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

PRODUCT ASSESSMENT REPORT OF A BIOCIDAL PRODUCT FOR NATIONAL AUTHORISATION APPLICATIONS

Insect Repellent Lotion IR3535® 10%

Product type 19

Ethyl butylacetylaminopropionate
(Further referred to as IR3535®)

Case Number in R4BP: BC-QE019739-30

Evaluating Competent Authority: Belgium

Date: 4/11/2019

TABLE OF CONTENTS

1 CONCLUSION

Insect Repellent Lotion IR3535® 10% can be authorised according to Art. 19(1) of Regulation (EU) No 528/2012 as a ready-to-use repellent (PT19) to be used against mosquitoes and ticks in temperate areas and should only be applied on uncovered parts of the face, hands, arms, legs and feet.

The assessment of the endocrine disrupting (ED) properties of the substances used in the biocidal product Insect Repellent Lotion IR3535® 10% was performed according to the Regulation (EU) 528-2012 and Regulation (EU) 2017-2100. Based on the existing knowledge and the data provided by the applicant, there is no indication of concern regarding the ED properties of the substances used in the biocidal product Insect Repellent Lotion IR3535® 10%.

Remark:

- This product is not authorised for use in tropical conditions, due to lack of efficacy studies.

2 ASSESSMENT REPORT

2.1 SUMMARY OF THE PRODUCT ASSESSMENT

2.1.1 Administrative information

2.1.1.1 Identifier of the product

Identifier	**Country (if relevant)**
Insect Repellent Lotion IR3535® 10%	Belgium

2.1.1.2 Authorisation holder

Name and address of the authorisation holder	**Name**	Merck KGaA
	Address	Frankfurter Straße 250 64293 Darmstadt Germany
Authorisation number	BE2019-0057	
Date of the authorisation	4/11/2019	
Expiry date of the authorisation	4/11/2029	

2.1.1.3 Manufacturer(s) of the products of the family

Name of manufacturer	Merck KGaA
Address of manufacturer	Frankfurter Straße 250 64293 Darmstadt Germany
Location of manufacturing sites	Frankfurter Straße 250 64293 Darmstadt Germany

2.1.1.4 Manufacturer(s) of the active substance(s)

Active substance	Ethyl butylacetylaminopropionate
Name of manufacturer	Merck S.L.U.
Address of manufacturer	Calle Maria de Molina 40 28006 Madrid Spain
Location of manufacturing sites	Poligono Merck 08100 Mollet de Vallés Barcelona Spain
Name of manufacturer	Merck KGaA
Address of manufacturer	Frankfurter Straße 250 64293 Darmstadt Germany
Location of manufacturing sites	Poligono Merck 08100 Mollet de Vallés Barcelona Spain

2.1.2 Product composition and formulation

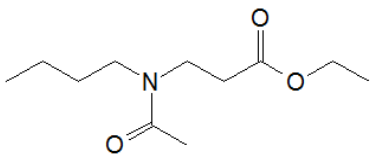
NB: the full composition of the product according to Annex III Title 1 should be provided in the confidential annex.

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

Yes ☐

No ☒

2.1.2.1 Identity of the active substance

Main constituent(s)	
ISO name	IR3535
IUPAC or EC name	ethyl 3-[N-acetyl-N-butyl] aminopropionate
EC number	257-835-0
CAS number	52304-36-6
Index number in Annex VI of CLP	
Minimum purity / content	> 99 % w/w
Structural formula	

2.1.2.2 Candidate(s) for substitution

The active substance IR3535® is not a candidate for substitution.

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

Common name	IUPAC name	Function	CAS number	EC number	Content (%)
IR3535®	ethyl 3-[N-acetyl-N-butyl] aminopropionate	Active substance	52304-36-6	257-835-0	10 % (technical) ≥9.9% (pure) purity: ≥99%

Full composition is available in the confidential annex.

2.1.2.4 Information on technical equivalence

Not needed, since the manufacturer is the same as included in the Union list of approved active substances.

