-life of the products is considered to be 2 years. Please refer to chapter 2.3.1 for a detailed evaluation.

2.3 Physico/chemical properties and analytical methods

The applicant has access to the Annex I dossier. The physical and chemical properties for the active substance DEET are detailed in the Annex I dossier, Doc IIIA, Section 3.

Table 1a: Physical and chemical properties of the biocidal product: Mosquito Milk Spray 9.5% DEET

	Method	Purity/Specification	Results	Reference
Physical state and nature	Visual examination	9.5% DEET, Batch G2370	Transparent liquid	Kohnen, M., 2013a
Colour	Visual examination	9.5% DEET, Batch G2370	Weak yellow	Kohnen, M., 2013a
Odour	Organoleptic examination	Not stated	Mild, pleasant odour	No reference given; data from summary
Explosive properties	Statement	n.a.	Considering the molecular structures and the composition of the formulation, explosive properties are not expected.	Mak, W.A, 2006a
Oxidizing properties	Statement	n.a.	Considering the molecular structures and the composition of the formulation, oxidizing properties are not expected.	Mak, W.A, 2006a
Flash point	EC method A.9	9.5% DEET, batch: A3472	29.1 °C at 99.5 kPa	Wenighofer, T., 2011a
Auto-flammability	EC method A.15	9.5% DEET, batch: A3472	420 °C at 99.4 kPa	Wenighofer, T., 2011b

	Method	Purity/Specification	Results	Reference
Other indications of flammability			n.a.	
Acidity / Alkalinity	SOP QC-4002/02	9.5% DEET, Batch G2370	pH 10% solution = 5.6 ± 1	Kohnen, M., 2013a
Relative density / bulk density	EC method A.3	9.5% DEET, batch: E1649	0.9408 at 20 °C	Mak, W.A, 2006a
Storage stability – stability and shelf life	In-house methods	9.5% DEET, Batch G2370	Storage for 5 months at 54 °C and 60 % RH in PP. Tested properties: pH (10%), a.i. content, appearance, density See table 1b for details.	Kohnen, M., 2013a
Effects of temperature			See above	
Effects of light			Not investigated. Product should be stored in the dark.	
Reactivity towards container material			See above	
Technical characteristics in dependence of the formulation type			n.a.	
Compatibility with other products			n.a.	
Surface tension			n.a.	
Viscosity			n.a.	
Particle size distribution			n.a.	

Table 1b – storage stability data (at 54°C, 60%RH, in 75mL polypropylene container)

t (months)	0	1/2	1	2	3	4	5
DEET content (%w/v)	9.4	10.0	10.0	9.9	9.7	10.0	10.0
pH (10%)	5.6	5.2	5.5	5.4	5.3	5.5	5.5
Density (mg/mL)	959	951	947	918	934	932	941

Table 2a: Physico-chemical properties of the biocidal product: Mosquito Milk Spray 20% DEET

	Method	Purity/Specification	Results	Reference
Physical state and nature	Visual examination	20 % DEET, Batches 100517D, 100517E, 100519A	Transparent liquid	Kohnen, M., 2013b
Colour	Visual examination	Not stated	Weak yellow	Kohnen, M., 2013b
Odour	Organoleptic examination	Not stated	Mild, pleasant odour	
Explosive properties	Statement	n.a.	Considering the molecular structures and the composition of the formulation, explosive properties are not	

	Method	Purity/Specification	Results	Reference
			expected.	
Oxidizing properties	Statement	n.a.	Considering the molecular structures and the composition of the formulation, oxidizing properties are not expected.	
Flash point	EC method A.9	20 % DEET, batch: A3512	32.1 °C at 99.5 kPa	Wenighofer, T., 2011c
Auto-flammability	EC method A.15	20 % DEET, batch: A3512	415 °C at 99kPa	Wenighofer, T., 2011d
Other indications of flammability			n.a.	
Acidity / Alkalinity	SOP QC-4002/02	20 % DEET, Batches 100517D, 100517E, 100519A	pH 10% solution = 5.5 ± 1	Kohnen, M., 2013b
Relative density / bulk density	EC method A.3	20 % DEET, batch: E1649	0.9409at 20 °C	Wenighofer, T., 2011e
Storage stability – stability and shelf life	In-house methods	20 % DEET, Batches 100517D, 100517E, 100519A	Storage for 5 months at 54 °C and 60 % RH in PP. Tested properties: pH, a.i. content, appearance, density. See table 2b for details.	Kohnen, M., 2013b
Effects of temperature			See above	
Effects of light			Not investigated. Product should be stored in the dark.	
Reactivity towards container material			See above	
Technical characteristics in dependence of the formulation type			n.a.	
Compatibility with other products			n.a.	
Surface tension			n.a.	
Viscosity			n.a.	
Particle size distribution			n.a.	

Table 2b – storage stability data (at 54°C, 60%RH, in 75mL polypropylene container)

t (months)	0	1/2	1	2	3	4	5
DEET content (%w/v)	20.0	20.6	20.8	21.26	22.15	No data	23.5
pH	5.8	4.3	3.6	3.7	3.7	No data	3.5
Density (mg/mL)	925	925	926	925	927	No data	928

Table 3a: Physico-chemical properties of the biocidal product: Mosquito Milk Roll On 20% DEET

	Method	Purity/Specification	Results	Reference
Physical state and nature	Visual examination	20 % DEET, batch: G2303	Opaque liquid	Kohnen, M., 2013d
Colour	Visual examination	20 % DEET, batch: G2303	White	Kohnen, M., 2013d
Odour	Organoleptic examination	Not reported	Mild, pleasant odour	No reference given, data from summary
Explosive properties	Statement	n.a.	Considering the molecular structures and the composition of the formulation, explosive properties are not expected.	Mak, W.A., 2007a
Oxidizing properties	Statement	n.a.	Considering the molecular structures and the composition of the formulation, oxidizing properties are not expected.	Mak, W.A., 2007a
Flash point	EC method A.9, GLP	20 % DEET, batch: F1989	92.5 °C at 100 kPa	Mak, W.A., 2007a
Auto-flammability	EC method A.15, GLP	20 % DEET, batch: F1989	430°C at 100 kPa	Mak, W.A., 2007a
Other indications of flammability			n.a.	
Acidity / Alkalinity	SOP QC-4002/02	20 % DEET, batch: G2303	pH 10 % solution = 6.7 ± 1	Kohnen, M., 2013d
Relative density / bulk density	EC method A.3, GLP	20 % DEET, batch: F1989	0.9599 at 20 °C	Mak, W.A., 2007a
Storage stability – stability and shelf life	In-house methods, CIPAC MT46.3	20 % DEET, batch: G2303	Storage for 5 months at 54 °C and 60 % RH in glass. Tested properties: pH, a.i. content, appearance, density. See table 3b for details.	Kohnen, M., 2013d
Effects of temperature			See above	
Effects of light			Not investigated. Product should be stored in the dark.	
Reactivity towards container material			See above	
Technical characteristics in dependence of the formulation type			n.a.	
Compatibility with other products			n.a.	
Surface tension			n.a.	
Viscosity			n.a.	
Particle size distribution			n.a.	

Table 3b – storage stability data (at 54°C, 60%RH, in 50mL glass container)

t (months)	0	1/2	1	2	3	4	5
DEET content (%w/v)	20.06	20.02	19.83	20.17	19.39	20.02	19.91
pH	6.7	6.2	6.4	6.2	6.4	6.4	6.2
Density (mg/mL)	952	953	954	957	950	933	941

Table 4a: Physico-chemical properties of the biocidal product: Mosquito Milk Lotion 20% DEET

	Method	Purity/Specification	Results	Reference
Physical state and nature	Visual examination	20 % DEET, batch: A3497	Opaque liquid	Kohnen, M., 2013i
Colour	Visual examination	20 % DEET, batch: A3497	White	Kohnen, M., 2013i
Odour	Organoleptic examination	Not reported	Mild, pleasant odour	No reference given, study report not submitted.
Explosive properties	Statement	n.a.	Considering the molecular structures and the composition of the formulation, explosive properties are not expected.	No reference given
Oxidizing properties	Statement	n.a.	Considering the molecular structures and the composition of the formulation, oxidizing properties are not expected.	No reference given
Flash point	EC method A.9	20 % DEET, batch: A3497	29.4 °C at 98.8 kPa	Wenighofer, T., 2011t
Auto-flammability	EC method A.15	20 % DEET, batch: A3497	415 °C at 98.8kPa	Wenighofer, T., 2011u
Other indications of flammability			n.a.	
Acidity / Alkalinity	SOP QC-4002/02	20 % DEET, batch: A3497	pH 10 % solution = 5.5 ± 1	Kohnen, M., 2013i
Relative density / bulk density	EC method A.3	20 % DEET, batch: A3497	0.9319 at 20 °C	Wenighofer, T., 2011v
Storage stability – stability and shelf life	Various	20 % DEET, batch: A3497	Storage for 5 months at 54 °C and 60 % RH in HDPE. Tested properties: pH, a.i. content, appearance, viscosity, density. See table 4b for details.	Kohnen, M., 2013i
Effects of temperature			See above	
Effects of light			Not investigated. Product should be stored in the dark.	

	Method	Purity/Specification	Results	Reference
Reactivity towards container material			See above	
Technical characteristics in dependence of the formulation type			n.a.	
Compatibility with other products			n.a.	
Surface tension			n.a.	
Viscosity	Brookfield viscometer	20 % DEET, batch: A3497	3100	Kohnen, M., 2013i
Particle size distribution			n.a.	

Table 4b – storage stability data (at 54°C, 60%RH, in 75mL polypropylene container)

t (months)	0	1/2	1	2	3	5
DEET content (%w/v)	20.42	21.00	20.43	21.80	22.52	22.43
pH	5.5	5.5	5.1	5.0	5.0	4.9
Density (mg/mL)	938	944	953	952	954	950
Viscosity (mPa.s)	3100	1120	660	520	500	550

Table 5a: Physico-chemical properties of the biocidal product: Mosquito Milk Stick 20% DEET

	Method	Purity/Specification	Results	Reference
Physical state and nature	Visual examination	20 % DEET, batch: G2407	Opaque semi-solid	Kohnen, M., 2013j
Colour	Visual examination	20 % DEET, batch: G2407	White	Kohnen, M., 2013j
Odour	Organoleptic examination	Not reported	Mild, pleasant odour	No reference given, study report not submitted.
Explosive properties	Statement	n.a.	Considering the molecular structures and the composition of the formulation, explosive properties are not expected.	Mak, W.A, 2007b
Oxidizing properties	Statement	n.a.	Considering the molecular structures and the composition of the formulation, oxidizing properties are not expected.	Mak, W.A, 2007b
Flash point	EC method A.9	20 % DEET, batch: D1485	>110 °C at 98.8 kPa	Mak, W.A, 2007b
Flammability	EC method A.10	20 % DEET, batch: D1485	Not highly flammable.	Mak, W.A, 2007b
Auto-flammability	EC method A.16	20 % DEET, batch: D1485	Not self-igniting	Mak, W.A, 2007b
Other indications of flammability			n.a.	
Acidity / Alkalinity	SOP QC-4002/02	20 % DEET, batch: G2407	pH 10 % solution = 8.8 ± 1	Kohnen, M., 2013j
Relative density / bulk density	EC method A.3	20 % DEET, batch: D1485	1.0526 at 20 °C	Mak, W.A., 2007b

	Method	Purity/Specification	Results	Reference
Storage stability – stability and shelf life	Various	20 % DEET, batch: G2407	Storage for 5 months at 54 °C and 60 % RH in HDPE. Tested properties: pH, a.i. content, appearance. See table 5b for details.	Kohnen, M., 2013j
Effects of temperature			See above	
Effects of light			Not investigated. Product should be stored in the dark.	
Reactivity towards container material			See above	
Technical characteristics in dependence of the formulation type			n.a.	
Compatibility with other products			n.a.	
Surface tension			n.a.	
Viscosity			n.a.	
Particle size distribution			n.a.	

Table 5b – storage stability data (at 54°C, 60%RH, in 50mL HDPE bottle)

t (months)	0	1/2	1	2	3	5
DEET content (%w/v)	19.94	19.89	20.44	19.28	19.86	19.78
pH	8.8	9.2	9.2	8.9	9.0	8.8

Summary and discussion

Sufficient data was provided regarding the physical and chemical properties of the various DEET products. None of the products are auto-flammable, explosive or oxidising. The products are all considered flammable.

Because the products are all ready to use, no data on technical properties is considered required.

Shelf-life

For all products applied for, (accelerated) stability data was provided in the packaging proposed for the European market. Generally speaking, a shelf-life of at least two years for all products is considered supported because of the properties of the individual components; none of the components are sensitive to hydrolysis or are heat sensitive.

A shelf-life of 5 years was claimed. Considering none of the reports contain detailed information on storage conditions (it is unlikely a RH of 60% can be maintained at 54 °C in an oven) and no real-time data is available for the various products, it is insufficiently clear whether the products will be physically stable for the total claimed shelf-life. Additional data should be submitted to support the claimed shelf-life of 5 years.

Flammability

The spray, roll on and lotion products contain flammable components and, based on their composition, are expected to be category 3 flammable liquids with a flashpoint between 23 and 60°C.

The reported flash point for the 20% Roll on at 92.5°C is considered unlikely to be correct, taking into account the composition of the product. The applicant, nor the performing lab was able to give an explanation for the values reported. Considering the 20% Spray contains the same amount of flammable constituents as the 20% Roll on, the flashpoint of the 20% Spray is considered representative for the Roll on product with 20% DEET (flashpoint 32.1°C).

2.3.1 Analytical methods

Analytical method for determination of the active substance in the biocidal product

The methods for the active substance DEET and the impurities in the technical active substance are detailed in the Annex I dossier, Doc IIIA, Section 4.1.

For the product, a GC-FID method was provided, which was used for all products. However, validation includes the 20% DEET Roll On only (Trouwers, A., 1995).

Specificity
No interference based on representative chromatograms.
Linearity
r = 0.999, y = 1.364x - 0.007, n = 4x5 (5 sets of 4 measurements), range 60 – 140% of the theoretical concentration (100% = 2g/L).
Accuracy
Mean recovery 101.7%
Precision
0.545% SD, 0.54%RSD

The analytical method is based on dilution with acetone, using an amount of product to achieve 0.5g DEET in 25mL acetone, diluting 10 times with acetone, followed by filtration through a 0.45µm filter and injection into the GC system.

The substances that may interfere with the accurate determination in other products are mainly perfumes and solvents. In all products, the same perfumes and solvents are used and the other components are not expected to cause problems during analysis. Therefore, it is considered acceptable to extrapolate validation data to all other DEET products.

Analyte	Principle of method
Technical active substance as manufactured:	GC-FID
Impurities in technical active substance:	GC-FID with GC-MS for confirmation of the identity
Active substance in the formulations	GC-FID (SOP QC 4001 04)

Residue analytical method in air
The EU review of DEET concluded that a residue analytical method for air may be required at the product authorisation stage. Considering the vapour pressure of DEET, a residue analytical method is required. The Technical Notes of Guidance state that an analytical method is required if the vapour pressure exceeds 0.01 Pa and/or the product is sprayed or occurrence in air is otherwise probable (IIA4.2b).

A new residue analytical method (Miller, C., 2013) was developed and validated according to the latest legislatory requirements (SANCO/825/00 rev 8.1).

Method description
Air is drawn through a Tenax cartridge for 6 hours at 1L/min (360L air) at 35°C and 80%RH and at 20°C and 30%RH, followed by desorption with acetone and dilution in methanol, followed by analysis by HPLC-MS/MS with external standardisation.

Conditions

Instrument:	AB Sciex API 4000 (Analyst 1.4.2 software), Waters Acquity UPLC		
Mode:	Ion spray		
Column:	C18, 2.1mmx50mm, 1.7µm.		
Mobile phase A:	water:methanol:formic acid (90:10:0.1 v:v:v) + 0.01M ammonium formate		
Mobile phase B:	methanol:formic acid (100:0.1 v:v)		
Gradient	Time	%A	%B
	0	40	60
	1	40	60
	1.5	5	95
	2.5	5	95
	3	40	60
	4	40	60
Injection volume:	10 µL		
Flow rate:	0.5 mL/min		
Retention time:	approx. 0.6 minutes		

Validation data
The method validation is reported in table 2.3.2-1.

No matrix effect of the Tenax sorbent was observed.

Discussion and conclusion
The LC-MS/MS method submitted is acceptable and complies with SANCO/825/00 rev 8.1 and TNsG validation requirements. The required LOQ of 0.225mg/m^3, based on the lowest AEL_{acute} of 0.75 mg/kg bw/day, is met.

At 35°C and 80%RH breakthrough was detected at 10% of the nominal fortification rate. At 20°C and 30%RH, the breakthrough was 6%. The lab considers this to be acceptable. Considering the accuracy (87 – 110% overall, mean 90 – 103% per fortification level) and the repeatability (RSD ≤6% per fortification level) of the method are acceptable, the breakthrough volume of up to 10% still allows sufficiently accurate measurements and is therefore considered a minor deficiency.

In August 2011, RMS Sweden evaluated additional data, including a residue analytical method for water (Sadgrove, L., 2010). This method was validated using two transitions (192->119m/z and 192->91m/z). Considering the method for water is highly specific, the method for air can be considered highly specific as well. No additional confirmatory method is required.

Table 2.3.2-1 validation data for the residue analytical method for air

Target analyte	Method / equipment	Specificity	Linearity	Accuracy (min-max (mean)) (%)		Repeatability (% RSD)	Reference
DEET	LC-MS/MS 192->119 m/z 35°C, 80%RH	No interference	0.2 – 5ng/L, n=9 r^2 = 0.9994 y=799154x+ 54527.8	Control (n=2)	Not detected	-	Miller, C., 2013
				0.225mg/m^3	101 - 105 (103)	1.7 (n=5)	
				2.25mg/m^3	87 – 93 (90)	3.3 (n=5)	
	LC-MS/MS	No		Control (n=2)	Not detected	-	

	192->119 m/z 20°C, 30%RH	interference		0.225mg/m^3	94 – 110 (101)	6.0 (n=5)	
				2.25mg/m^3	97 - 105 (101)	2.8 (n=5)	

2.4 Risk assessment for Physico-chemical properties

General information

No new data relevant to the risk assessment was provided. None of the products applied are auto-flammable, explosive or oxidising. However, except for the 20% DEET Stick, all products are classified as flammable (cat 3 flammable liquids).

2.5 Effectiveness against target organisms

2.5.1 Function

Mosquito Milk DEET products are insect repellents (PT19) based on 9.5%-20% (w/w) DEET.

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

Mosquito Milk DEET products are used to repel mosquitoes (Culicidae).
Mosquito Milk DEET products are insect repellents that should be applied to the skin of exposed body parts with the purpose to protect humans from mosquito bites.

2.5.3 Effects on target organisms

DEET (*N*,*N*-Diethyl-*m*-toluamide) repels mosquitoes (Culicidae) 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.