2.1.2.5 Information on the substance(s) of concern

According to the Guidance on BPR: Volume II Parts B+C, a substance corresponding to the following condition has to be considered as substance of concern: Active substances, other than those included in Annex I of the BPR, for which a draft final Competent Authority Report (CAR) (with agreed reference values) is available (including draft final CARs for Product Types other than the one of the actual biocidal product under evaluation). This

criterion identifies other active substances in the biocidal product that act as co-formulants (e.g. in-can preservatives). It is noted that active substances (acting as co-formulants in a product) should be regarded as SoCs because, due to their intrinsic biological activity, they are likely to possess toxicological activity. It is also noted that as many active substances do not hold harmonised classifications under the CLP Regulation, they may fail to be identified as SoCs by the first two indents of Art 3(f) of the BPR. These substances should be considered SoCs if they are present in the biocidal product at a concentration ≥ 0.1%.

Regarding the environment, Citric Acid is registered as active substance in the Review programme for PT 2. It is not included in the Annex I of the BPR and, as such, must thus be considered as a substance of concern.

However Citric Acid has no environmental classification.

Regarding environment, the substances considered due to their classification or because they are registered as active substance showed no risk and were not considered to be of concern.

For more information, please refer to the Confidential Annex.

2.1.2.6 Type of formulation

EW Emulsion, oil in water (RTU)

2.1.3 Hazard and precautionary statements

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

Classification	
Hazard category	None
Hazard statement	None
Labelling	
Signal words	None
Hazard statements	None
Precautionary statements	P102 Keep out of reach of children P103 Read label before use
Note	

2.1.4 Authorised use(s)

2.1.4.1 Use description

Table 1. Use # 1 – Application to human skin to repel mosquitoes (general public)	
Product Type	PT19 – Repellents and attractants (Pest control)
Where relevant, an exact description of the authorised use	Repellent
Target organism (including development stage)	**Scientific name** **Common name** Culicidae Mosquitoes - *Culex*, *Aedes* and *Anopheles* spp. Adults only in temperate areas
Field of use	Indoors (only in well ventilated area) and outdoors Insect repellent lotion IR3535® 10% is a ready-to-use insect repellent used to protect humans against mosquitoes in temperate areas only.
Application method(s)	manual application
Application rate(s) and frequency	Application rate for mosquitoes (1.16 µl/cm²) – protection time 8 hours : o Adult : 10.58 ml / application on uncovered body parts*. Apply sparingly to uniformly cover uncovered parts of the face, hands, arms, legs and feet. The product can be reapplied 2 times maximum per day. o Child (6-12y) : 5.87 ml / application on uncovered body parts*. Maximum one application per day. o Child (2-6y) : 4.33 ml / application on uncovered body parts*. Maximum one application per day. o Toddler (1-2y) : 3.06 ml / application on uncovered body parts*. Maximum one application per day. o Infant (0-1y) : 2.61 ml / application on uncovered body parts*. Maximum one application per day. * The product can be applied on uncovered parts of the body, limited to the face, arms, legs and feet. Do not apply on the whole body.
Category(ies) of users	General public (non-professional)
Pack sizes and packaging material	**Types and Materials** • Squeeze tube - with snap cap, screw cap, top cap or flip top cap (PP) - (PE; HDPE; LDPE; PP; HDPE/LDPE ; HDPE/EVOH; HDPE/F; HDPE/PA ; LDPE/EVOH ; LDPE/F ; LDPE/PA) • Squeeze tube - with snap cap, screw cap, top cap or flip top cap (PP) - (in aluminium with inner layer of: PE; HDPE; LDPE; PP; HDPE/LDPE ; HDPE/EVOH; HDPE/F; HDPE/PA ; LDPE/EVOH ; LDPE/F ; LDPE/PA) • Bottle - with screw cap, top cap or pump dispenser- (PE; HDPE; LDPE; PP; HDPE/LDPE ; HDPE/EVOH; HDPE/F; HDPE/PA ; LDPE/EVOH ; LDPE/F ; LDPE/PA) For all packaging types, size: 25-250 mL in steps of 5 ml