Mosquito Milk products differ from the product described in the CAR of DEET since the concentrations of the active ingredient and the formulation of the products are different. Therefore new laboratory studies have been provided with *Culex quinquefasciatus*, *Aedes aegypti* and *Anopheles stephensi* mosquitoes using Mosquito Milk DEET products. The resulting complete protection times (CPT's) are presented in Table 2.5.3.0 and are discussed in the text below.

Data requirements

The TNsG on PT18 and PT19* states that to show efficacy of products intended for use as repellent on skin or clothes against mosquitoes, both simulated-use tests (arm-in-cage) and field studies showing repellence in the field need to be provided. However, this guidance was not available during the process of data collection by the applicant. In line with the draft note for guidance discussed at PA&MRFG** 'competent authorities should therefore accept data based on the latest available guidance published (or applicable) on the date when the applicant can reasonably be expected to start collecting data, and not require re-alignment to any subsequently published guidance for the purpose of granting authorisation or mutual recognition'.

In the TNsG on product evaluation*** that was available during data collection, no details are given on the data requirements for repellents. The CA of the Netherlands is of the opinion that the simulated-use laboratory tests (arm-in-cage studies) are worst case scenarios and that field studies can be waived under the prerequisite that comparable product, comparable dosage and a sufficient number of test persons are used in lab studies provided.

According to the TNsG on PT18 and PT19, personal repellents for outdoor use have to be tested against at least two mosquito species, in particular *Aedes* spp*.* and *Culex* spp*. Culex* spp. are the most common species in Europe and bites mainly between dusk and dawn. *Aedes* mosquitoes are less common in Europe and more common in tropical areas where they are vectors of Yellow fever. *Aedes* species are more aggressive than *Culex* spp and mostly active during the day. Mosquito Milk DEET products were therefore tested with arm-in-cage tests against both these mosquito species at the Swiss Tropical and Public Health Institute in 2011 according to WHO guidelines (WHOPES 2009.4). In addition also efficacy data were provided for Mosquito Milk DEET products against the malaria mosquito *Anopheles stephensi* in a variety of different clinical tests performed at the Institute of Tropical Medicine in Antwerp (ITMA).

References:

* BPD 98/8/EC: Technical Notes for Guidance: TNsG on Product Evaluation, Insecticides, acaricides and products to control other arthropods (PT 18) and Repellents and attractants (only concerning arthropods) (PT 19). *European Commission, Directorate-General Environment,* CA-Dec12-Doc.6.2.a.-Final

****** Draft note for guidance. Relevance of new guidance becoming available during the process of authorisation and mutual recognition of authorisations of biocidal products. CA-July 12-Doc.6.2d. PA&MRFG-July 12-Doc.8.

*** TNsG on Product Evaluation, ECB, February 2008.

Complete Protection Time (CPT) calculation

Complete Protection Time (CPT) is the time from application of a repellent until the first confirmed event showing efficacy failure i.e., the first landing, bite, confirmed within 30 minutes by another similar event.

There are different possibilities to present a protection time on the label. The CA NL is of the opinion it is best to derive a mean CPT-value between the different tests provided and to use this value as the average protection time on the label. For the calculation of the mean CPT-value, we use those studies which fulfil the requirements of the official guidelines (EPA, WHO) and which were conducted with at least 8-10 test persons. Taking into account the high inter-individual variability among test persons, studies with lower numbers of tests persons are less valuable. Tests with lower numbers of test persons can be used, however, for rounding up or down the protection time to full hours.

A mean CPT-value is calculated and this value is given on the label as an average protection time (PT) in whole hours. Values are generally rounded up from 30 minutes upwards and taking the test results into account. As the efficacy against different species groups of mosquitoes may differ considerably the CA NL is of the opinion that the protection times should be specified per mosquito species group tested. This leads to the following label statements on the Dutch label: *Protects on average for x hours against mosquitoes in NW-Europe. For tropical mosquitoes the protection time may be shorter: y hours against yellow fever mosquitoes and z hours against malaria mosquitoes ".*

Tabel 2.5.3.0 Summary of the CPT results of the efficacy studies

Product name	***Culex***		***Aedes***		***Anopheles***		**Comments**
	Test	**PT****	**Test**	**PT****	**Test**	**PT****	

	results*		results*		results*		
Spray 9.5% DEET	6h 26	**6**	1h 38	**2**	5-6h	**5**	
Spray 20% DEET	6h 26	**6**	2h 49	**3**	4.5h	**4**	
Roll On 20% DEET	7h 23	**7**	3h 56	**4**	5-8h	**6**	
Lotion 20% DEET	7h 41	**8**	4h 00	**4**	nt***	**6**	Expert judgement used for PT against
Stick 20% DEET	6h 51	**7**	2h 45	**3**	2h	**5**	

* Mean complete protection time (CPT) calculated from the tests
** Average protection time as put on the Dutch label in whole hours
*** Not tested

Studies on *Culex quinquefasciatus* and *Aedes aegypti*
Simulated-use studies (arm-in-cage tests) on *Culex quinquefasciatus* and *Aedes aegypti* were performed according WHO guidelines (WHOPES 2009.4). The Mosquito Milk product was applied to the bare forearm between the wrist and elbow at a concentration of 1 ml test material per 600 cm^2. Eight volunteers exposed their treated forearm for 3 minutes in mosquito cages containing 200 hungry females every 30 minutes over 8-12 hours post application. Before and after exposure of the treated arm, the readiness of mosquitoes to bite was assessed by inserting an untreated arm into the cage for 1 minute or until 10 probings/bites were counted (negative control). As a positive control DEET 20% was used. The results of these tests are summarized in Table 2.5.3.0.

The results of the arm-in-cage studies show (Table 2.5.3.0.) that Mosquito Milk DEET products repel *Culex quinquefasciatus* for periods of 6 to more than12 hours. The higher concentrations give the longest protection times. The roll on products appear to give a somewhat longer protection time at comparable concentrations of DEET than the spray products, this can be caused by the formulation or the amount of product that was applied. Against *Aedes aegypti* the Mosquito Milk DEET products give protection times between 2 and 7 hours.

Studies on *Anopheles*
The efficacy data provided for Mosquito Milk DEET products against *Anopheles stephensi* include a variety of different clinical tests performed at the Institute of Tropical Medicine in Antwerp (ITMA) with different DEET products . Some of these studies show the efficacy against *Anopheles stephensi* in laboratory studies using mice, these were not used in the evaluations. Arm-in-cage studies on human volunteers (with 5-9 test persons) were done for some of the Mosquito Milk DEET products (see Table 2.5.3.0). Also a limited number of field trials with very low numbers of volunteers were done. The product was applied to different body parts. The applicant also refers to public literature to support the claim for efficacy against *Anopheles* species.

Because a solid series of tests with the Mosquito Milk DEET products were provided on Culex quinquefasciatus and Aedes aegypti and the data provided on the efficacy of Mosquito Milk DEET products against Anopheles stephensi is in line with these data and with the general data available on efficacy of DEET against Anopheles species, the CA NL is of the opinion that the data are acceptable and can be used as a basis to decide on protection times for Mosquito Milk DEET products against Anopheles species to be put on the label.

The summarized data on protection times from these tests are included into Table 2.5.3.0. Against *Anopheles stephensi* the protection times range from 4 to 10 hours. For some

Mosquito Milk DEET products no tests were done and only general literature data were provided. In those cases the CA NL has decided on a protection time against *Anopheles* species to be put on the label, based on data provided for Mosquito Milk DEET products with comparable DEET concentrations but with different formulations. These are indicated in table 2.5.3.0 as " Expert judgement used for PT against *Anopheles".*

The results with Mosquito Milk DEET products against the different species are in compliance with the public literature data on repellency by DEET products against different mosquito species (Re-evaluation Decision document RRD2002-01, PMRA Canada, April 2002). These data show that *Aedes* species (yellow fever vectors), that are more aggressive in their behaviour than *Anopheles* (malaria vectors) and *Culex* species *(virus vectors*) are more difficult to repel and show shorter protection times. Culex species are generally most easily repelled by DEET and have the longest protection times.

Other information provided
In addition, a literature overview was provided with 11 DEET efficacy trials on other products with various DEET concentrations on other insect species such as flies, midges and chiggers, showing protection times from 2 hrs up to 2 weeks (B5.10.2, no original study reports send in).
The CA NL is of the opinion that these data are not sufficient to support a claim for protection against other insect species than mosquitoes.

Effect of added perfumes
A laboratory study was provided to assess whether removing the active ingredient N-diethly-3-methyl-benzamide (DEET) from a *Mosquito Milk* skin repellent formulation containing up to 1.75% perfume, would still give protection against biting mosquitoes. The formulation without DEET was tested in a WHO arm-in-cage test, alongside the actual formulation containing 20% DEET against *C. quinquefasciatus*, on two female and two male volunteers. In the tests, the readiness of the mosquitoes to land and bite prior testing was 0.174 bites per second (mean) corresponding to 10.4 bites in 1 minute. Similar to the negative control, the formulation without DEET already failed during the first exposure at 5 minutes. All four volunteers received at least 2 bites within the first exposure. From these results it is concluded that the active ingredient DEET contained in the original formulation provides the protection against the biting mosquito, while the remainder of the formulation shows no protective effect. This is corroborated by the observation that the original formulation provided complete protection for up to 8 hours under the same experimental conditions.
It is therefore concluded by CA NL that Mosquito Milk perfume additives are not repellent at the tested concentration and are not to be considered active ingredients.

2.5.3.1 Dose

Use as topical application on exposed body parts, applied 1-2 times a day.
Apply sparingly on the uncovered parts of the body. Spread equally. Repeat application once if necessary and when allowed (see label instructions). For use on face, spray into palm of hand before applying.

The efficacy studies were done according to WHO-guidelines with a standard dose of 1 ml product per 600 cm^2. The 600 cm^2 roughly corresponds with a human male bare forearm. For the determination of the amount of product applied on the skin per application, the applicant refers to RIVM Report 320005002/2006: Pest control Products Fact Sheet, H.J. Bremmer et al. In Chapter 5: Insect repellents, p. 61 Dermal exposure: instant application model, it is argued that the default value and the amount of repellent applied per application is set at 6 g of product for adults (2 arms, 2 legs and face). This corresponds with the use dosage used in the arm-in-cage tests of about 1 ml per 600 cm^2 of skin (=one adult male arm). The amount of repellent used for a child of 10.5 months is defined to be 1.5 g product per application. The applied amount was derived using the agreed values for

cosmetics such as suntan creams and body lotions. Therefore, extrapolation to relatively viscous formulations (lotion, roll on and stick) is acceptable.

For spray application adults will have to pump 30 - 35 times in order to reach the proposed amount. For children, this is about 8 times. A small user test done by the applicant learned that this value is overestimated and that real use will be around 12 – 18 pumps per application. In addition, some of the product is lost with spray applications, hence not all of the product will reach the skin. Taking into account the above, it is clear that for spray applications, an amount of 6 g of product applied for adults and 1.5 g for children of 10.5 months is an overestimation for spray applications.

This topic was also discussed during the EU Technical Meetings concerning the active substance IR3535. For this comparable substance (insect repellent to be applied to human skin) it was agreed to use a lower amount of 3 g per application for adults. The applicant proposes to use the same principle also for DEET products.

The CA NL is of the opinion that a practical use dose between 3 and 6 grams of product per adult per application seems reasonable . For children up to 12 years the practical use dose will generally lie between 1 and 3 grams per application.

2.5.3.2 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.

2.5.3.3 Limitations

Repeat application of the product after swimming, showering or when the efficacy diminishes.

2.5.3.4 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.

2.5.4 Evaluation of the label claim

The applicant has provided a Dutch label (WG/GA). This has been adapted to our standards. For the convenience of the competent authorities authorising this product through mutual recognition the Dutch label claim, translated in English, is added to the PAR (see Annex 9).

2.5.5 General conclusions on efficacy

Considering that:

- simulated-use studies (arm-in-cage tests) on *Culex quinquefasciatus* and *Aedes aegypti* were done according WHO-guidelines and showed efficacy for the products tested
- additional efficacy data were provided for identical products against *Anopheles stephensi*
- the data provided allowed the determination of the average protection times for all the different Mosquito Milk DEET products

The CA NL is of the opinion that the following Mosquito Milk Deet products:

- *Mosquito Milk Spray 9.5% DEET*
- *Mosquito Milk Spray 20% DEET*
- *Mosquito Milk Roll On 20% DEET*

- *Mosquito Milk Lotion 20% DEET*
- *Mosquito Milk Stick 20% DEET*

are effective in repelling mosquitoes (Culicidae) from human skin, when used according to the instructions on the label, providing the average protection times as given in Table 2.5.3.0.

2.6 Exposure assessment

2.6.1 Description of the intended use(s)

Mosquito Milk products are mosquito repellents based on DEET that should be applied to the skin of exposed body parts with the purpose to protect humans from mosquito bites. The product is for non-professional use.

Practical use dosages are between 3 and 6 grams of product per adult per application. For children up to 12 years the practical use dose will generally lie between 1 and 3 grams per application. The maximum application frequency is 1-2 times a day, depending on the DEET concentration (see table 1.5.2. Intended use: use restrictions). The protection times of the various products are summarized in Table 2.5.3.0 and depend on the DEET concentration, the formulation and the mosquito species.

2.6.2 Assessment of exposure to humans and the environment

General information toxicology

The applicant has submitted an effect and exposure assessment for the Mosquito Milk DEET products. The human health exposure and risk assessment of the Mosquito Milk DEET products were examined by the Ctgb appropriately according to standard requirements. Studies with different Mosquito Milk DEET products have been provided. No new studies have been provided concerning the active substance and human health exposure. The products were not reference products in the EU-review program for inclusion of the active substance in Annex I of Directive 98/8/EC. The CA NL has revised this risk assessment for the human health aspect. See for more detail section 2.7.

General information environment

The environmental exposure and risk assessment of the Mosquito Milk DEET products from the applicant was examined appropriately according to standard requirements. No new studies have been provided concerning environmental exposure. The products were not reference products in the EU-review program for inclusion of the active substance in Annex I of Directive 98/8/EC. The applicant has submitted an effect and exposure assessment for the Mosquito Milk DEET products. The CA NL has revised this risk assessment for the environmental aspect. See for more detail section 2.8 below.

2.7 Risk assessment for human health

General information

Mosquito Milk DEET products are ready-to-use sprays (one spray with a pure DEET concentration of 9.8% w/w and one spray with a pure DEET concentration of 19.4% w/w) roll on (pure DEET concentration of 20.7% w/w, lotion (pure DEET concentration of 19.4% w/w) or stick (pure DEET concentration of 19.4% w/w) products for non-professional use. During the Annex I active review stage a product with an DEET concentration of 15% has been evaluated.

For these authorisation applications, no new studies were submitted with the active substance or concerning human exposure that were not already evaluated during the

Annex I active review stage. Detailed data on the toxicity of the active substance can be consulted in Doc IIA of the final Assessment Report (March 2010) for DEET, PT19.

New studies were submitted with the products, because these products were not reference products in the EU-review program for inclusion of the active substance in Annex I of Directive 98/8/EC. These studies have not been evaluated in the CAR of DEET. The applicant has submitted studies with the products to address acute oral, dermal, skin and eye irritation (see 2.7.1.3 for results). For dermal absorption of DEET from the formulations the applicant provided a statement that the value of 20% used in the CAR of DEET can be used in the risk assessment.

2.7.1 Hazard potential

2.7.1.1 Toxicology of the active substance

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

2.7.1.2 Toxicology of the substance(s) of concern

All products contain ethanol as a substance of concern. The highest content of ethanol in the formulations is 36.9% (DEET Anti-Insect Spray 9.5% DEET).

Ethanol is notified according to the biocides review programme (for PT1, 2 and 4). A draft CA-report is yet available, although not discussed in the working groups. For ethanol a Council's Dutch Expert Committee on Occupational Standards (DECOS) evaluation (2006) is available.

List of Endpoints

At the request of the Minister of Social Affairs and Employment of The Netherlands, the Health Council of the Netherlands has set health-based recommended occupational exposure limits for chemicals in air at the workplace in 2006. These recommendations were made by the Council's Dutch Expert Committee on Occupational Standards (DECOS). For ethanol at the workplace, DECOS calculated a health-based calculated occupational cancer risk value (HBC-OCRV) of 1300 mg/m^3, resulting in a breast cancer risk of 4 additional death cases per 1000 (4*10^{-3}) deaths for 40 years. In addition, DECOS recommended a short-term exposure limit (STEL) of 1900 mg/m^3 TWA 15 minutes and a skin notation, as dermal exposure can substantially contribute to the body burden of ethanol. In the report of DECOS it is stated that, as a worst case estimate, a penetration rate of 0.7 mg/cm^2/h can be used to calculate the internal dose after dermal exposure. Although there are no exact values available for dermal absorption of ethanol, values of 1-2% dermal absorption are usually used for ethanol based on studies and the penetration rate recommended by DECOS in the Netherlands. The EFSA guidance on dermal absorption (2012)[1] recommends the value of 25% for formulations containing >5% substance. Therefore the RMS has performed the risk assessment by considering two values for dermal absorption of ethanol: 25% and 1-2%.

Epidemiological studies suggest that consumption levels below 10-12 grams of ethanol per day will probably not cause liver cirrhosis. However, the Committee on Alcohol consumption
and reproduction concluded that at these consumption levels effects on fertility and development may occur. Even long term oral exposure to levels of 1-12 gram ethanol per day might result in effects on the development (like increased incidence of spontaneous

[1] EFSA Guidance on dermal absorption. EFSA Journal 2012;10(4):2665

abortion, foetal death, pre-term delivery and decreased length of gestation) and fertility, according to the Committee on Alcohol consumption and reproduction. From the available meta-analysis and pooled studies, the committee concluded that drinking of one glass of alcoholic beverage per day the internal intake will be 10 gram ethanol.

Considering the fact that the maximal alcohol concentration in blood after one (oral) drink is approximately 10-100 times higher than the ethanol concentration in blood after inhalatory exposure to 1300 mg/m^3, DECOS was of the opinion that a HBC-OCRV of 1300 mg/m^3 is low enough to protect against these effects. Other toxic effect manifest themselves after exposure to higher exposure levels.

2.7.1.3 Toxicology of the biocidal product

The toxicology of the biocidal products was examined appropriately according to standard requirements. The products were not (dummy) products in the EU-review program for inclusion of the active substance in Annex I of Directive 98/8/EC.

GLP-compliant studies with the products have been submitted by the applicant to address acute oral and dermal toxicity, skin and eye irritation. The results of these studies are presented below.

Mosquito Milk Spray 9.5% DEET

Acute oral toxicity
The test item **Mosquito Milk Spray 9.5% DEET** was administered to a group of 6 female Sprague Dawley rats at the single dose of 2000 mg/kg body weight. The experimental protocol was compliant with the OECD guideline No. 423 and Directive 96/54/EEC test method B.1tris.

No mortality occurred during the study. No clinical signs related to the administration of the test item were observed. The body weight evolution of the animals remained normal throughout the study. The macroscopical examination of the animals at the end of the study did not reveal treatment related change.

In conclusion, the LD50 of the test item **Mosquito Milk Spray 9.5% DEET** is higher than 2000 mg/kg body weight by oral route in the rat.

According to the criteria for classification, packaging and labelling of dangerous substances and preparations in accordance with the EEC Directives 67/548, 2001/59 and 99/45, the test item **Mosquito Milk Spray 9.5% DEET** must not be classified. No symbol or risk phrase is required. In accordance with the Regulation (EC) No. 1272/2008 on classification, labelling and packaging of substances and mixtures, the test item must not be classified. No signal word or hazard statement is required.

Acute dermal toxicity
The test item **Mosquito Milk Spray 9.5% DEET** was applied onto the intact skin of 10 Sprague Dawley rats (5 males and 5 females) at the single dose of 2000 mg/kg body weight. The experimental protocol was compliant with the OECD guideline No. 402 and Directive 96/54/EEC test method B.3.

No mortality occurred during the study. Neither cutaneous reactions nor systemic clinical signs related to the administration of the test item were observed. The body weight evolution of the animals remained normal throughout the study. The macroscopical examination of the animals at the end of the study did not reveal treatment-related changes.

In conclusion, the LD50 of the test item **Mosquito Milk Spray 9.5% DEET** is higher than 2000 mg/kg body weight by dermal route in the rat.

According to the criteria for classification, packaging and labelling of dangerous substances and preparations in accordance with the EEC Directives 67/548, 2001/59 and 99/45, the test item **Mosquito Milk Spray 9.5% DEET** must not be classified. No symbol or risk phrase is required. In accordance with the Regulation (EC) No. 1272/2008, the test item must not be classified. No signal word or hazard statement is required.

Acute dermal irritation
The test item **Mosquito Milk Spray 9.5% DEET** was applied, as supplied, at the dose of 0.5 mL, under semi-occlusive dressing during 4 hours on an undamaged skin area of 3 rabbits. The experimental protocol was compliant with the OECD guideline No. 404 and Directive 96/54/EEC test method B.4.

A slight to well defined erythema in three animals, associated with a very slight oedema in one animal, were noted on the treated area of the animals, 1 hour after the patch removal. The oedematous reactions were totally reversible on day 2; the erythematous reactions were totally reversible between days 1 and 2. On the cutaneous structure, dryness was noted on day 2 in one animal. The average scores at 24, 48 and 72 hours for both erythema and oedema were 0.33.

The results obtained, under these experimental conditions, enable to conclude that the test item **Mosquito Milk Spray 9.5% DEET** must not be classified, according to the criteria for classification, packaging and labelling of dangerous substances and preparations in compliance with the EEC Directives 67/548, 2001/59 and 99/45. No symbol or risk phrase is required.
In accordance with the Regulation (EC) No. 1272/2008, the test item must not be classified. No signal word or hazard statement is required.

Acute eye irritation
The test item **Mosquito Milk Spray 9.5% DEET** was instilled as supplied, into the eye of 3 New Zealand rabbits at the dose of 0.1 mL. The experimental protocol was compliant with the OECD guideline No. 405 and Directive 96/54/EEC test method B.5.

The ocular reactions observed during the study have been moderate to significant and totally reversible in the three animals:
- at the conjunctivae level: a moderate to significant redness noted 1 hour after the test item instillation and totally reversible between days 9 and 15, associated with a moderate to significant chemosis noted 1 hour after the test item instillation and totally reversible between days 7 and 14,
- at the iris level: a congestion, noted 1 or 24 hours after the test item instillation, and totally reversible between days 2 and 3.
- at the corneal level: a slight to moderate corneal opacity, noted 1 or 24 hours after the test item instillation, and totally reversible between days 6 and 8.
Moreover, white spots on the nictitating membrane were noted on day 2 in one animal. The average scores for cornea, iris, conjunctivae and chemosis at 24, 48 and 72 hours were 1.2, 0.5, 2.7 and 2.3, respectively.

In conclusion, the results obtained, under these experimental conditions, enable to conclude that the test item **Mosquito Milk Spray 9.5% DEET** must be classified R36 “Irritating to eyes” according to the criteria for the classification, packaging and labelling of dangerous substances in compliance with the EEC Directive No. 67/548, 2001/59 and 99/45. The item is to be characterised by the symbol “Xi” and the warning label “irritant”. In accordance with the Regulation (EC) No. 1272/2008 on classification, labelling and packaging of substances and mixtures, the test item must be classified in category 2

“Irritating to eyes”. The signal word “Warning” and hazard statement H319 “Causes serious eye irritation**”** are required.

Mosquito Milk Spray 20% DEET

In April 2016 the applicant has submitted an application for a major change, which included a change of the composition of the product. Please refer to the document ‘Annex 10 of PAR Mosquito Milk Products’ in the asset NL-0003044-0000.

~~*Acute oral toxicity*~~
~~The test item **Mosquito Milk Spray 20% DEET** was administered to a group of 6 female Sprague Dawley rats at the single dose of 2000 mg/kg body weight. The experimental protocol was compliant with the OECD guideline No. 423 and Directive 96/54/EEC test method B.1tris.~~

~~No mortality occurred during the study. No clinical signs related to the administration of the test item were observed. The body weight evolution of the animals remained normal throughout the study. The macroscopical examination of the animals at the end of the study did not reveal treatment related change.~~

~~In conclusion, the LD50 of the test item **Mosquito Milk Spray 20% DEET** is higher than 2000 mg/kg body weight by oral route in the rat.~~

~~According to the criteria for classification, packaging and labelling of dangerous substances and preparations in accordance with the EEC Directives 67/548, 2001/59 and 99/45, the test item **Mosquito Milk Spray 20% DEET** must not be classified. No symbol or risk phrase is required. In accordance with the Regulation (EC) No. 1272/2008 on classification, labelling and packaging of substances and mixtures, the test item must not be classified. No signal word or hazard statement is required.~~

~~*Acute dermal toxicity*~~
~~The test item **Mosquito Milk Spray 20% DEET** was applied onto the intact skin of 10 Sprague Dawley rats (5 males and 5 females) at the single dose of 2000 mg/kg body weight. The experimental protocol was compliant with the OECD guideline No. 402 and Directive 69/54/EEC test method B.3.~~

~~No mortality occurred during the study. Neither cutaneous reactions nor systemic clinical signs related to the administration of the test item were observed. The body weight evolution of the animals remained normal throughout the study. The macroscopical examination of the animals at the end of the study did not reveal treatment-related changes.~~

~~In conclusion, the LD50 of the test item **Mosquito Milk Spray 20% DEET** is higher than 2000 mg/kg body weight by dermal route in the rat.~~

~~According to the criteria for classification, packaging and labelling of dangerous substances and preparations in accordance with the EEC Directives 67/548, 2001/59 and 99/45, the test item **Mosquito Milk Spray 20% DEET** must not be classified. No symbol or risk phrase is required. In accordance with the Regulation (EC) No. 1272/2008, the test item must not be classified. No signal word or hazard statement is required.~~

~~*Acute dermal irritation*~~
~~The test item **Mosquito Milk Spray 20% DEET** was applied, as supplied, at the dose of 0.5 mL, under semi-occlusive dressing during 4 hours on an undamaged skin area of 3 rabbits. The experimental protocol was compliant with the OECD guideline No. 404 and Directive 69/54/EEC test method B.4.~~

~~No cutaneous reactions (erythema and oedema) were observed at any examination time (1, 24, 48 and 72 hours). The average scores for erythema and edema at 24, 48 and 72 hours were 0.~~

~~The results obtained, under these experimental conditions, enable to conclude that the test item **Mosquito Milk Spray 20% DEET** must not be classified, according to the criteria for classification, packaging and labelling of dangerous substances and preparations in compliance with the EEC Directives 67/548, 2001/59 and 99/45. No symbol or risk phrase is required. In accordance with the Regulation (EC) No. 1272/2008, the test item must not be classified. No signal word or hazard statement is required.~~

~~*Acute eye irritation*~~
~~The test item **Mosquito Milk Spray 20% DEET** was instilled as supplied, into the eye of 3 New Zealand rabbits at the dose of 0.1 mL. The experimental protocol was compliant with the OECD guideline No. 405 and Directive 69/54/EEC test method B.5.~~

~~The ocular reactions observed during the study have been moderate to significant and partially reversible:~~
~~- at the conjunctivae level: a moderate redness, noted 24 hours after the test item instillation and totally reversible between days 7 and 10, associated with an significant chemosis, noted 1 hour after the test item instillation and totally reversible between days 7 and 15.~~
~~- at the iris level: a congestion, noted 24 or 72 hours after the test item instillation and totally reversible on day 4.~~
~~- at the corneal level: a moderate corneal opacity, noted 24 hours after the test item instillation. The corneal opacity was totally reversible in two animaks on day 7 or day 8 and remained on day 21 (last day of the test) in the last animal (slight intensity).~~
~~A corneal neovascularisation was noted from day 8 in one animal and was still observed on day 21.~~
~~Whitish secretions requiring a physiological rinse were noted in one animal on days 2 and 3.~~
~~The average scores for cornea, iris, conjunctivae and chemosis at 24, 48 and 72 hours were 1.9, 0.7, 2.5 and 2.5, respectively.~~

~~In conclusion, taking into account the irreversibility of lesions observed, the results obtained, under these experimental conditions, enable to conclude that the test item **Mosquito Milk Spray 20% DEET** must be classified R41 "Risk of serious damage to eyes", according to the criteria for the classification, packaging and labelling of dangerous substances in compliance with the EEC Directives 67/548, 2001/59 and 99/45. It must be characterised by the symbol “Xi” and the danger label “irritant”. In accordance with the Regulation (EC) No. 1272/2008, the test item must be classified in category 1 “irreversible effects on the eye”. The signal word “Danger” and hazard statement H318 “Causes serious eye damage” are required.~~

<u>Mosquito Milk Roll On 20% DEET</u>

Acute oral toxicity
The test item **Mosquito Milk Roll On 20% DEET** was administered to a group of 6 female Sprague Dawley rats at the single dose of 2000 mg/kg body weight. The experimental protocol was compliant with the OECD guideline No. 423 and Directive 96/54/EC test method B.1tris.

No mortality occurred during the study. No clinical signs related to the administration of the test item were observed. The body weight evolution of the animals remained normal

throughout the study. The macroscopical examination of the animals at the end of the study did not reveal treatment related change.

In conclusion, the LD50 of the test item **MOSQUITO MILK ROLL ON 20% DEET** is higher than 2000 mg/kg body weight by oral route in the rat.

According to the criteria for classification, packaging and labelling of dangerous substances and preparations in accordance with the EEC Directives 67/548, 2001/59 and 99/45, the test item **Mosquito Milk Roll On 20% DEET** must not be classified. No symbol or risk phrase is required. In accordance with the Regulation (EC) No. 1272/2008 on classification, labelling and packaging of substances and mixtures, the test item must not be classified. No signal word or hazard statement is required.

Acute dermal toxicity
The test item **Mosquito Milk Roll On 20% DEET** was applied onto the intact skin of 10 Sprague Dawley rats (5 males and 5 females) at the single dose of 2000 mg/kg body weight. The experimental protocol was compliant with the OECD guideline No. 402 and Directive 96/54/EC test method B.3.

No mortality occurred during the study. Neither cutaneous reactions nor systemic clinical signs related to the administration of the test item were observed. The body weight evolution of the animals remained normal throughout the study. The macroscopical examination of the animals at the end of the study did not reveal treatment-related changes.

In conclusion, the LD50 of the test item **Mosquito Milk Roll On 20% DEET** is higher than 2000 mg/kg body weight by dermal route in the rat.

According to the criteria for classification, packaging and labelling of dangerous substances and preparations in accordance with the EEC Directives 67/548, 2001/59 and 99/45, the test item **Mosquito Milk Roll On 20% DEET** must not be classified. No symbol or risk phrase is required. In accordance with the Regulation (EC) No. 1272/2008, the test item must not be classified. No signal word or hazard statement is required.

Acute dermal irritation
The test item **Mosquito Milk Roll On 20% DEET** was applied, as supplied, at the dose of 0.5 g, under semi-occlusive dressing during 4 hours on an undamaged skin area of 3 rabbits. The experimental protocol was compliant with the OECD guideline No. 404 and Directive 96/54/EC test method B.4
.
A very slight erythema was noted in one animal on day 1 and was totally reversible on day 3. The average scores for erythema and oedema at 24, 48 and 72 hours were 0.23 and 0.

The results obtained, under these experimental conditions, enable to conclude that the test item **Mosquito Milk Roll On 20% DEET** must not be classified, according to the criteria for classification, packaging and labelling of dangerous substances and preparations in compliance with the EEC Directives 67/548, 2001/59 and 99/45. No symbol or risk phrase is required. In accordance with the Regulation (EC) No. 1272/2008, the test item must not be classified. No signal word or hazard statement is required

Acute eye irritation
The test item **Mosquito Milk Roll On 20% DEET** was instilled as supplied, into the eye of 3 New Zealand rabbits at the dose of 0.1 mL. The experimental protocol was compliant with the OECD guideline No. 405 and Directive 96/54/EC test method B.5.

The ocular reactions observed during the study have been slight to significant and partially reversible:
- at the conjunctivae level: a moderate redness, noted 24 hours after the test item instillation and totally reversible between days 7 and 13, associated with a slight to important chemosis, noted 1 hour after the test item instillation and totally reversible between days 7 and 13.
- at the iris level: a congestion, noted 24 hours after the test item instillation and totally reversible between days 6 and 7.
- at the corneal level: a moderate corneal opacity, noted 24 hours after the test item instillation. The corneal opacity was totally reversible in two animals on day 10 or day 17 and remained on day 21 (last day of the test) in the last animal (slight intensity).
A corneal neovascularisation was noted between days 2 and 4 in one animal, from day 6 and still observed on day 21 in the second animal, and on day 8 in the last animal.
White spots were noted on the nictitating membrane in one animal on days 2 and 3 and on day 8.
The average scores for cornea, iris, conjunctivae and chemosis were 1.9, 1, 2.77 and 2.1, respectively.

In conclusion, taking into account the irreversibility of lesions observed, the results obtained, under these experimental conditions, enable to conclude that the test item **Mosquito Milk Roll On 20% DEET** must be classified R41 "Risk of serious damage to eyes", according to the criteria for the classification, packaging and labelling of dangerous substances in compliance with the EEC Directives 67/548, 2001/59 and 99/45. It must be characterised by the symbol “Xi” and the danger label “irritant”. In accordance with the Regulation (EC) No. 1272/2008, the test item must be classified in category 1 “irreversible effects on the eye”. The signal word “Danger” and hazard statement H318 “Causes serious eye damage” are required.

Mosquito Milk Lotion 20% DEET

Acute oral toxicity
The test item **Mosquito Milk Lotion 20% DEET** was administered to a group of 6 female Sprague Dawley rats at the single dose of 2000 mg/kg body weight. The experimental protocol was compliant with the OECD guideline No. 423 and Directive 96/54/EC test method B.1tris.

No mortality occurred during the study. On the first days of the study, decreases in spontaneous activity (6/6) and in muscle tone (1/6), myosis (1/6), partial ptosis (1/6), piloerection (4/6), increase lachrymation (1/6) and staggering gait (1/6) were noted. The animals recovered a normal behaviour on day 3. The mean body weight evolution of the animals remained normal throughout the study. In one animal, a decrease of the body weight (-5.8%) was recorded at 48-hours post dose. The macroscopical examination of the animals at the end of the study did not reveal treatment related change.

In conclusion, the LD50 of the test item **Mosquito Milk Lotion 20% DEET** is higher than 2000 mg/kg body weight by oral route in the rat.

According to the criteria for classification, packaging and labelling of dangerous substances and preparations in accordance with the EEC Directives 67/548, 2001/59 and 99/45, the test item **Mosquito Milk Lotion 20% DEET** must not be classified. No symbol or risk phrase is required. In accordance with the Regulation (EC) No. 1272/2008 on classification, labelling and packaging of substances and mixtures, the test item must not be classified. No signal word or hazard statement is required.

Acute dermal toxicity

The test item **Mosquito Milk Lotion 20% DEET** was applied onto the intact skin of 10 Sprague Dawley rats (5 males and 5 females) at the single dose of 2000 mg/kg body weight. The experimental protocol was compliant with the OECD guideline No. 402 and Directive 96/54/EC test method B.3.

No mortality occurred during the study. Neither cutaneous reactions nor systemic clinical signs related to the administration of the test item were observed. The body weight evolution of the animals remained normal throughout the study. The macroscopical examination of the animals at the end of the study did not reveal treatment-related changes.

In conclusion, the LD50 of the test item **Mosquito Milk Lotion 20% DEET** is higher than 2000 mg/kg body weight by dermal route in the rat.

According to the criteria for classification, packaging and labelling of dangerous substances and preparations in accordance with the EEC Directives 67/548, 2001/59 and 99/45, the test item **Mosquito Milk Lotion 20% DEET** must not be classified. No symbol or risk phrase is required. In accordance with the Regulation (EC) No. 1272/2008, the test item must not be classified. No signal word or hazard statement is required.

Acute dermal irritation
The test item **Mosquito Milk Lotion 20% DEET** was applied, as supplied, at the dose of 0.5 g, under semi-occlusive dressing during 4 hours on an undamaged skin area of 3 rabbits. The experimental protocol was compliant with the O.E.C.D. guideline No. 404 and Directive 96/54/EC test method B.4.

No cutaneous reactions (erythema and oedema) were observed whatever the examination time (1, 24, 48 and 72 hours). The average scores of erythema and oedema at 24, 48 and 72 hours were 0.

The results obtained, under these experimental conditions, enable to conclude that the test item **Mosquito Milk Lotion 20% DEET** must not be classified, according to the criteria for classification, packaging and labelling of dangerous substances and preparations in compliance with the EEC Directives 67/548, 2001/59 and 99/45. No symbol or risk phrase is required. In accordance with the Regulation (EC) No. 1272/2008, the test item must not be classified. No signal word or hazard statement is required.

Acute eye irritation
The test item **Mosquito Milk Lotion 20% DEET** was instilled as supplied, into the eye of 3 New Zealand rabbits at the dose of 0.1 mL. The experimental protocol was compliant with the OECD guideline No. 405 and Directive 96/54/EC test method B.5.

The ocular reactions observed during the study have been moderate and partially reversible:
- at the conjunctivae level: a moderate redness, noted 1 hour after the test item instillation and totally reversible on day 9, associated with a moderate chemosis, noted 1 hour after the test item instillation and totally reversible on day 10.
- at the iris level: a congestion, noted 1 hour after the test item instillation and totally reversible on day 4.
- at the corneal level: a slight corneal opacity, noted 1 hour after the test item instillation and remaining on day 21 (last day of the test) (slight intensity).
A corneal neovascularisation was noted from day 8 and was still observed on day 21.