2.1.4.2 Use-specific instructions for use

See 2.1.5.1

2.1.4.3 Use-specific risk mitigation measures

See 2.1.5.2

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

See 2.1.5.3

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

See 2.1.5.4

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

See 2.1.5.5

2.1.4.7 Use description

Table 2. Use # 2 – Application to human skin to repel ticks (general public)	
Product Type	PT19 – Repellents and attractants (Pest control)
Where relevant, an exact description of the authorised use	Repellent
Target organism (including development stage)	**Scientific name** / **Common name** Ixodidae / Ticks – *I. ricinus* and *I. scapularis* nymphs and adults only in temperate areas
Field of use	Indoors (only in well ventilated area) and outdoors Insect repellent lotion IR3535® 10% is a ready-to-use insect repellent used to protect humans against ticks in temperate areas only.
Application method(s)	manual application
Application rate(s) and frequency	Application rate for ticks (1.01 µl/cm^2) – protection time 7 hours : ○ Adult : 9.20 ml / application on uncovered body parts*. The product can be reapplied 2 times maximum per day. ○ Child (6-12y) : 5.10 ml / application on uncovered body parts*. Maximum one application per day. ○ Child (2-6y) : 3.77 ml / application on uncovered body parts*. Maximum one application per day. ○ Toddler (1-2y) : 2.66 ml / application on uncovered body parts*. Maximum one application per day. ○ Infant (0-1y) : 2.27 ml / application on uncovered body parts*. Maximum one application per day. * The product can be applied on uncovered parts of the body, limited to the face, arms, legs and feet. Do not apply on the whole body.
Category(ies) of users	General public (non-professional)
Pack sizes and packaging material	**Types and Materials**

	• Squeeze tube - with snap cap, screw cap, top cap or flip top cap (PP) - (PE; HDPE; LDPE; PP; HDPE/LDPE ; HDPE/EVOH; HDPE/F; HDPE/PA ; LDPE/EVOH ; LDPE/F ; LDPE/PA) • Squeeze tube - with snap cap, screw cap, top cap or flip top cap (PP) - (in aluminium with inner layer of: PE; HDPE; LDPE; PP; HDPE/LDPE ; HDPE/EVOH; HDPE/F; HDPE/PA ; LDPE/EVOH ; LDPE/F ; LDPE/PA) • Bottle - with screw cap, top cap or pump dispenser- (PE; HDPE; LDPE; PP; HDPE/LDPE ; HDPE/EVOH; HDPE/F; HDPE/PA ; LDPE/EVOH ; LDPE/F ; LDPE/PA) For all packaging types, size: 25-250 mL in steps of 5 ml

2.1.4.8 Use-specific instructions for use

See 2.1.5.1

2.1.4.9 Use-specific risk mitigation measures

See 2.1.5.2

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

See 2.1.5.3

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

See 2.1.5.4

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

See 2.1.5.5

2.1.5 General directions for use

2.1.5.1 Instructions for use

Use repellent safely. Always read the label or leaflet before use and follow all the instructions provided.

Keep out of reach of children.

Place a right amount of lotion on the palm of the hand and distribute the lotion over the exposed skin. ONLY apply to uncovered parts of the body, limited to the face, arms, legs and feet. Do not apply on the whole body.

Make sure to protect the eyes. Do not apply to eye area.

Do not apply over cuts, wounds, freshly shaven or irritated skin. Do not use under clothing. Only for external use.

Applying sun care products or cosmetic formulations after repellent use will alter the efficacy of the repellent considerably. In case of a concomitant use of the product with sunscreen, first apply the sunscreen and wait 20 minutes before the application of the product.

In case of strong perspiration and after having taken a swim, the effectiveness will diminish. The product can be applied once a day for children under 12 years old and twice a day for adult and children above 12 years old.

Caution must be taken when using these products on infants and mechanical protection (clothing, mosquito nets) is to be preferred.

Avoid contact with synthetic materials. Synthetic materials should be protected during application.

The users should inform if the treatment is ineffective and report straightforward to the registration holder.

The use of the product with other repellent products is not recommended.

The protection time of 8 hours is only indicative. Environmental factors (e.g. high temperature, wind velocity) can modify it.