The average scores for cornea, iris, conjunctivae and chemosis at 24, 48 and 72 hours were 2.0, 1.0, 2.0 and 3.0, respectively.

In conclusion, taking into account the irreversibility of lesions observed, the results obtained, under these experimental conditions, enable to conclude that the test item **Mosquito Milk Lotion 20% DEET** must be classified R41 "Risk of serious damage to eyes", according to the criteria for the classification, packaging and labelling of dangerous substances in compliance with the EEC Directives 67/548, 2001/59 and 99/45. It must be characterised by the symbol “Xi” and the danger label “irritant”. In accordance with the Regulation (EC) No. 1272/2008, the test item must be classified in category 1 “irreversible effects on the eye”. The signal word “Danger” and hazard statement H318 “Causes serious eye damage” are required.

Mosquito Milk Stick 20% DEET

Acute oral toxicity
A sample of the formulation was examined for acute oral toxicity in an experiment with female rats (limit test), according to Directive 96/54/EC test method B.1 and OECD Guideline no. 423.

No mortality or distinct clinical signs were observed after treatment with a 2000 mg/kg b.w. dose level. Macroscopic examination of the surviving animals at the end of the observation period did not reveal any treatment-related gross changes.

Since all animals survived the 2000 mg/kg dose level, the oral LD50 of the test item is considered to be higher than 2000 mg/kg body weight.

According to the criteria for classification, packaging and labelling of dangerous substances and preparations in accordance with the EEC Directives 67/548, 2001/59 and 99/45, the test item **Mosquito Milk Stick 20% DEET** must not be classified. No symbol or risk phrase is required. In accordance with the Regulation (EC) No. 1272/2008 on classification, labelling and packaging of substances and mixtures, the test item must not be classified. No signal word or hazard statement is required.

Acute dermal toxicity
A sample of the formulation was examined for acute dermal toxicity in an experiment with male and female rats (limit test), according to Directive 96/54/EC test method B.3 and OECD Guideline no. 402. A dose level of 2000 mg per kg body weight was examined and the dermal contact period was 24 hours.

No mortality, dermal reactions or clinical signs were observed after treatment with a 2000 mg/kg b.w. dose level. Macroscopic examination of the surviving animals at the end of the observation period did not reveal any treatment-related gross changes.

Since all animals survived the 2000 mg/kg dose level, the oral LD50 of the test item is considered to be higher than 2000 mg/kg body weight.

According to the criteria for classification, packaging and labelling of dangerous substances and preparations in accordance with the EEC Directives 67/548, 2001/59 and 99/45, the test item **Mosquito Milk Stick 20% DEET** must not be classified. No symbol or risk phrase is required. In accordance with the Regulation (EC) No. 1272/2008 on classification, labelling and packaging of substances and mixtures, the test item must not be classified. No signal word or hazard statement is required.

Acute dermal irritation
A sample of the formulation was tested for acute dermal irritating properties in an experiment with three albino rabbits, according to Directive 92/69/EEC, method B.4 and OECD Guideline no. 404.

The test item did not cause skin effects in the three rabbits. The average scores for erythema and oedema at 24, 48 and 72 hours were 0.7 and 0.3, respectively.

According to the criteria for classification, packaging and labelling of dangerous substances and preparations in accordance with the EEC Directives 67/548, 2001/59 and 99/45, the test item **Mosquito Milk Stick 20% DEET** must not be classified. No symbol or risk phrase is required. In accordance with the Regulation (EC) No. 1272/2008 on classification, labelling and packaging of substances and mixtures, the test item must not be classified. No signal word or hazard statement is required.

Acute eye irritation
A sample of the formulation was tested for acute eye irritating properties in an experiment with three albino rabbits, according to Directive 92/69/EEC, method B.5 and OECD Guideline no. 405.

The test item generally caused moderate redness and moderate swelling of the conjunctivae and moderate or severe ocular discharge in the three rabbits. At 72 hours after treatment, all eye effects had cleared completely.

The average scores for cornea, iris, conjunctivae and chemosis at 24, 48 and 72 hours were 0.1, 0.1, 0.77 and 0.33, respectively.

According to the criteria for classification, packaging and labelling of dangerous substances and preparations in accordance with the EEC Directives 67/548, 2001/59 and 99/45, the test item **Mosquito Milk Stick 20% DEET** must not be classified. No symbol or risk phrase is required. In accordance with the Regulation (EC) No. 1272/2008 on classification, labelling and packaging of substances and mixtures, the test item must not be classified. No signal word or hazard statement is required.

For dermal absorption of DEET from the formulations the applicant provided a statement that the value of 20% used in the CAR of DEET can be used in the risk assessment.

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

2.7.2 Exposure

Mosquito Milk DEET products are ready-to-use spray, roll on, lotion or stick products for non-professional use at a N,N-diethyl-*m*-toluamide (DEET) concentration of 9.8%, 19.4 and 20% w/w dependent on product.
The intended use of the products is exclusively by dermal application. The exposure assessment is based on an application frequency of 1-2 times per day. Dermal route is the main path of exposure, but contributions to exposure via inhalation of the product during application of the repellent spray and via hand to mouth contact are possible. However, according to TNsG – human exposure to Biocidal products – Guidance on Exposure Estimation (European commission, 2002, part 2)) the inhalation route can be excluded for the use outdoors, and use indoors only takes place in the summer in situations where there is a high ventilation rate. On these grounds, the inhalation exposure to sprays is likely to be negligible. However, in the CAR of DEET it has been concluded that inhalation exposure cannot be fully ruled out and therefore a recommendation on ventilation is considered necessary on spray formulations.
Oral exposure by hand-to-mouth transfer is not considered to be a significant route of exposure because the smell and taste of DEET acts as a self-deterrent against this type of activity. More importantly, all products contain an ingredient that acts as a strong deterrent for ingestion (Bitrex). However, the efficacy of Bitrex was discussed at a Technical Meeting where it was concluded that Bitrex may not be effective in preventing ingestion in all age groups, in particular children < 12 years old. Therefore the oral route is still considered to

be possible and the calculations for hand to mouth transfer are included by the RMS in the worst case exposure calculations. The potential for exposure to DEET is summarized in the table below.

Potential for exposure to DEET:

Exposure path	Industrial use	Professional use	General public	Via the environment
Inhalation	-	-	X	-
Dermal	-	-	X	-
Oral	-	-	X	-

2.7.2.1 Exposure of professional users

The products are not intended for professional use.

2.7.2.2 Exposure of non-professional users and the general public

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

Active substance DEET:
A user survey study has been performed in the USA involving human use and exposure to insect repellents containing DEET (Boomsma and Parthasarathy, 1990 (III-A6.14)). This study is part of the data package for DEET and is presented in Doc III of the final CAR. The human health exposure scenario for adult consumers at the 75th percentile of use, applying the representative product containing DEET as an insect repellent was used for the risk characterizations. The use of the 75th percentile was considered acceptable since the user study had a large number of study subjects and the measured exposure was similar to the default exposure value of the TNsG. In this study, the average active ingredient content was estimated to be 26.1%. The 75th percentile of human dermal exposure per application of the formulation containing 26.1% DEET is estimated to be 1.5 g active substance for males, 1.0 g for females, 1.66 g for children aged 13-17 years and 1.42 g for children aged <12 years based on the results of the survey study. Daily exposure for different age groups was calculated by considering a body weight of 70, 60, 62.8 and 25.5 kg for males, females, children > 12 years of age and children <12 years of age, respectively. The same values for body weight were also used in the CAR of DEET.

Exposure due to hand to mouth transfer has also been included in the calculations as a worst-case approach. According to the TNsG on human exposure, part II, 2002 it is expected that adults will ingest the amount applied to fingers. The surface of the fingers is approximately 4% of the treated body surface. The oral exposures are for the age groups 13-17 years and < 12 years are 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).

A dermal absorption value of 20% was used to calculate internal exposure in humans.

Substance of concern ethanol:
The highest exposure to ethanol is expected for the formulation with the highest ethanol content (DEET Anti-Insect Spray 9.5% DEET). Based on the USA user survey study with DEET-containing repellants the 75th percentile of human dermal exposure per application is estimated to be 5.7 g product for males, 3.8 g product for females, 6.4 g product for children aged 13-17 years and 5.4 g product for children aged <12 years. As a consequence for DEET Anti-Insect Spray 9.5% DEET with the highest ethanol concentration of 36.9% the 75th percentile of external dermal exposure per application is

estimated to be 2.10 g ethanol for males, 1.40 g ethanol for females, 2.36 g ethanol for children aged 13-17 years and 1.99 g ethanol for children aged <12 years.

Indirect exposure of general public
The degree of indirect exposure is considered negligible as the primary route of exposure is direct application to the skin.

2.7.2.3 Exposure to residues in food

The application of the DEET products does not result in residues to which consumers might become exposed.

2.7.3 Risk Characterisation

2.7.3.1 Risk for Professional Users

The products are not intended for professional use.

2.7.3.2 Risk for non-professional users and the general public

Active substance DEET:
It was decided at TM I and II 2009 that risk characterisation for DEET products should be performed for two daily applications and by using the 75th percentile of human dermal exposure based on the USA survey study. When using this method the estimated exposures for different contents of DEET in the products after dermal application in percentages of the $AEL_{repeated\ dermal}$ for adult males, adult females, children >12 years and < 12 years are presented in Table 1.

Table 1. The ratio of the estimated dermal exposure to $AEL_{repeated\ dermal}$ for different contents of DEET in the formulations. Two applications per day have been considered.

Exposure/$AEL_{repeated\ dermal}$	**9.8% DEET**	**19.4% DEET**	**20.7% DEET**
Dermal			
Male:	0.39	0.78	0.83
Female:	0.30	0.60	0.64
>12 yr:	0.48	0.96	1.02
<12 yr:	1.02	2.38	2.15

Taking into account only **dermal** exposure, the use of the product with 9.8% DEET, **Mosquito milk spray 9.5% DEET**, 2 times per day is considered acceptable for adults, children >12 years old and children <12 years old. Moreover, although the risk characterisation ratio for children < 12 years is 1.02, the calculated risk characterisation ratio of 1.02 is considered to be at the limit of acceptable risks. The dermal absorption value of 20% is based on a 15% (w/w) solution in ethanol and ethanol is known to enhance dermal permeation. The concentration ethanol in the product **Mosquito milk spray 9.5% DEET** is lower compared to this reference. Therefore RMS considers it justified to accept the risk characterisation ratio of 1.02. Furthermore eCA is of the opinion that the benefit of a longer protection time prevails here.
The use of the products with 19.4 and 20.7% DEET, **Mosquito Milk Spray 20% DEET**, **Mosquito Roll On 20% DEET, Mosquito Milk Lotion 20% DEET** and **Mosquito Milk Stick 20% DEET** 2 times per day is considered acceptable for adults and children >12 years old. Although, the risk characterisation ratio for children > 12 years is 1.02 for the 20.7% Roll-on product, the calculated risk characterisation ratio of 1.02 is considered to be at the limit of acceptable risks (as the worst dermal absorption percentage is taken into

account and the benefit of a longer protection time as described for the 9.8% DEET product for children < 12 years old).

The restriction of the product use to maximal use once per day was considered to be one of the possible risk management measures. Therefore daily exposures for different contents of DEET in the products following a single exposure have also been calculated by the RMS. The results are presented in table 2.

Table 2. The ratio of the estimated dermal exposure to $AEL_{repeated\ dermal}$ for different contents of DEET in the formulations. One application per day has been considered.

Exposure/$AEL_{repeated\ dermal}$	**9.8% DEET**	**19.4% DEET**	**20.7% DEET**
Dermal			
Male:	0.20	0.39	0.41
Female:	0.15	0.30	0.32
>12 yr:	0.24	0.48	0.51
<12 yr:	0.51	1.01	1.08

If only dermal exposure is considered, the use of the product with 9.8% DEET, **Mosquito Milk Spray 9.5% DEET** once per day is considered acceptable for adults, children > 12 years old and children <12 years old. The use of the products with 19.4% and 20.7% DEET, **Mosquito Milk Spray 20% DEET** (pure a.i. 19.4%), **Mosquito Roll On 20% DEET** (pure a.i. 20.7%), **Mosquito Milk Lotion 20% DEET** (pure a.i. 19.4%) and **Mosquito Milk Stick 20% DEET** (pure a.i. 1.5%) once per day is considered acceptable for adults and children >12 years old. Considering the group of children < 12 years is the most vulnerable group and already after only one application the risk index is above 1, no safe use is anticipated for this group.

As a worst-case approach, the RMS has also performed the assessment of the oral exposure, considering potential ingestion of 4% of the total applied product by adults (amount on fingers) and 8% by children (amount on hands). The resulting oral exposure estimates were compared with $AEL_{acute\ oral}$ of 0.75 mg/kg bw/day. From the calculation given in Annex 7 it can be seen that higher risk characteriation ratios are calculated for oral exposure in comparison with dermal exposure. Furthermore, reverse reference calculations in Annex 7 show how many times per day products containing different concentrations of DEET can be applied dermally without exceeding the AELs. For example, if only dermal exposure is considered, to exceed the $AEL_{repeated\ dermal}$ of 8.2 mg/kg bw/day, a formulation with the lowest content of DEET (9.8% DEET) can be applied 5.09, 6.56, 4.12 and 1.96 times per day for adult male, adult female, child >12 years and <12 years respectively. Thus based on the 1.96 value for children < 12 years old the application of the formulation containing 9.8% DEET twice per day is not considered acceptable. However, as described above for the risk characterisation ratio of 1.02 the value of 1.96 is considered to be at the same limit of acceptable values taken into account the worst dermal absorption percentage and the benefit of a longer protection time.

The reverse dose calculations in Annex 7 further show that for a formulation with the lowest content of DEET (9.8% DEET) only 9.3, 12, 7.5 and 3.6% of the estimated external dose per application at the 75th percentile of use for males, females, children >12 years and children< 12 years respectively can be ingested before an $AEL_{acute\ oral}$ of 0.75 mg/kg bw/day is exceeded. If as a worst-case an ingestion of 8% of the applied product is considered for the age groups 13-17 years and < 12 years, the exposure area in children would have to be reduced to avoid exceeding the AEL even for the formulation with the lowest content of DEET (9.8%). However, in the PA-MRFG meeting it has been agreed that labelling instructions with the intent to reduce the treated skin area are not accepted as an adequate risk mitigation measure; thus this restriction cannot be considered by the RMS.

Although considering oral exposure represents the worst-case approach, the high RCR values for oral exposure suggest that oral contribution cannot be considered negligible especially in case of children < 12 years old (see Annex 7). However, in the CAR of DEET it was concluded that the oral dose is likely to be largely overestimated given the short half-life after oral exposure in dogs and rats and the rapid achievement of C_{max}. The hand to mouth behaviour is more frequent in small children and based on concerns that Bitrex may not be sufficiently effective in protecting small children from ingestion of product, an age limit of 2 years was proposed in the CAR together with the recommendation "restrict the use on children between three and twelve years old". Furthermore, a recommendation not to use the products on hands of children < 12 years old has been included in the CAR in order to limit the potential oral exposure. However, as stated above, limiting the treated skin area was not considered an acceptable risk management measure by the PA&MRFG meeting. Therefore this restriction was not considered by the RMS.

In summary, an age limit of 2 years is proposed by the RMS as a cut-off for considering oral exposure in accordance with the approach used in the CAR of DEET. As a consequence the RMS considers the contribution of oral exposure negligible for children > 2 years old and adults. As a restriction, the phrase "Do not use on children < 2 years old and restrict the use on children between two and twelve years old" needs to be put on the label of the products, in accordance with the inclusion directive of DEET in Annex I of Directive 98/8/EC (Commission Directive 2010/51/EU).

Substance of concern ethanol:
Based on the survey study the 75th percentile of human dermal exposure per application of DEET Anti-Insect Spray 9.5% DEET is estimated to be 2.10 g ethanol for males, 1.40 g ethanol for females, 2.36 g ethanol for children aged 13-17 years and 1.99 g ethanol for children aged <12 years. Although the exact dermal absorption percentage is unknown, the values of 1-2% are usually used in the Netherlands based on studies and the penetration rate recommended by DECOS. The EFSA Guidance on dermal absorption recommends a value of 25% for formulations containing > 5% substance. If as a worst-case 25% dermal absorption is considered, the expected internal dermal exposure to ethanol will be 5.3% of the expected ethanol intake by drinking one glass of alcoholic beverage (10 g ethanol per day) for males, 3.5% for females, 5.9% for children aged 13-17 years and 5.0% for children aged <12 years. The 1-2% dermal absorption percentages result in internal dermal exposure of 0.21-0.42% of the expected ethanol intake by drinking one glass of alcoholic beverage (10 g ethanol per day) for males, 0.14-0.28% for females, 0.24-0.47% for children aged 13-17 years and 0.20-0.40% for children aged <12 years. Based on these results the RMS NL concludes that no unacceptable risk results from the presence of ethanol as a substance of concern in the formulations.

Conclusions
Because the products are intended for intentional exposure on skin and to be used by the general public, including elderly, children and unhealthy subjects, a conservative approach should be taken when approving products. Special care should also be taken when approving products for use in children <12 years old. When approving spray products, recommendations on ventilation should apply since the inhalational fraction is excluded in the risk characterisation calculations. Therefore the products which will be applied by spraying, need to be carrying safety phrases S23 according to Directive 1999/45/EC or P260 according to Regulation 1272/2008/EC ("Do not breathe spray") and S51 according to Directive 1999/45/EC or P271 according to Regulation 1272/2008/EC ("Use only in well ventilated areas").

Based on the presented risk evaluation the use of the product with 9.8% DEET, **Mosquito Milk Spray 9.5% DEET**, 2 times per day is considered acceptable for adults and children from 2 to 17 years old. The product should be labelled with "**Do not use on children less than two years old and** restrict the use on children between two and twelve years old" in accordance with the inclusion directive of DEET in Annex I of Directive 98/8/EC (Commission Directive 2010/51/EU).

As the product will be applied by spraying, it should be labelled with the safety phrases S23 according to Directive 1999/45/EC or P260 according to Regulation 1272/2008/EC ("Do not breathe spray") and S51 according to Directive 1999/45/EC or P271 according to Regulation 1272/2008/EC ("Use only in well ventilated areas").

The use of the products with 19.4% or 20.7% DEET, **Mosquito Milk Spray 20% DEET (pure a.i. 19.4%)**, **Mosquito Roll On 20% DEET (pure a.i. 20.7%)**, **Mosquito Milk Lotion 20% DEET (pure a.i.19.4%)** and **Mosquito Milk Stick 20% DEET** (pure a.i. 19.4%) 2 times per day is considered acceptable for adults and children >12 years old. The products must not be used on children < 12 years old. The restriction "Do not use on children < 12 years old" has to be written on a prominent position on the label. As **Mosquito Milk Spray 20% DEET** will be applied by spraying, it should be labelled with the safety phrases S23 according to Directive 1999/45/EC or P260 according to Regulation 1272/2008/EC ("Do not breathe spray") and S51 according to Directive 1999/45/EC or P271 according to Regulation 1272/2008/EC ("Use only in well ventilated areas").

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

2.8.1 Effect Assessment

No studies were submitted with the product authorisation application for the active substance or for the products that were not already evaluated during the Annex I active review stage or studies. Detailed data on the fate and distribution of DEET in the environment and the effect of the active substance on environmental organisms can be consulted in Doc IIA of the final Assessment Report (March 2010) for N,N-diethyl-*m*-toluamide (DEET, PT19). Fate and effects data are only provided in this Assessment Report for the parent structure, as DEET is ready biodegradable and no major (>10%) transformation products were formed in studies of hydrolysis and aquatic phototransformation.
The PNEC derivation is also described in detail in the Assessment Report for diethyl-*m*-toluamide (DEET), section 4.3.1 of Doc IIA and a summary is included in the table below.

Table 2.8.1-1 Summary of the PNECs derived for DEET in the different compartments.

Compartment	Organism	Endpoint	AF	PNEC
Freshwater	Green algae (*Selenastrum capricornutum*)	ErC_{50} = 43 mg/L	1000	0.043 mg/L
STP	Microorganisms from an activated sludge	EC_{50} > 1000 mg/L	100	10 mg/L
Sediment	Sediment-dwelling organisms	Equilibrium partitioning	-	0.0741 mg/kg ww
Soil	Green algae (*Selenastrum capricornutum*)	Equilibrium partitioning	-	0.0379 mg/kg ww

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 (0.23 Pa) higher than 0.01 Pa, the Henry´s law constant is low (3.93E-3 Pa*m^3/mol and DT50 is less than 2d; cf the TNsG on Annex I inclusion), ozone depletion in the stratosphere (atmospheric lifetime is <<1 year, and it does not contain Cl, Br or F substituents) or acidification (the AP, Acidification Potential is low[2]).

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). No further avian data were required, because DEET has a low potential for bioconcentration and bioaccumulation (log Kow <3; cf TGD II3.8.2).

2.8.2 Exposure Assessment

Major emissions from the application of mosquito repellents result from indoor showering, bathing or laundry with emission via the STP to surface water and sediment (waste phase). Direct emission to surface water and sediment can result from outdoor showering or bathing after application of the product on the skin (waste phase).
Emission to fresh water is expected to be worst case. Therefore risk for the marine environment is considered covered by the freshwater risk assessment.
For the proposed applications emissions during the application phase and the service life of the products are also considered less relevant and these routes are therefore not assessed.

Indirect emission
The water compartment (both inland and marine) is expected to be indirectly exposed to DEET mainly from STP effluents, 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). The most relevant environmental compartment of concern for DEET is therefore the aquatic.
According to a usage study described in Boomsma & Parthasarathy (section III-B6.6(2) of the final CAR of DEET), on average 1.2 g of active ingredient of a repellent containing 20% DEET is consumed per application, of which 0.9 g (75%) is applied to the skin and 0.3 g (25%) to the clothes. One can also assume some of the product to be “spilled” during application (a direct release to the air compartment) and absorbed by the skin during the “leave on phase
In IC5, UC36 (cosmetic odour agents; p 226 in the TGD II), 5% of the applied amount (for substances having vapour pressure below 100 Pa) is assumed to be emitted to the air. This figure was therefore adopted. All absorbed DEET (6.4%) is assumed to be metabolized (and excreted primarily as urine metabolites). Therefore, the rest of the initially applied dose (88.7%) is assumed to be released to the STP (see Figure 1).

[2] De Leeuw F. 1993. Assessment of the atmospheric hazards and risks of new chemicals: Procedures to estimate ”hazarard potentials”. Chemosphere 27(8): 1313-1328. AP=(MWSO2/MWDEET)*(nN+ nCl + nF + 2*nS)/2= (64.06/191.28)*1/2 = 0.17).

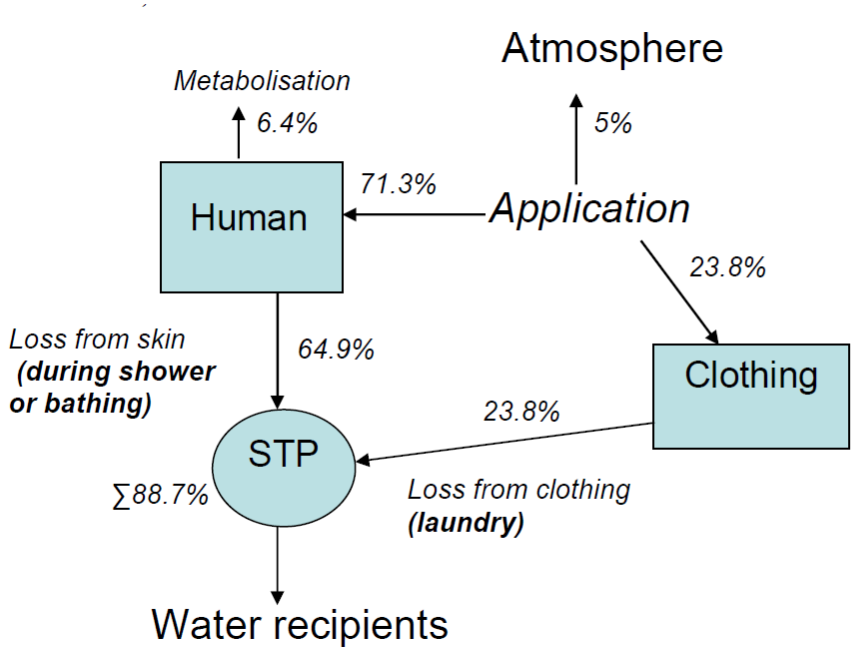

Figure 1 Assumed flows of DEET into the STP and environment. All percentages are referring to the initially applied dose.

Final environmental exposure will to a large extent depend on whether households are connected to STPs equipped with at least secondary (biological) treatment. Other efficient treatment processes include ozonation and PAC (Powdered Activated Carbon) addition, although these are more common in drinking water treatment[3].
In the following sections, PECs are derived by using the Emission Scenario Document (ESD) for PT 1 (Human hygiene products)[4]and equations in the TGD Part II (since there is not yet an ESD developed for PT 19). These calculations are based on data on amount consumed by individuals. The TNsG on human exposure sets a default value for the amount of dermally applied repellent product to 6 g. Estimated PEC values are compared to monitoring data found in some recent publications in scientific peer reviewed journals.

Direct emission
At the Technical Meeting I 2009 several member states had questions about possible direct emissions due to swimming for this kind of products.
DE presented a swimming scenario at TM II 2011 (draft CAR for lauric acid) and proposed to include this scenario in the ESD for PT19 which DE is drafting. DE requested other member states to submit data on natural swimming lakes in order to revise the swimming scenario for inclusion in the draft ESD for PT19.
NL has recently developed a swimming scenario based on data from the more isolated freshwater swimming lakes to which officially the function 'swimming water' is assigned and has recently submitted these data to DE for inclusion in the future PT19 ESD.
Both the DE and NL swimming scenarios are applied in this PAR.

2.8.2.1 PEC_{STP}, $PEC_{surface\ water}$ and $PEC_{sediment}$ – indirect emission

PEC_{STP} and local concentrations in surface water (Clocalwater, or $PEC_{surface\ water}$) were calculated using the ESD for PT1 because there is no corresponding ESD for PT 19 yet.

[3] In a study of simulated treatment processes on spiked raw water samples for drinking water use, the most efficient DEET removal process was ozonation, although high reduction also can be achieved by PAC addition (dose dependent). The simulated treatment processes compared were chemical (Alum coagulation, Ferric coagulation, Softening), PAC treatment and oxidation (chlorination and ozonation). Westerhoff et al. 2005. Fate of endocrine-disruptor, pharmaceutical and personal care product chemicals during simulated drinking water treatment processes. Environ Sci Technol 39: 6649-6663

[4] Environmental Emission Scenarios for biocides used as human hygiene biocidal products (Product type 1). European Commission DG ENV/RIVM. Jan 2004. [TMI 04-env-item4-PT1.doc]

However, 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, the Mosquito Milk DEET products can for exposure modelling purposes be considered as a “leave on” Personal Care Product (PCP) and would thus fit into this scenario.
According to the calculation formula for emission rate to STP (cf table 4.2 in ESD for PT1), Elocalwater (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:
$E_{localwater} = N_{local}*N_{appl}*F_{inh}*F_{water}*Q_{formappl}*C_{formweight}*F_{penetr}*10^{-6}$

If using the input values in table 2.8.1.2-1, $Elocal_{water}$ is 1.08-2.28kg/d for the Mosquito Milk DEET products. These values are used as input for the PT1 scenario in EUSES 2.1.2.

Table 2.8.1.2-1 Input values used to estimate Elocalwater (Emission rate to wastewater) in accordance with ESD for PT 1.

Input parameters (abbrev.)	Explanations	Input value	Remark
N_{local}	Number of inhabitants feeding one STP	10 000	Default according to ESD PT1 and TGD Part II
N_{appl}	Number of applications per day	2	According to the list of intended uses, the product is applied 1-2 times per day. Applying 2 applications per day for the calculation is a worst case assumption since the calculated exposure reflects the use of all inhabitants using the product (and it may be considered less likely that all users would apply the product at the maximum number per day).
F_{inh}	Fraction of inhabitants using product	0.37	According to the final CAR for DEET 37% (F_{inh} = 0.37) of the population is using any insect repellent.
F_{water}	Fraction released to wastewater	0.887	See figure 1
$Q_{formappl}$	Consumption of product per application	6 g	The TNsG on human exposure sets a default value for the amount of dermally applied repellent product to 6 g.
$C_{formweight}$	Amount of active substance in product	98-207 g/kg	i.e. 9.8-20.7% (information submitted by the applicant)
F_{penetr}	Market share of products applied for this purpose	0.28	According to the final CAR for DEET (Default value in ESD for PT 1 is 0.5.)

Table 2.8.2.1-2 summarises the concentrations in STP effllluent as well as the PECs in surface water and sediment.

Table 2.8.2.1–2 PEC_{STP}, $PEC_{surface\ water}$ and $PEC_{sediment}$ for indirect emission to surface water and sediment via the STP due to body cleaning and washing of treated clothes.

Amount of a.s. in product (g/kg)	PEC_{STP} (mg/L)	$PEC_{surface\ water}$ (mg/L)	$PEC_{sediment}$ (mg/kg ww)
98	$6.81x10^{-2}$	$6.81x10^{-3}$	$1.17x10^{-2}$
194	$1.35x10^{-1}$	$1.35x10^{-2}$	$2.33x10^{-2}$
207	$1.44x10^{-1}$	$1.44x10^{-2}$	$2.48x10^{-2}$

2.8.2.2 $PEC_{surface\ water}$ and $PEC_{sediment}$ – direct emission

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

DE swimming scenario

In general the calculation based on the given equations in EU TGD (2003):

- PEClocal_surfacewater according to equation 48, chapter 2.3.8.3, EU TGD (2003);
- PEClocal_sediment according to equation 50, chapter 2.3.8.4, EU TGD (2003),

but some values are substituted depending on the chosen scenario "e.g. swimming".

Germany made a proposal to calculate the local concentrations in water for the swimming emission route. This proposal is based on the equations of the EU TGD (2003) and on a specific scenario developed by Germany that simulates the release of an active substances into natural and artificial lakes by swimming of persons treated with biocidal product. Germany developed this new scenario because the specific use pattern of biocidal products in PT19 wherefore no applicable emission scenario was found in the available ESD's.

- As a worst case assumption the lake is set to 1 million m^3 (1 000 000 000 L). This is seen as representative for a medium quarry pond and for natural and other freshwater lakes for swimming.
- For the worst case estimation the average number of persons, who are swimming at the same day in one lake or pond while using the biological product is set to 20 (Fmainsource = 0.002).
- The fraction of the product which is emitted to the water is set to 1 in the proposed scenario.
- The rate constant for the biodegradability is set according to Table 7 (EU TGD, 2003) to k = 0.047 d^{-1} for surface water. DEET is readily biodegradable therefore formation of metabolites is considered as not relevant.
- The time of swimming during the year is limited by the temperature of the air and the water, therefore it was estimated that swimming will take place for 1 hour a day on 150 days per year as a maximum limit.
- For PEC localwater three situations are calculated: concentration in STP influent (C localinf), local concentration in water (C localwater) after 1 day and annual concentration in water (C localwater_annual) after 150 days.

Calculation steps:

1) Calculation of „Elocalwater" according to equation No. 5 of EU TGD.
As specific data for the use of b.p. are available (e.g. amount of b.p. used per person and application), the daily emission to the lake Elocal, water can be simply estimated by: Number of applications per day x amount of b.p. used per application x mean amount of a.s. in the b.p.

The TNsG on human exposure sets a default value for the amount of dermally applied repellent product to 6 g. According to the list of intended uses, the product is applied 1-2 times per day. Applying 2 applications per day for the calculation is a worst case assumption since the calculated exposure reflects the use of all inhabitants using the product (and it may be considered less likely that all users would apply the product at the maximum number per day).

Elocalwater = 0.02-0.05 kg/d^{-1}

2) Calculation of „C localinf" according to modification of equation No. 32 of EU TGD, where „EFFLUENTstp" is replaced by the volume of the lake Vwaterbody = 1,000,000,000 L/d
C localinf = Elocalwater / Vwaterbody

3) Calculation of „C local$_{water}$“ according to the modified equation no. 7.16 from the OECD emission scenario document for PT 8 (wood preservatives) for the release into a static water body (input of a.s. for 1 day):

$$Clocal_{water} := \frac{Elocal_{water}}{V_{waterbody} \cdot k} \cdot \left[1 - \frac{\left[1 - e^{\left(- T_{1d} \cdot k \right)} \right]}{T_{1d} \cdot k} \right]$$

With k = rate constant for biodegradation in surface water = 0.047 d^{-1}
Vwaterbody = 1,000,000,000 L
T1d = 1 d

4) Calculation of „C local$_{water}$_annual“ according to the modified equation no. 7.16 from the OECD emission scenario document for PT 8 (wood preservatives) for the release into a static water body (continuously input of a.s. for one season):

$$Clocal_{water\_ann} := \frac{Elocal_{water}}{V_{waterbody} \cdot k} \cdot \left[1 - \frac{\left[1 - e^{\left(- T_{emission} \cdot k \right)} \right]}{T_{emission} \cdot k} \right]$$

With k = rate constant for biodegradation in surface water
Vwaterbody = 1,000,000,000 L
Temission = 150 d

Calculation of the PEC in the sediment according to the equation no. 50 of the TGD:

$$PEClocal_{sed} = \frac{K_{susp\text{-}water}}{RHO_{susp}} \cdot PEClocal_{water} \cdot 1000 \qquad (50)$$

Explanation of symbols

$PEClocal_{water}$	concentration in surface water during emission episode	[mg.l^{-1}]	eq. (48)
$K_{susp\text{-}water}$	suspended matter-water partitioning coefficient	[m^3.m^{-3}]	eq. (24)
RHO_{susp}	bulk density of suspended matter	[kg.m^{-3}]	eq. (18)
$PEClocal_{sed}$	predicted environmental concentration in sediment	[mg.kg^{-1}]	

$PEC_{surface\ water}$ used for the risk assessment is selected by comparing the three local concentrations and choosing the highest value calculated $Clocal_{inf}$ or $Clocal_{water}$ or $Clocal_{water\_annual}$ representing the worst-case situation. As the highest values were obtained for $Clocal_{water\_annual}$ these concentrations were used as $PEC_{surface\ water}$ for the risk assessment, see Table 2.8.2.2-1.

Table 2.8.2.2–1 $Clocal_{inf}$, $Clocal_{water}$, $Clocal_{water\_annual}$ for direct emission to surface water due to swimming.

Amount of a.s. in product (g/kg)	$Clocal_{inf}$ (mg/L)	$Clocal_{water}$ (mg/L)	$Clocal_{water\_annual}$ (mg/L)
98	2.35×10^{-5}	1.17×10^{-5}	4.30×10^{-4}
194	4.66×10^{-5}	2.32×10^{-5}	8.50×10^{-4}
207	4.97×10^{-5}	2.47×10^{-5}	9.07×10^{-4}

Table 2.8.2.2-2 summarises the PECs in surface water and sediment for direct emission to surface water and sediment due to swimming based on the German swimming scenario.

Table 2.8.2.2–2 $PEC_{surface\ water}$ and $PEC_{sediment}$ for direct emission to surface water and sediment due to swimming based on the German swimming scenario including biodegradation.

Amount of a.s. in product (g/kg)	$PEC_{surface\ water}$ (mg/L)	$PEC_{sediment}$ (mg/kg ww)
98	$4.30x10^{-4}$	$7.41x10^{-4}$
194	$8.50x10^{-4}$	$1.47x10^{-3}$
207	$9.07x10^{-4}$	$1.56x10^{-3}$

NL swimming scenario

There are 450 official swimming locations in the Netherlands which are owned by one of the 19 regional waterboards and concern the more isolated lakes. There are an additional 220 official swimming locations owned by Rijkswaterstaat (the executive arm of the Dutch Ministry of Infrastructure and the Environment), these locations concern swimming locations along side rivers etcetera.

The swimming lakes from waterboards are included in the data analysis as these concern the more isolated swimming lakes. For each waterboard approx. 5-10 swimming locations have been selected, the total number of swimming lakes selected is 71. Parameters collected are the average and high number of swimmers per day during the period of access (swimming season from 1 May till 30 September) and the volume of the swimming area or of the entire lake. The water depth in the swimming area is estimated to be 1.5 m if not reported and in case a chain with balls borders the swimming area. According to the Dutch ''protocol zwemwaterlocaties in binnenwater'' (protocol swimming locations in inland waters) a swimming area should be delineated at a depth of 1.5 m in case the swimming area is defined.

Deep lakes can be stratified and thus only a certain part of the lake is susceptible to mixing. Information on which water volume of the lake gets mixed is mostly lacking and therefore mixing of the entire water volume of a lake is assumed in the data analysis.

Please be aware that mixing/dilution can have a big impact on the PECs for the water and sediment compartments.

It is assumed that 1% of the swimmers uses a repellent and that the entire amount of a single application applied is washed off daily during swimming. The TNsG on human exposure sets a default value for the amount of dermally applied repellent product to 6 g. As a worst-case it is assumed that the products are applied twice a day.

Using these data the 10 percentile, 90 percentile and average $PEClocal_{water}$ with and without degradation (TWA 30 days) was calculated. For these $PEC\ local_{water}$ the $PEC\ local_{sediment}$ was calculated with the equilibrium partitioning method according to equation no. 50 of the TGD, see Table 2.8.2.2-3.

Table 2.8.2.2–3 90 percentile $PEC_{surface\ water}$ and $PEC_{sediment}$ for direct emission to surface water and sediment from swimming based on 30 days TWA concentrations. Calculations are based on the Dutch swimming scenario.