2.1.5.2 Risk mitigation measures

ONLY apply to uncovered parts of the body, limited to the face, arms, legs and feet.

Do not use on children's hands. An adult should apply the product to children below 12 years of age and wash his hands after application.

Wash hands before handling food. Do not apply directly on or near food, feed or drinks, or on surfaces or utensils likely to be in direct contact with food, feed, drinks. To prevent contamination of food, avoid contact of treated skin with food.

Only apply outdoor or in well ventilated area.

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

In case of inhalation: bring to fresh air.

In case of eye contact: check for and remove any contact lenses if easy to do. Rinse out with plenty of water. Call in ophthalmologist.

In case of skin contact: in case of skin lesions, redness or persistent pain after application, consult a doctor.

In case of swallowing: immediately make victim drink water (two glasses at most). Consult a physician.

Most important symptoms and effects, acute or delayed: no description of any toxic symptoms

Indication of any immediate medical attention and special treatment needed: No information available

Environmental precautions: Do not discharge superfluous fluids to the drain.

2.1.5.4 Instructions for safe disposal of the product and its packaging

Waste material must be disposed of in accordance with the Directive on waste 2008/98/EC as well as other national and local regulations. Leave chemicals in original containers. No mixing with other waste. Handle uncleaned containers like the product itself.

Do not discharge superfluous fluids to the drain.

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

Storage conditions: Keep container tightly closed in a dry and well-ventilated place.

Recommended storage temperature: Room temperature (18-25°C). The product should not be stored for a prolonged period at temperatures >40°C.

Shelf-life: 18 months

Environmental exposure controls: Do not let product enter drains.

2.1.6 Other information

The authorisation holder must provide the eCA with a new long term stability test at ambient temperature which supports the 18 month stability within a 2 year period post-approval; or - if a 2 year stability is sought - within a 2,5 year period post-approval.

2.1.7 Packaging of the biocidal product

Type of packaging	Size/volume of the packaging	Material of the packaging	Type and material of closure(s)	Intended user (e.g. professional, non-professional)	Compatibility of the product with the proposed packaging materials (Yes/No)
Squeeze tube	25-250 mL in steps of 5 ml	PE HDPE LDPE PP HDPE/LDPE HDPE/EVOH HDPE/F HDPE/PA LDPE/EVOH LDPE/F LDPE/PA	Snap cap Screw cap Top cap Flip top cap mostly PP	Non-professional	Yes
Bottle	25-250 mL in steps of 5 ml	PE HDPE LDPE PP HDPE/LDPE HDPE/EVOH	Screw cap Top cap Pump dispenser	Non-professional	Yes

		HDPE/F HDPE/PA LDPE/EVOH LDPE/F LDPE/PA			
Squeeze tube	25-250 mL in steps of 5 ml	Aluminium with inner layer of: PE HDPE LDPE PP HDPE/LDPE HDPE/EVOH HDPE/F HDPE/PA LDPE/EVOH LDPE/F LDPE/PA	Snap cap Screw cap Top cap Flip top cap mostly PP	Non-professional	Yes

2.1.8 Documentation

2.1.8.1 Data submitted in relation to product application

Please see §3.1 list of studies for the biocidal product.

2.1.8.2 Access to documentation

The applicant of this product is the same as the review programme participant for the active substance and is thus the owner of all data on the active substance.