	90 percentile $PEClocal_{water}$ (TWA 30 days, mg/L)			
Amount of a.s. in product (g/kg)	**High density swimmers in lake**	**High density swimmers in swimming area**	**Average density swimmers in lake**	**Average density swimmers in swimming area**
98	$5.18x10^{-3}$	$4.15x10^{-2}$	$1.74x10^{-3}$	$1.23x10^{-2}$
194	$1.03x10^{-2}$	$8.21x10^{-2}$	$3.44x10^{-3}$	$2.43x10^{-2}$
207	$1.09x10^{-2}$	$8.76x10^{-2}$	$3.67x10^{-3}$	$2.59x10^{-2}$
	90 percentile $PEClocal_{sediment}$ (mg/kg wwt)			
Amount of a.s. in product (g/kg)	**High density swimmers in lake**	**High density swimmers in swimming area**	**Average density swimmers in lake**	**Average density swimmers in swimming area**

98	$8.93x10^{-3}$	$7.15x10^{-2}$	$3.00x10^{-3}$	$2.12x10^{-2}$
194	$1.78x10^{-2}$	$1.42x10^{-1}$	$5.93x10^{-3}$	$4.19x10^{-2}$
207	$1.88x10^{-2}$	$1.51x10^{-1}$	$6.33x10^{-3}$	$4.46x10^{-2}$

2.8.2.3 Exposure monitoring – data published in the open literature

Publications in scientific peer reviewed journals regarding DEET concentrations in the environment were used to compare the calculated values with measured data.
Before making comparisons between measured and modelled data one needs to be aware of the uncertainty associated with measured values, due to temporal and spatial variation. Temporal fluctuations are of special concern when it comes to PEC estimations of DEET; the highest values expected during peak bug season. There may also be geographical variations. These monitoring data should therefore only be regarded as examples of DEET concentrations found in order to evaluate the calculated PEC values, not as substitutes.
The highest surface freshwater concentration found in a study of 56 american streams was 1.1 µg/L, which is 73 times lower than the worst case $Clocal_{water}$ of 0.08 mg/L, see table 2.8.2.2-3.

A few data on DEET in American raw waste water influents (150 and 365 ng/L) have been found in the open literature (Snyder et al. 2006)[5]. These values are at least 1479 times lower than the lowest concentration in influent calculated (0.54 mg/L).
DEET concentrations in Norwegian and German STP effluents (10-60 ng/L and 130 ng/L respectively)[6], are at least 538 times lower than what was estimated through model calculations (0.07 mg/L). The Norwegian data are from an STP without biological treatment whereas the German data are from an STP with biological treatment. The DEET concentrations found in the German influent was 0.21 µg/L, before the biological treatment step, which is more than 2571 times lower than estimated from the calculations.

Table 2.8.2.3-1 Environmental monitoring data for DEET from open peer reviewed scientific literature.

Area information	**Analytical information**	**Concentrations found**	**Reference**
Seawater North Sea Sampling locations mostly coastal	Polymeric sorbent extraction + GC-MS LOQ: 26 pg/L Sampling period: June-July 1998 2x10L samples at 5m depth 15 sampling locations	Highest values 1.09 and 1.06 ng/L respectively [found in the German Bight; (53°40.00'N; 06°25.00'E) and (54°15.00'N; 07°48.00'E)] DEET was detected in all but two samples.	Weigel *et al.* 2002.

[5] Snyder et al, 2006. Role of membranes and activated carbon in the removal of endocrine disruptors and pharmaceuticals. Desalination. In press.

[6] Ref no 8066. Weigel et al. 2004. Determination of selected pharmaceuticals and caffeine in sewage and seawater from Tromsø/Norway with emphasis on ibuprofen and its metabolites. Chemosphere 56: 583-592

Seawater Tromsø Sound (Norway), (into which sewage is discharged)	Glass fibre filtration, sorbent extraction + GC/MS LOQ: 0.20 ng/L Sampling period: 2002 (most samples taken in April, the rest in October) 2.5L samples. 12 sampling locations	Range: 0.4-13 ng/L (STP data: 10 and 60 ng/L in April and October respectively)	Weigel *et al.* 2004. [Ref no. 8066] Chemosphere 56: 583-592
Surface freshwater Las Vegas Wash, a waterway receiving tertiary treated municipal effluent from the city of Las Vegas, NV.	Whole water (incl dissolved and particulate phases) Solid Phase Extraction + LC/MS/MS 1L samples 3 replicates Reporting level: 1.0 ng/L	Average: 40 ng/L	Vanderford *et al.* 2003.
Surface freshwater 56 streams across the USA, some bias to streams downstreams intense urbanization and livestock	Whole water (incl dissolved and particulate phases) Continuous Liquid- Liquid Extraction + GC/MS Sampling period: 2000 Reporting level: 40 ng/L[a] Duplicate composite samples (from 4-6 vertical profiles)	Highest value: 1.1 µg/L (measured at urban site) Median concentration: 0.05 µg/L (all sites) Frequency of detection: 73.2%	Kolpin *et al.* 2002

[a] Reporting level: lowest concentration standard that could be quantitated reliably. Initially set to 0.04 µg/l, and then revised to 0.08 µg/l, but lower contrations reported if GC/MS criteria (retention time and abundance of three characteristic ions in the same ratio as that of standard) were met. Sandstrom et al, 2005.

Compared to monitoring data from STP influents/effluents all estimated values are conservative. Similarly, the estimated values were in the range of, or above the peak maximum measured concentration in fresh surface water.

DEET has been on the Dutch market for > 3 years (authorised since 1986). This period is sufficiently large to consider the market share to be established. Although DEET is observed in both groundwater and surface water in the Netherlands, DEET is not included in the list of substances of concern relevant for surface water at drinking water abstraction points as established by VEWIN/CTGB.
Furthermore, the RIVM did not include this active substance on the recommended list of surface water to be monitored for drinking water from surface water[7] because all measured concentrations in the Rhine and Meuse were below the drinking water limit of 0.1 µg/L.
From the general scientific knowledge collected by the CTGB about the products and their active substance, the CTGB concludes that there are no concrete indications for concern about the consequences of these products for surface water from which drinking water is produced when used in compliance with the directions for use. The standards for surface water destined for the production of drinking water are met.

[7] Bakker, J. Biociden in oppervlaktewater voor drinkwaterproductie, National Institute of Public Health and the Environment, RIVM report 601712007, 2010, Bilthoven, The Netherlands.

2.8.2.4 PEC_{soil} and $PEC_{groundwater}$ – indirect emission

The estimation of the local PECs for the terrestrial compartment includes soil and groundwater:

- PEC_{soil} according to equation 66, chapter 2.3.8.5, EU TGD (2003);
- $PEC_{porewater}$ according to equation 68, chapter 2.3.8.6, EU TGD (2003) as a first worst-case estimation.

The estimation of releases to the soil compartment premises calculation of predicted concentrations of the a.s. in dry sewage sludge as part of a.s. load leaving a STP. Accumulation of the acute substance may occur when sludge is applied over consecutive years for persistent substances. Table 2.8.2.4-1 summarises the concentration in dry sewage sludge C_{sludge} as well as the PECs in soil and porewater.

Table 2.8.2.4–1 Csludge, PEC_{soil} and $PEC_{groundwater}$ for indirect emission to soil and groundwater due to body cleaning and washing of treated clothes.

Amount of a.s. in product (g/kg)	C_{sludge} (mg/kg)	PEC_{soil} (µg/kg ww)	$PEC_{porewater\ grassland}$ (µg/L)	$PEC_{porewater\ agricultural\ soil}$ (µg/L)
98	5.58	5.78	0.77	2.05
194	11.05	11.44	1.52	4.06
207	11.79	12.20	1.62	4.34

The calculated PECs for porewater were addressed further by the RMS as they exceed the drinking water limit for groundwater of 0.1 µg/L. PECgw for the nine FOCUS groundwater scenarios, as developed for plant protection products, were calculated. Model used, input data and assumptions are shown in Table 2.8.2.4-2. The overall assumption being that the only exposure route to groundwater is via the application of sludge from STPs.

Table 2.8.2.4–2 Summary of data used and assumptions made to calculate PECgroundwater 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:	0.028-0.059 kg/ha[a]
Application method:	To the soil surface
Date of application:	1 October annually for 20 years[b]
Molar mass:	191.3 g/mol
Vapour pressure:	0.23 Pa (25°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 SimpleTreat output concentration of DEET in dry sewage sludge of 5.58-11.79 mg/kg (see table 2.8.2.4-1), and application of 5000 kg dry sludge/ha and year to agricultural land (at a single event as suggested in the TGD, Part II 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 PECgw (as FOCUS standard output; 80th percentile annual average PECgw at 1 m depth) are shown in Table 2.8.1.4-3. These results show that the predicted groundwater concentrations of DEET following the intended use of this substance are <0.1 µg/L for all FOCUS scenarios.

Table 2.8.2.4-3 80th precentile 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.

	PECgw, µg/L		
Scenario	**98 g/kg a.s. in product**	**194 g/kg a.s. in product**	**207 g/kg a.s. in product**
Chateaudun	< 0.001	< 0.01	< 0.01
Hamburg	< 0.1	< 0.1	< 0.1
Jokioinen	< 0.001	< 0.01	< 0.01
Kremsmuenster	< 0.01	< 0.1	< 0.1
Okehampton	< 0.1	< 0.1	< 0.1
Piacenza	< 0.1	< 0.1	< 0.1
Porto	< 0.1	< 0.1	< 0.1
Sevilla	< 0.001	< 0.001	< 0.01
Thiva	< 0.001	< 0.01	< 0.01

As agreed at the Technical Meeting I in 2009, the Netherlands submitted available groundwater monitoring data on DEET to the RMS. In addition to a report[8] (in Dutch) presenting the results from screening the presence of 149 pesticides and some biocides in groundwater at 189 locations in the Netherlands in 2007, the results on DEET were also presented in an Excel file. Hence, details with regard to DEET from this monitoring program appear not to be available in the open literature. The monitoring data were collected by two provinces and two drinking water companies from the Southern part of the Netherlands. The majority of the samples were taken during July-December. DEET was the substance that was found above the detection limit (0.01 µg/L) at the highest number of occasions (30%). In 189 samples from 189 groundwater monitoring points 57 samples had a concentration >0.01 ug/L, and out of these three samples (1.6%) were above the drinking water limit, i.e. > 0.1 ug/L (range was 0.36-1.48 µg/L). The report also referred to monitoring data from 2003 during which DEET was found above the detection limit in 5% of the samples, and in no sample concentrations >0.1 µg/L were measured.

In the Netherlands, surplus sludge of public STPs is not applied for fertilization and soil improvement of agricultural soil. Therefore, leaching to groundwater is not expected and thus monitoring data for groundwater are not required for the Dutch authorisation of the Mosquito Milk DEET products.

2.8.2.5 PEC_{Soil} and $PEC_{groundwater}$ – direct emission

In the scenario for the swimming pathway the terrestrial compartment is not exposed and therefore not assessed.

2.8.2.6 PEC_{air}

The active substance DEET is moderately volatile. The vapour pressure is 0.11 Pa at 20°C. A Henry's law constant of 3.93×10^{-3} Pa m^3 mol^{-1} is reported, confirming its relatively low volatility.

AOPWIN model calculation estimates that DEET in the atmosphere reacts with photochemically produced hydroxyl radicals in air, with a half-life of 0.634 days (24 hr day; 0.5×10^6 OH/cm^3). This calculated half life is below the trigger of < 2 days that is used as cut-off value to identify chemicals that could be of potential concern for with the potential for long-range transport through the atmosphere. As the substance unlikely shows significant long-range transport, it is considered of no concern for ozone depletion.

[8] Verhagen, de Coninck, Vervest (2008) Brede screening Bestrijdingsmiddelen Maasstroomgebied 2007. Royal Haskoning, pp 71.

Criteria for the examination of environmental risks to air are not specified in the form of a numerical standard. Therefore, effects on air quality only are taken into account when adverse effects are foreseen. The assessment of potential impacts on air quality, yet, is aimed to minimize the risk for stratospheric ozone depletion. There are no indications that this substance contributes to depletion of the ozone layer and the compounds are furthermore not listed as 'controlled substance' listed in Annex I of Regulation (EC) No 1005/2009 of the European Parliament, the environmental risk to air is considered acceptable.

2.8.2.7 Primary and secondary poisoning of birds and mammals

As the log K_{ow} is < 3 (2.4), a risk for bioconcentration and biomagnification is not expected (conform the biomagnification trigger value proposed for K_{ow} in the TGD).
As DEET is not bioaccumulative and the concentrations in surface water are low, the risk for the primary and secondary poisoning is considered acceptable.

2.8.3 Risk Assessment

The risk characterisation for the environment is the comparison of the toxicity of the substance to the exposure estimates. Both aspects were already discussed in section 2.8.1 and 2.8.2, respectively, and only the relevant values are summarised below.

2.8.3.1 Aquatic compartment (incl. sediment and STP)

The PNEC values for the water compartment and STP microorganisms were calculated from toxicity data by using recommended assessment factors, see section 2.8.1. The PNEC for STP microorganisms is 10 mg/L which is based on and EC_{50} > 1000 mg/L and an assessment factor of 100.
Because only three acute aquatic tests were performed, all on freshwater species, the assessment factor for the freshwater compartment was 1000. For the sediment compartment, there are no toxicity data available. The low Koc value indicates that sorption to sediment is not likely. Nevertheless, a PNEC value of 0.0741 mg/kg ww for sediment has been calculated based on the equilibrium partitioning theory and PNECwater of 0.043 mg/L. As both the PEC and PNEC for sediment are based on equilibrium partioning with the PEC and PNEC for surface water, the risk assessment for the aquatic environment covers the surface water and sediment compartments.

Indirect emission

Even when making worst case assumptions for the local environment, none of the PEC/PNEC ratios exceed 1, see table 2.8.3.1-1.

Table 2.8.3.1–1 PEC/PNEC ratios for indirect emission to the aquatic environment via the STP due to body cleaning and washing of treated clothes.

Amount of a.s. in product (g/kg)	PEC (mg/L)	PNEC (mg/L)	PEC/PNEC
Microorganisms in STP			
98	$6.81x10^{-2}$	10	$6.81x10^{-3}$
194	$1.35x10^{-1}$	10	$1.35x10^{-2}$
207	$1.44x10^{-1}$	10	$1.44x10^{-2}$
Aquatic environment			
98	$6.81x10^{-3}$	0.043	$1.58x10^{-1}$
194	$1.35x10^{-2}$	0.043	$3.14x10^{-1}$
207	$1.44x10^{-2}$	0.043	$3.35x10^{-1}$

Direct emission

In Tables 2.8.3.1-2, 2.8.3.1-3 and 2.8.3.1-4 the PEC/PNEC ratios for direct emission to surface water and sediment due to swimming are indicated, the PECs were calculated using both the swimming scenarios developed by Germany and The Netherlands for the future PT19 ESD.

The PEC/PNEC ratios for both surface water and sediment are < 1 for PECs calculated with the German scenario for Mosquito Milk products containing 98, 194 and 207 g/kg DEET.

Table 2.8.3.1–2 PEC/PNEC ratios for direct emission to the aquatic environment due to swimming based on the German swimming scenario including biodegradation.

Amount of a.s. in product (g/kg)	PEC (mg/L)	PNEC (mg/L)	PEC/PNEC
98	4.30×10^{-4}	0.043	1.00×10^{-2}
194	8.50×10^{-4}	0.043	1.98×10^{-2}
207	9.07×10^{-4}	0.043	2.11×10^{-2}

The PEC/PNEC ratios for both surface water and sediment are > 1 for PECs calculated with the Dutch scenario for the Mosquito Milk products containing 194 and 207 g/kg DEET for a high density of swimmers in the swimming area and < 1 for an average density of swimmers in the swimming area (see Table 2.8.3.1-3).
The presence of a high density number of swimmers in a swimming area will be occassional and the release of DEET into the swimming area can be considered intermittent. Furthermore, the DT50 of DEET is 15 days at 12°C but degradation will be even more rapid at higher water temperatures, not unusual in shallow swimming areas warmed by the sun during the swimming season. During release the PEC/PNEC ratios are thus expected to be above 1 just for a short period of time and therefore the risk to aquatic and sediment organisms is considered acceptable for the Mosquito Milk products containing 98, 194 and 207 g/kg DEET.

Table 2.8.3.1–3 90 percentile (30 d TWA) PEC/PNEC ratios for direct emission to the aquatic environment due to swimming based on the Dutch swimming scenario calculated with a DT50 of 15 days at 12°C.

Scenario	90th percentile PEC (mg/L)	PNEC (mg/L)	PEC/PNEC	Number out of 71 lakes with PEC/PNEC > 1
98 g/kg a.s. in product				
High density swimmers in lake	5.18×10^{-3}	0.043	1.20×10^{-1}	0
High density swimmers in swimming area	4.15×10^{-2}	0.043	9.65×10^{-1}	6
Average density swimmers in lake	1.74×10^{-3}	0.043	4.05×10^{-2}	0
Average density swimmers in swimming area	1.23×10^{-2}	0.043	2.86×10^{-1}	2
194 g/kg a.s. in product				
High density swimmers in lake	1.03×10^{-2}	0.043	2.40×10^{-1}	1
High density swimmers in swimming area	8.21×10^{-2}	0.043	**1.91**	27
Average density swimmers in lake	3.44×10^{-3}	0.043	8.00×10^{-2}	0
Average density swimmers in swimming area	2.43×10^{-2}	0.043	5.65×10^{-1}	3
207 g/kg a.s. in product				
High density swimmers in lake	1.09×10^{-2}	0.043	2.53×10^{-1}	2

High density swimmers in swimming area	$8.76x10^{-2}$	0.043	**2.04**	27
Average density swimmers in lake	$3.67x10^{-3}$	0.043	$8.53x10^{-2}$	0
Average density swimmers in swimming area	$2.59x10^{-2}$	0.043	$6.02x10^{-1}$	3

2.8.3.2 Terrestrial compartment

For the soil compartment, there are no toxicity data available. The low Koc value indicates that sorption to soil is not likely. Nevertheless, PNEC values have been calculated based on equilibrium partitioning theory and PNECwater.

Even when making worst case assumptions for the local environment, none of the PEC/PNEC ratios exceed 1.

Table 2.8.3.2–1 PEC/PNEC ratios for indirect emission to soil due to body cleaning after product use and washing of treated clothes.

Amount of a.s. in product (g/kg)	PEC_{soil} (µg/kg ww)	PNEC (µg/kg ww)	PEC/PNEC
98	5.78	37.9	0.15
194	11.44	37.9	0.30
207	12.20	37.9	0.32

2.8.3.3 Groundwater compartment

In the EUSES modelling the porewater PEC in agricultural soil was above 1 µg/L. This result was further addressed by the RMS by calculating PECgw at 1 m soil depth for nine FOCUS groundwater scenarios in FOCUS PEARL v. 4.4.4 model, assuming that sludge from STP is applied to agricultural soil. The 80th percentile annual average PECgw were below the drinking water limit of 0.1 µg/L for all FOCUS scenarios.

Finally, monitoring data from The Netherlands indicate that DEET may have a potential to leach to groundwater. In 189 samples of groundwater in 2007, DEET was detected at >0.01 µg/L in 57 samples (30%) and in 3 of these samples (1.6%) concentrations were reported as >0.1 µg/L (range 0.36-1.48 µg/L).

2.8.3.4 Atmosphere

Although PEC/PNEC ratios could not be calculated, the physiochemical properties of DEET do not suggest that this substance will pose a significant threat to the atmospheric environment, see section 2.8.2.6.

2.8.3.5 Primary poisoning and secondary poisoning (non compartment specific effects relevant to the food chain)

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 2.8.2.7.

2.9 Measures to protect man, animals and the environment

The instructions for use must contain the following indications:

Mosquito Milk Spray 9.5% DEET:

- Do not breathe spray
- Use only outdoors or in a well-ventilated area
- Do not use on children less than two years old, and restrict the use on children between two and twelve years old.

Mosquito Milk Spray 20% DEET:

- Not for use on children under 13 years
- Do not breathe spray
- Use only outdoors or in a well-ventilated area

Mosquito Roll On 20% DEET:

- Not for use on children under 13 years

Mosquito Milk Lotion 20% DEET:

- Not for use on children under 13 years

Mosquito Milk Stick 20% DEET:

- Not for use on children under 13 years

For the Mosquito Milk DEET products containing 9.8% w/w, 19.4% w/w and 20.7% w/w DEET no unacceptable risks were identified for the environment and no risk mitigation measures are required.

In the assessment report for annex 1 inclusion the following Elements to be taken into account by Member States when authorising Products are defined:

a. Member states may require monitoring methods for analysing residues of DEET in the air compartment might be required for authorisation of DEET containing biocidal products, whose use pattern result in significant exposure to the air compartment.
b. Member states may need to consider inclusion of DEET in national programs for monitoring groundwater.
c. Member states should address any potential for direct exposure to surface water as a consequence of swimming etc, which has not been assessed at the European level.

Ad. a: The opinion of the Ctgb is that is it not needed to design monitoring methods for analysing residues of DEET in the air compartment as the calculated half life of DEET is below the trigger of < 2 days that is used as cut-off value to identify chemicals that could be of potential concern for with the potential for long-range transport through the atmosphere. The substance unlikely shows significant long-range transport, and it is considered of no concern for ozone depletion.

Ad. b: In the Netherlands, surplus sludge of public STPs is not applied for fertilization and soil improvement of agricultural soil. Therefore, emission to soil and groundwater of this type of use is considered as negligible and thus monitoring data for groundwater are not required for the Dutch authorisation of the Mosquito Milk DEET products.

Ad. c: The exposure and risk for surface water due to swimming is assessed in the current assessment report using both the German and Dutch swimming scenarios to be implemented in the future ESD for PT19.

Additionally the Ctgb would like to stress that in order to gain information on the use of repellents by consumers a usage study representative for the different member states in European market needs to be carried out. Furthermore, DEET should be included in national programs for monitoring of surface water.

For the measures to protect humans we refer to the “elements to be taken into account by Member States when authorising products” from the Assessment Report and inclusion directive 2010/51/EC for DEET which shall be duly taken into consideration for a clear labelling of Mosquito Milk DEET products.

3 Proposal for decision

The Dutch CA considers that sufficient information has been provided to verify the outcome and conclusions, and permits the authorisation of Mosquito Milk Spray 9,5% DEET, Mosquito Milk Spray 20% DEET, Mosquito Milk Roll On 20% DEET, Mosquito Milk Lotion 20% DEET and Mosquito Milk Stick 20% DEET.

The Mosquito Milk products have been applied for and evaluated as insect repellents that should be applied to the skin of exposed body parts with the purpose to protect humans from mosquito bites.

Based on the assessment, the Dutch CA concludes that these products can be safely used by non-professional users.

4 Annexes:

1. **Summary of product characteristics: see separate document**
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**
9. **Translated Dutch EXAMPLE label**

Separate document in asset of Mosquito Milk 20% Spray (NL-0003044-0000):

10. **Confidential annex related to major change application of Mosquito Milk 20% Spray product**

Annex 1: Summary of product characteristics

See SPC in asset of each product

Annex 2: List of studies reviewed

List of <u>new data</u>[9] 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
A4.2	01	Miller, C.	2013	DEET: Validation of Methodology for the Determination of Residues in Air Huntingdon Life Sciences Report RQN0001 GLP Unpublished	Vertellus Performance Materials Inc.	☒	☐	☒	☐

List of <u>new data</u> submitted in support of the evaluation of the biocidal products

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
						Yes	No	Yes	No
B3.4	01	Mak, W.A.	2007a	Some physico-chemical properties of “muggenmelk roll-on” Source: TNO Defence, Security and Safety Report no: TNO-DV 2007 C047 GLP: Yes unpublished	Jaico RDP NV	☐	☒	☒	☐

9 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	
	02	Mak, W.A.	2007b	Some physico-chemical properties of “Muggenmelk Stick” Source: TNO Defence, Security and Safety Report no: TNO-DV 2007 C046 GLP: Yes unpublished	Jaico RDP NV	☐	☒	☒	☐
B3.4.1	01	Wenighofer, T.	2011a	“Mosquito Milk Spray 9.5% DEET” Flash Point Source: Seibersdorf Labor GmbH Report no: SL-LT-148/11 GLP: Yes unpublished	Jaico RDP NV	☐	☒	☒	☐
	02	Wenighofer, T.	2011c	“Mosquito Milk Spray 20% DEET” Flash Point Source: Seibersdorf Labor GmbH Report no: SL-LT-151/11 GLP: Yes unpublished	Jaico RDP NV	☐	☒	☒	☐
	03	Wenighofer, T.	2011t	“Mosquito Milk Lotion 20% DEET” Flash Point Source: Seibersdorf Labor GmbH Report no: SL-LT-144/11 GLP: Yes unpublished	Jaico RDP NV	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
B3.4.2	01	Wenighofer, T.	2011b	"Mosquito Milk Spray 9.5% DEET" Auto-Ignition Temperature Source: Seibersdorf Labor GmbH Report no: SL-LT-149/11 GLP: Yes unpublished	Jaico RDP NV	☐	☒	☒	☐
	02	Wenighofer, T.	2011d	"Mosquito Milk Spray 20% DEET" Auto-Ignition Temperature Source: Seibersdorf Labor GmbH Report no: SL-LT-152/11 GLP: Yes unpublished	Jaico RDP NV	☐	☒	☒	☐
	03	Wenighofer, T.	2011u	"Mosquito Milk Lotion 20% DEET" Auto-Ignition Temperature Source: Seibersdorf Labor GmbH Report no: SL-LT-145/11 GLP: Yes unpublished	Jaico RDP NV	☐	☒	☒	☐
B3.6	01	Mak, W.A.	2006a	Some physico-chemical properties of "Muggenmelk Spray" Source: TNO Defence, Security and Safety Report no: TNO-DV2 2006 C040 GLP: Yes Unpublished	Jaico RDP NV	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
	02	Wenighofer, T.	2011e	"Mosquito Milk Spray 20% DEET" Relative Density Source: Seibersdorf Labor GmbH Report no: SL-LT-150/11 GLP: Yes unpublished	Jaico RDP NV	☐	☒	☒	☐
	03	Wenighofer, T.	2011v	"Mosquito Milk Lotion 20% DEET" Relative Density Source: Seibersdorf Labor GmbH Report no: SL-LT-143/11 GLP: Yes unpublished	Jaico RDP NV	☐	☒	☒	☐
B3.7	01	Kohnen, M.	2013a	Stability tests on Mosquito Milk Spray 9.5% DEET Source: Jaico RDP nv Report no: 9 juli 2013 Not to GLP Unpublished	Jaico RDP NV	☐	☒	☒	☐
	02	Wenighofer, T.	2013	Stability tests on Mosquito Milk Spray 20% DEET Source: Jaico RDP nv Report no: 9 juli 2013 Not to GLP Unpublished	Jaico RDP NV	☐	☒	☒	☐
	03	Neve, D. de	2011	Stabiliteitsstudie NG-29 Source: Medgenix Benelux Report no: DOC-QA-23 GLP: Yes unpublished	Jaico RDP NV	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
	04	Kohnen, M.	2013d	Stability tests on Mosquito Milk Roll On 20% DEET Source: Jaico RDP nv Report no: 9 juli 2013 Not to GLP Unpublished	Jaico RDP NV	☐	☒	☒	☐
	05	Kohnen, M.	2013i	Stability tests on Mosquito Milk Lotion 20% DEET Source: Jaico RDP nv Report no: 9 juli 2013 Not to GLP Unpublished	Jaico RDP NV	☐	☒	☒	☐
	06	Kohnen, M.	2013j	Stability tests on Mosquito Milk Stick 20% DEET Source: Jaico RDP nv Report no: 9 juli 2013 Not to GLP Unpublished	Jaico RDP NV	☐	☒	☒	☐
B4.1	01	Trouwers, A.	1995	Identification and Quantification of the active ingredient N,N-diethyl-m-toluamide Source: jaico RDP nv Report no: SOP 10.1/B Not to GLP Unpublished	Jaico RDP NV	☐	☒	☒	☐
B5.10.1	01	Jaico RDP nv	2011	Summary of the Efficacy Trials on Mosquito Milk Spray 9.5% DEET	Jaico RDP NV	☐	☒	☒	☐
	02		2011	Summary of the Efficacy Trials on Mosquito Milk Spray 20% DEET	Jaico RDP NV	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
	03		2011	Summary of the Efficacy Trials on Mosquito Milk Roll On 20% DEET	Jaico RDP NV	☐	☒	☒	☐
	04		2011	Summary of the Efficacy Trials on Mosquito Milk Stick 20% DEET	Jaico RDP NV	☐	☒	☒	☐
	05		2011	Summary of the Efficacy Trials on Mosquito Milk Lotion 20% DEET	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.1	01	Swiss TPH	2011	Laboratory efficacy evaluation of the mosquito repellent Mosquito Milk Spray DEET 9.5% against Culex quinquefasciatus	Jaico RDP NV	☐	☒	☒	☐
	02		2011	Laboratory efficacy evaluation of the mosquito repellent Mosquito Milk Spray DEET 20% against Culex quinquefasciatus	Jaico RDP NV	☐	☒	☒	☐
	03		2011	Laboratory efficacy evaluation of the mosquito repellent Jungle Formula Sensitive Skin against Culex quinquefasciatus	Jaico RDP NV	☐	☒	☒	☐
	04		2011	Laboratory efficacy evaluation of the mosquito repellent Mosquito Milk Roll On DEET 20% against Culex quinquefasciatus	Jaico RDP NV	☐	☒	☒	☐
	05		2011	Laboratory efficacy evaluation of the mosquito repellent Mosquito Milk Roll On DEET 20% against Culex quinquefasciatus	Jaico RDP NV	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
	06		2011	Laboratory efficacy evaluation of the mosquito repellent Mosquito Milk Stick DEET 20% against Culex quinquefasciatus	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.2	01	Swiss TPH	2011	Laboratory efficacy evaluation of the mosquito repellent Mosquito Milk Spray DEET 9.5% against Aedes aegypti	Jaico RDP NV	☐	☒	☒	☐
	02		2011	Laboratory efficacy evaluation of the mosquito repellent Mosquito Milk Roll On DEET 20% against Aedes aegypti	Jaico RDP NV	☐	☒	☒	☐
	03		2011	Laboratory efficacy evaluation of the mosquito repellent Mosquito Milk Stick DEET 20% against Aedes aegypti	Jaico RDP NV	☐	☒	☒	☐
	04		2011	Laboratory efficacy evaluation of the mosquito repellent Mosquito Milk Lotion DEET 20% against Aedes aegypti	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3	01	Jaico RDP nv	2011	Efficacy tests Mosquito Milk @ ITMA Mosquito Milk Spray 9.5 % DEET	Jaico RDP NV	☐	☒	☒	☐
	02		2011	Efficacy tests Mosquito Milk @ ITMA Mosquito Milk Spray 20% DEET	Jaico RDP NV	☐	☒	☒	☐
	03		2011	Efficacy tests Mosquito Milk @ ITMA Mosquito Milk Roll on 20% DEET	Jaico RDP NV	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
	04		2011	Efficacy tests Mosquito Milk @ ITMA Mosquito Milk Stick 20% DEET	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.1	01	ITM Antwerp	1994	Comparative Mosquito Repellent test between two Finnish commercial products and Jaico Mosquito Milk	Jaico RDP NV	☐	☒	☒	☐
	02		2010	Repellents experiment As_20100910 Test Report	Jaico RDP NV	☐	☒	☒	☐
	03		2010	Repellents experiment As_20100803 Test Report	Jaico RDP NV	☐	☒	☒	☐
	04		2005	Repellents experiment As_20051109 Test Report	Jaico RDP NV	☐	☒	☒	☐
	05		1987	Repellent effect of the product “Mosquito Milk (Muggenmelk)” to mosquitoes (preliminary observations)	Jaico RDP NV	☐	☒	☒	☐
	06		1999	Mosquito Repellent Activity	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.10	01	ITM Antwerp	1989	Vergelijking van verschillende repellent produkten	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.12	01	ITM Antwerp	1993	Comparative Mosquito Repellent test between four experimental Jaico Products	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.13	01	ITM Antwerp	1994	Comparative Mosquito Repellent test between two Jaico Products	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.14	01	ITM Antwerp	1994	Comparison between Mosquito Repellent Activities of Formulation T and Mosquito Milk (Jaico)	Jaico RDP NV	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
	02		1994	Comparison between Mosquito Repellent Activities of Formulation T and Mosquito Milk (Jaico)	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.15	01	ITM Antwerp	1994	Mosquito Repellent Activity of Mosquito Milk (Jaico)	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.16	01	ITM Antwerp	1995	Comparative Mosquito Repellent Test between two Portuguese commercial products and Jaico Mosquito Milk	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.17	01	ITM Antwerp	1995	Mosquito Repellent Activity of Mosquito Milk (Jaico)	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.18	01	ITM Antwerp	1995	Comparative Mosquito Repellent Test between one commercial product, two experimental suspensions and Jaico Mosquito Milk	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.19	01	ITM Antwerp	1996	Comparative Mosquito Repellent Test between products “Yellow”, “Green” and Muggenmelk Roller	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.2	01	ITM Antwerp	1994	Comparative Mosquito Repellent test between two Jaico products	Jaico RDP NV	☐	☒	☒	☐
	02		2010	Repellents experiment As_20080226 Test Report	Jaico RDP NV	☐	☒	☒	☐
	03		1987	Comparative repellent effect of the product “Mosquito Milk (Muggenmelk)” and “Mot Mygg” to mosquitoes (preliminary observations)	Jaico RDP NV	☐	☒	☒	☐
	04		2010	Repellents experiment As_20080226 Test Report	Jaico RDP NV	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
B5.10.1.3.20	01	ITM Antwerp	1997	Deugdelijkheid van Jaico Muggenmelk (Roller 50ml)	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.21	01	ITM Antwerp	2002	Report of repellent experiment As_20020813	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.22	01	ITM Antwerp	2002	Report of repellent experiment As_20021015	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.23	01	ITM Antwerp	1997	Repellent effect on local mosquitoes with human subjects	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.24	01	ITM Antwerp	2008	Mission Report Camargue 6-10 October 2008	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.3	01	ITM Antwerp	1994	Comparative Mosquito Repellent test between “Pick Out” and “Jaico Mosquito Milk”	Jaico RDP NV	☐	☒	☒	☐
	02	ITM Antwerp	1988	Comparative repellent effect of the product “Mosquito Milk (Muggenmelk)” and “Sketolene” to mosquitoes (preliminary observations)	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.4	01	ITM Antwerp	1995	Repellent effect of Jaico “Muggenmelk” (spray) against local mosquitoes belonging to Culex sp. On a human volunteer	Jaico RDP NV	☐	☒	☒	☐
	02		1988	Comparative repellent effect of the product “Mosquito Milk (Muggenmelk)” and “Everglades” to mosquitoes (preliminary observations)	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.5	01	ITM Antwerp	2008	Repellents experiment As_20080226 Test Report	Jaico RDP NV	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
	02		1988	Comparative repellent effect of the product “Mosquito Milk (Muggenmelk)” and “Off” to mosquitoes (preliminary observations)	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.6	01	ITM Antwerp	1988	Comparative repellent effect of the product “Mosquito Milk (Muggenmelk)” and “Aerogard” to mosquitoes (preliminary observations)	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.7	01	ITM Antwerp	1988	Comparative repellent effect of the product “Mosquito Milk (Muggenmelk)”, “Tabard Lotion” (origin South Africa) and Bayer product Jasmine (origin Thailand) to mosquitoes (preliminary observations)	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.8	01	ITM Antwerp	1988	Vergelijking van verschillende repellent produkten	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.3.9	01	ITM Antwerp	1988	Essai Comparatif de Répulsif	Jaico RDP NV	☐	☒	☒	☐
B5.10.1.4	01	Jaico RDP nv	2008	The presence of Plant Oils: background.	Jaico RDP NV	☐	☒	☒	☐
	02	Jaico RDP nv	2008	The presence of Plant Oils: background.	Jaico RDP NV	☐	☒	☒	☐
B5.10.2	01	Jaico RDP nv	2011	International Literature Overview Efficacy Trials on Other Insect Species	Jaico RDP NV	☐	☒	☒	☐
B5.10.3	02	Swiss Tropical and Public Health Institute	2012	Laboratory study to assess the repellent activity of Mosquito Milk perfume for use in a skin repellent formulation	Jaico RDP NV	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
B6.1.1	01	Phycher Bio Développement	2011	Evaluation of acute oral toxicity in rats with the test item: Mosquito Milk Spray 9.5% DEET	Jaico RDP NV	☐	☒	☒	☐
	02	Phycher Bio Développement	2011	Evaluation of acute oral toxicity in rats with the test item: Mosquito Milk Lotion 20% DEET	Jaico RDP NV	☐	☒	☒	☐
	03	TNO Nutrition and Food Research	2003	Acute oral toxicity study with Jaico Muggenmelk Stick in rats	Jaico RDP NV	☐	☒	☒	☐
B6.1.2	01	Phycher Bio Développement	2011	Evaluation of acute dermal toxicity in rats with the test item: Mosquito Milk Spray 9.5% DEET	Jaico RDP NV	☐	☒	☒	☐
	02	Phycher Bio Développement	2011	Evaluation of acute dermal toxicity in rats with the test item: Mosquito Milk Lotion 20% DEET	Jaico RDP NV	☐	☒	☒	☐
	03	TNO Nutrition and Food Research	2003	Acute dermal toxicity study with Jaico Muggenmelk Stick in rats	Jaico RDP NV	☐	☒	☒	☐
B6.2.1	01	Phycher Bio Développement	2011	Assessment of acute dermal irritation with the item: Mosquito Milk Spray 9.5% DEET	Jaico RDP NV	☐	☒	☒	☐
	02	Phycher Bio Développement	2016	Assessment of acute dermal irritation with the item: Mosquito milk 20% DEET spray	Omega Pharma nv	☐	☒	☒	☐
	03	Phycher Bio Développement	2011	Assessment of acute dermal irritation with the item: Mosquito Milk Lotion 20% DEET	Jaico RDP NV	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
	04	TNO Nutrition and Food Research	2003	Acute dermal irritation/corrosion study with Jaico Muggenmelk Stick in albino rabbits	Jaico RDP NV	☐	☒	☒	☐
B6.2.2	01	Phycher Bio Développement	2011	Assessment of acute eye irritation with the item: Mosquito Milk Spray 9.5% DEET	Jaico RDP NV	☐	☒	☒	☐
	02	Phycher Bio Développement	2011	Assessment of acute eye irritation with the item: Mosquito Milk Lotion 20% DEET	Jaico RDP NV	☐	☒	☒	☐
	03	TNO Nutrition and Food Research	2003	Acute eye irritation/corrosion study with Jaico Muggenmelk Stick in albino rabbits	Jaico RDP NV	☐	☒	☒	☐

Annex 3: Analytical methods residues – active substance

DEET

The analytical methods for residues are taken from the CA report to support the inclusion of DEET in annex I of Directive 98/8/EC. Where relevant, some additional remarks/information are given in italics.

Analytical methods for residues

Soil (principle of method and LOQ)	DEET: LC-MS/MS with 1 transition (LOQ: 0.01 mg/kg)
Air (principle of method and LOQ)	*DEET: LC-MS/MS (LOQ 0.225µg/m^3)**
Water (principle of method and LOQ)	DEET: LC-MS/MS (LOQ: 0.1 µg/L in surface water)
Body fluids and tissues (principle of method and LOQ)	DEET in blood plasma: HPLC-UV (LOQ 49.4µg/L) No confirmatory method is provided. No further data is required as DEET is not classified as toxic or highly toxic.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Not required as the use pattern of DEET will not result in any contact with food or feeding stuffs.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Not required as the use pattern of DEET will not result in any contact with food or feeding stuffs.

** new data; see paragraph 2.3.2*

Annex 4: Toxicology and metabolism –active substance

DEET

Threshold Limits and other Values for Human Health Risk Assessment

Summary			
	Value	Study	SF
AEL repeated dermal (general public)	8.2 mg/kg bw/day*	8-week study (dogs, oral capsule)	100
AEL acute oral (general public)	0.75 mg/kg bw/day	90 day study (rat dermal)	100
*Corrected for a dermal absorption of approximately 82 % in the rat			

Inhalative absorption	No data
Oral absorption	>80% based on urinary, faecal and tissue content (in the rat). In rats, 85-91% of administered radioactivity was found in urine.
Dermal absorption	Dermal rat approx. 82% (based on urinary excretion, faeces content, tissue content and skin). Humans: <20% based on urinary excretion, faecal and skin content, corrected for recovery). No information was provided on inhalational absorption.

Classification	
with regard to toxicological data (according to the criteria in Dir. 67/548/EEC)	Class of danger: Xn R phrases: 22 - 36/38
with regard to toxicological data (according to the criteria in Reg. 1272/2008)	Pictogram: GHS07 Signal word: Warning Acute Tox. 4, H302; Eye Irrit. 2, H319; Skin Irrit. 2, H315.

Annex 5: Toxicology – biocidal product

Mosquito Milk Spray 9,5% DEET:

General information

Formulation Type	Spray
Active substance(s) (incl. content)	DEET (9.8%)
Category	PT19

Acute toxicity, irritancy and skin sensitisation of the preparation (Annex IIIB, point 6.1, 6.2, 6.3)	
Rat LD50 oral (OECD 423)	> 2000 mg/kg bw
Rat LD50 dermal (OECD 402)	> 2000 mg/kg bw
Rat LC50 inhalation (OECD 403)	No study was submitted
Skin irritation (OECD 404)	Not irritating
Eye irritation (OECD 405)	Irritating (R36) Causes serious eye irritation (H319)
Skin sensitisation (OECD 429; LLNA)	No study was submitted

Classification and labelling proposed for the preparation with regard to toxicological properties (Annex IIIB, point 9)	
Directive 1999/45/EC	Xi Irritant R10, R36, R52/53 S2, S23, S46, S51 DPD11
Regulation 1272/2008/EC	GHS02, GSH07 Warning H226, H319 P102, P210, P260, P270, P271, P305+351+338 EUH208

Mosquito Milk Spray 20% DEET:

General information

Formulation Type	spray
Active substance(s) (incl. content)	DEET (19.4%)
Category	PT19

Acute toxicity, irritancy and skin sensitisation of the preparation (Annex IIIB, point 6.1, 6.2, 6.3)	
Rat LD50 oral (OECD 423)	No study was submitted
Rat LD50 dermal (OECD 402)	No study was submitted
Rat LC50 inhalation (OECD 403)	No study was submitted
Skin irritation (OECD 404)	Not irritating
Eye irritation (OECD 405)	No study was submitted
Skin sensitisation (OECD 429; LLNA)	No study was submitted

Classification and labelling proposed for the preparation with regard to toxicological properties (Annex IIIB, point 9)	
Directive 1999/45/EC	Xi Irritant R10, R36, R52/53 S2, S23, S26, S39, S46, S51 DPD11

Regulation 1272/2008/EC	GHS02, GHS07 Warning H226, H319 P102, P210, P260, P270, P271, P305+P351+P338+P310 EUH208 (contains citronellal. May produce an allergic reaction

Mosquito Milk Roll On 20% DEET:

General information

Formulation Type	Liquid with a roll-on applicator
Active substance(s) (incl. content)	DEET (20.7%)
Category	PT19

Acute toxicity, irritancy and skin sensitisation of the preparation (Annex IIIB, point 6.1, 6.2, 6.3)	
Rat LD50 oral (OECD 423)	> 2000 mg/kg bw
Rat LD50 dermal (OECD 402)	> 2000 mg/kg bw
Rat LC50 inhalation (OECD 403)	No study was submitted
Skin irritation (OECD 404)	Not irritating
Eye irritation (OECD 405)	Risk of serious damage to eyes (R41) Causes serious eye damage (H318)
Skin sensitisation (OECD 429; LLNA)	No study was submitted

Classification and labelling proposed for the preparation with regard to toxicological properties (Annex IIIB, point 9)	
Directive 1999/45/EC	Xi Irritant R10, 41, R52/53 S2, S26, S39, S46
Regulation 1272/2008/EC	GHS02, GHS05 Danger H226, H318 P101, P102, P210, P270, P305+351+338+310.

Mosquito Milk Lotion 20% DEET:

General information

Formulation Type	liquid
Active substance(s) (incl. content)	DEET (19.4%)
Category	PT19

Acute toxicity, irritancy and skin sensitisation of the preparation (Annex IIIB, point 6.1, 6.2, 6.3)	
Rat LD50 oral (OECD 423)	> 2000 mg/kg bw
Rat LD50 dermal (OECD 402)	> 2000 mg/kg bw
Rat LC50 inhalation (OECD 403)	No study was submitted
Skin irritation (OECD 404)	Not irritating
Eye irritation (OECD 405)	Risk of serious damage to eyes (R41) Causes serious eye damage (H318)
Skin sensitisation (OECD 429; LLNA)	No study was submitted

Classification and labelling proposed for the preparation with regard to toxicological properties

(Annex IIIB, point 9)	
Directive 1999/45/EC	Xi Irritant R10, R41, R52/53 S2, S26, S39, S46 DPD11
Regulation 1272/2008/EC	GHS02, GHS05 Danger H226, H318 P101, P102, P210, P270, P305+P351+P338+P310 EUH208

Mosquito Milk Stick 20% DEET:

General information

Formulation Type	stick
Active substance(s) (incl. content)	DEET (19.4%)
Category	PT19

Acute toxicity, irritancy and skin sensitisation of the preparation (Annex IIIB, point 6.1, 6.2, 6.3)	
Rat LD50 oral (OECD 423)	> 2000 mg/kg bw
Rat LD50 dermal (OECD 402)	> 2000 mg/kg bw
Rat LC50 inhalation (OECD 403)	No study was submitted
Skin irritation (OECD 404)	Not irritating
Eye irritation (OECD 405)	Not irritating
Skin sensitisation (OECD 429; LLNA)	No study was submitted

Classification and labelling proposed for the preparation with regard to toxicological properties (Annex IIIB, point 9)	
Directive 1999/45/EC	R52/53
Regulation 1272/2008/EC	P102, P103

Annex 6: Safety for professional operators

Products are not intended for professonal use.

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

General information	
Formulation Type	Spray (9.8% and 19.4%), liquid with a roll on applicator (20.7%), lotion (19.4%), stick (19.4%)
Active substance(s) (incl. content)	DEET 9.8%, 19.4% and 20%
Category	PT19
Data base for exposure estimation	
according to	Appendix: Toxicology and metabolism – active substance/CAR

Exposure scenarios for intended uses (Annex IIIB, point 6.6)	
Primary exposure	Non-professional users (consumers; adults and children)
Secondary exposure, acute	Not relevant
Secondary exposure, chronic	Not relevant

The internal dermal exposure is calculated according to the following formula:

Internal dermal dose a.s. = (Number of applications) × (amount of product (75th percentile based on survey data)) × (content a.s.) × (% dermal absorption) / body weight

The internal oral exposure is calculated based on the following formula:

Internal oral dose a.s. = (Number of applications) × (Amount of product (75th percentile based on survey data)) × (content a.s.) × (% ingested amount) / body weight

The number of applications is considered to be two (first tier) or one (second tier) per day. For dermal absorption the value of 20% is used for DEET based on the CAR. Oral absorption is considered to be 100% as a worst-case approach. The % of the ingested amount is considered to be 4% for adults (product on fingers) and 8% for children (product on hands).

Primary exposure for two applications for adults and children:

Internal exposure for two applications	**9.8% DEET**	**19.4% DEET**	**20.7% DEET**
Dermal* (mg/kg bw/day)			
Male (0.329 mg/kg bw/day per 1% DEET)	3.22	6.38	6.81
Female (0.255 mg/kg bw/day per 1%)	2.50	4.95	5.28
>12 yr (0.405 mg/kg bw/day per 1%)	3.97	7.86	8.38
<12 yr: (0.853 mg/kg bw/day per 1%)	8.36	16.55	17.66
Oral (mg/kg/bw/day)**			
Male (0.066 mg/kg bw/day per 1% DEET)	0.65	1.28	1.37
Female (0.051 mg/kg bw/day per 1%)	0.50	0.99	1.06
>12 yr (0.162 mg/kg bw/day per 1%)	1.59	3.14	3.35
<12 yr (0.341 mg/kg bw/day per 1%)	3.34	6.62	7.06

**Based on the 75th percentile of human use rate (Boomsma and Parthasarathy, 1990) and considering two applications per day corrected for a conservative dermal absorption of 20% in humans and body weights of 70 kg for male adult, 60 kg for female aduls, 62.8 kg for*

children >12 years old and 25.5 kg for children < 12 years old. For clarity, in the first column the exposure values per 1% DEET based on theresults of the user survey study are given.
*** Internal oral exposure is calculated by considering adults ingesting 4% of the external dermal dose (product on fingers) and children ingesting 8% of the external dermal dose (product on hands). Oral exposure is considered to be 100% as a worst-case approach. For clarity, in the first column the exposure values per 1% DEET based on the results of the user survey study are given.*

Risk characterisation ratio per two applications for adults and children (internal exposure)

Risk Characterisation Ratio*	**9.8% DEET**	**19.4% DEET**	**20.7% DEET**
Dermal			
Male:	0.39	0.78	0.83
Female:	0.30	0.60	0.64
>12 yr:	0.48	0.96	1.02
<12 yr:	1.02	2.38	2.15
Oral			
Male:	0.87	1.71	1.83
Female:	0.67	1.32	1.41
>12 yr:	2.12	4.19	4.47
<12 yr:	4.45	8.83	9.41

** Based on the 75th percentile of human use rate (Boomsma and Parthasarathy, 1990) and considering two applications per day corrected for a conservative dermal absorption of 20% in humans and body weights of 70 kg for male adult, 60 kg for female aduls, 62.8 kg for children >12 years old and 25.5 kg for children < 12 years old. The $AEL_{repeated\ dermal}$ of 8.2 mg/kg bw/da is used for the calculation of the RCR after dermal exposure. The $AEL_{acute\ oral}$ of 0.75 mg/kg bw/day is used for the calculation of the RCR after oral exposure.*

Primary exposure for one application for adults and children:

Internal exposure for one application	**9.8% DEET**	**19.4% DEET**	**20.7% DEET**
Dermal* (mg/kg bw/day)			
Male (0.164 mg/kg bw/day per 1% DEET)	1.61	3.18	3.39
Female (0.128 mg/kg bw/day per 1%)	1.25	2.48	2.65
>12 yr (0.203 mg/kg bw/day per 1%)	1.99	3.94	4.20
<12 yr: (0.427 mg/kg bw/day per 1%)	4.18	8.28	8.84
Oral (mg/kg/bw/day)**			
Male (0.033 mg/kg bw/day per 1% DEET)	0.32	0.64	0.68
Female (0.026 mg/kg bw/day per 1%)	0.25	0.50	0.54
>12 yr (0.081 mg/kg bw/day per 1%)	0.79	1.57	1.68
<12 yr (0.171 mg/kg bw/day per 1%)	1.68	3.32	3.54

**Based on the 75th percentile of human use rate (Boomsma and Parthasarathy, 1990) and considering one applications per day corrected for a conservative dermal absorption of 20% in humans and body weights of 70 kg for male adult, 60 kg for female aduls, 62.8 kg for children >12 years old and 25.5 kg for children < 12 years old. For clarity, in the first column the exposure values per 1% DEET based on the results of the user survey study are given.*

*** Internal oral exposure is calculated by considering adults ingesting 4% of the external dermal dose (product on fingers) and children ingesting 8% of the external dermal dose (product on hands). Oral exposure is considered to be 100% as a worst-case approach. For clarity, in the first column the exposure values per 1% DEET based on the results of the user survey study are given.*

Risk characterisation ratio per application for adults and children (internal exposure)

Risk Characterisation Ratio*	**9.8% DEET**	**19.4% DEET**	**20.7% DEET**
Dermal			
Male:	0.20	0.39	0.41
Female:	0.15	0.30	0.32
>12 yr:	0.24	0.48	0.51
<12 yr:	0.51	1.01	1.08
Oral			
Male:	0.43	0.85	0.91
Female:	0.33	0.67	0.72
>12 yr:	1.05	2.09	2.24
<12 yr:	2.24	4.43	4.72

** Based on the 75th percentile of human use rate (Boomsma and Parthasarathy, 1990) and considerin gone application per day corrected for a conservative dermal absorption of 20% in humans and body weights of 70 kg for male adult, 60 kg for female aduls, 62.8 kg for children >12 years old and 25.5 kg for children < 12 years old. The $AEL_{repeated\ dermal}$ of 8.2 mg/kg bw/da is used for the calculation of the RCR after dermal exposure. The $AEL_{acute\ oral}$ of 0.75 mg/kg bw/day is used for the calculation of the RCR after oral exposure.*

Reverse reference scenario for one application per day for adults and children*

	External dermal exposure per application (mg/kg bw/day)	**Internal dermal exposure per application (mg/kg bw/day)**	**$AEL_{acute\ oral}$/External dermal exposure**	**$AEL_{repeated\ dermal}$/ Internal dermal exposure**
9.8% DEET				
Male:	8.05	1.61	0.093	5.09
Female:	6.25	1.25	0.12	6.56
>12 yr:	9.95	1.99	0.075	4.12
<12 yr:	20.9	4.18	0.036	1.96
19.4% DEET				
Male:	15.9	3.18	0.047	2.58
Female:	12.4	2.48	0.060	3.31
>12 yr:	19.7	3.94	0.038	2.08
<12 yr:	41.4	8.28	0.018	0.99
20.7% DEET				
Male:	19.85	3.39	0.038	2.42
Female:	13.25	2.65	0.057	3.09
>12 yr:	21	4.20	0.036	1.95

<12 yr:	44.2	8.84	0.017	0.93

**Based on the 75th percentile of human use rate (Boomsma and Parthasarathy, 1990) and considering one application per day corrected for a conservative dermal absorption of 20% in humans and body weights of 70 kg for male adult, 60 kg for female aduls, 62.8 kg for children >12 years old and 25.5 kg for children < 12 years old. The internal dermal exposure is compared with the $AEL_{repeated\ dermal}$ of 8.2 mg/kg bw/day. To estimate how much DEET applied to the skin can be ingested without exceeding the $AEL_{acute\ oral}$, the external dermal exposure is compared with the $AEL_{acute\ oral}$ of 0.75 mg/kg bw/day (considering 100% oral absorption this value also represents internal oral exposure).*

Conclusion:
Exposure of non-professionals and the general public to the biocidal products containing 9.4%, 19.4% and 20.7% DEET as active substance is considered acceptable, if the biocidal product is used as intended and all safety advices are followed.

Annex 8: 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.

Annex 9: Translated Dutch EXAMPLE label

The text below refers to the label that was used in the Netherlands for authorisations granted under transitional law and under the BPD. Over time, these have been replaced by product specific SPCs, which can be found in the asset of each product in R4BP.

As additional information on the intended use the translated Dutch legal instructions and directions for use are presented below.

A.
LEGAL INSTRUCTIONS FOR USE

This product can only be used to repel mosquitoes to protect people.

The use frequency and use instructions as stated in the directions for use (B) should be sustained.

This product is intended for non-professional use only.

B.
DIRECTIONS FOR USE

This product provides on average 6* hours of protection against the most common mosquito species in the Netherlands. For some tropical mosquito species the protection time can be much shorter: on average 2* hours against the yellow fever mosquito and 5* hours against the malaria mosquito.
Factors such as temperature, humidity and transpiration can influence the efficacy.

Apply softly and evenly over the bare skin that needs protection.
For use on the face apply the product first on the hand and than use the hand to apply it to the face.
Avoid contact with eyes, mucous membranes and damaged skin.
Avoid contact with food, plastics and lacquered surfaces.
Use only outdoors or in a well-ventilated area and do not inhale the product..

- Do not use more than once/twice** a day. Do not use on children younger than 2 years**. For children up to 12 years limit the use to once a day**. Not for use on children under 13 years **. Do not use on children (< 18 years old)**.

Re-apply, when allowed, after swimming, showering or when the effect diminishes.

Keep this product away from children.
Keep the product dry and do not place it in direct sunlight.
Close the bottle well.

Do not reuse the packaging and do not dump the product into the environment.

* this is an example, the protection hours differ per product, see table 2.5.3.0.
** this depends on the product, see table 1.5.2 Intended use: use restrictions.