2.2 ASSESSMENT OF THE BIOCIDAL PRODUCT

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

Table 3. Use # 1 – name of the use	
Product Type	PT19 – Repellents and attractants (Pest control)
Where relevant, an exact description of the authorised use	Insect Repellent Lotion IR3535® 10 % is a ready to use product. The repellent is applied onto the skin. 3 g Product is sufficient for the application to approximately 50% of the body surface (face, hands, arms and legs as assessed in the CAR for IR3535). For treatment of the face, distribute the lotion over the skin of the face thereby taking care to protect the eyes. Relevant codes: VI.1.1 and VI.9 (manual distribution over skin).
Target organism (including development stage)	**Scientific name** / **Common name** / **Development stage** Culicidae / Mosquitoes / Adults Ixodidae / Ticks / Nymphs Ixodidae / Ticks / Adults
Field of use	Other well ventilated areas
Application method(s)	manual application Description: The ready to use product is a lotion which is manually applied directly onto the exposed skin.
Application rate(s) and frequency	Dose: 3.0 g Dilution: 100% Insect Repellent Lotion IR3535® 10 % is intended to be used in Europe in summer when insects are frequent. It is usually applied once a day depending on outdoor activities, weather and presence of insects. The product can be applied (face, hands, arms and legs) up to 7 times per day for adults, up to 4 times for children > 10 years and maximally 2 times per day for smaller children and infants. The frequency must be reduced if more body parts are treated.
Category(ies) of users	General public (non-professional)
Pack sizes and packaging material	**Type** / **Material** / **Size** Bottle / Plastic: HDPE / >25.0 - < 250.0 mL The lightproof tube/flask is closed with a screw cap or a snap cap

2.2.2 Clarification on product composition and compositions tested

In the studies submitted several test materials were used. Below, the differences to the product Insect Repellent Lotion IR3535® 10% are described, whereas the full composition of the test materials is provided in the confidential part of the PAR.

- **Insect Repellent Lotion IR3535® 10%**
- **US Lotion Formulation:** In the US EPA formulation, the preservative Paragon II was contained at 1%. Insect Repellent Lotion IR3535® 10%is a preservative-free formulation which is buffered with a citric acid and disodium hydrogen phosphate (hydrated forms) at a total concentration of 1%. The triethanolamine concentration is very slightly lower than in Insect Repellent Lotion IR3535® 10%. The difference is compensated by water.
- **EU Lotion Formulation** or also **TMT-001** (efficacy test against *Aedes albopictus*): Identical to the US Lotion Formulation apart from a very slightly higher concentration of triethanolamine. The difference is compensated by water.

2.2.3 Physical, chemical and technical properties

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
Physical state at 20 °C and 101.3 kPa	Organoleptic	10.23 Insect Repellent Lotion IR3535® 10%	Liquid	Report no. 98322204, Fieseler, A. 2015
Colour at 20 °C and 101.3 kPa	Organoleptic	10.23 Insect Repellent Lotion IR3535® 10%	White	Report no. 98322204, Fieseler, A. 2015
Odour at 20 °C and 101.3 kPa	Organoleptic	10.23 Insect Repellent Lotion IR3535® 10%	Mild characteristic	Report no. 98322204, Fieseler, A. 2015
Acidity / alkalinity	CIPAC MT 75.3	10.23 Insect Repellent Lotion IR3535® 10%	Undiluted: pH = 6.4 At 1 %: pH = 7.0	Report no. 98322204, Fieseler, A. 2015
Relative density / bulk density	OECD 109	10.23 Insect Repellent Lotion IR3535® 10%	D_4^{20} = 1.008	Report no. 98322204, Fieseler, A. 2015
Storage stability test – **accelerated storage**	CIPAC MT 46.3 CIPAC MT 191 OECD 109 OECD 114	10.23 Insect Repellent Lotion IR3535® 10%	- No change in overall appearance of the test item: homogenous white liquid with characteristic odour. - No change in the packaging material: container and lid	Report no. 98322204, Fieseler, A. 2015

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
	[using HPLC-UV, as validated in section 2.2.5]		showed no cracking, fogging discoloration or distortion or significant change in weight. There is no seepage through the container walls or lid. - Change in pH (at 20 ± 1 °C): T0: 7.0 (1% dilution) – 6.4 undiluted T8w: 6.3 (1% dilution) – 5.6 undiluted - Change in density (kg/m3, at 20 ± 1 °C): T0: 1008.2 ± 0.4 T8w: 986.3 ± 0.3 - Change in viscosity (20 ± 0.3 °C; min-max; in mPa.s): T0: 534 - 1462 T8w: 387 - 986 - Change in viscosity (40 ± 0.5 °C; min-max; in mPa.s): T0: 238 - 597 T8w: 209 - 539 - Change in IR3535® (w/w %): T0: 10.23 T8w: 9.43 - Change in IR3535® free acid (w/w %): T0: 0.14 T8w: 0.82	

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
			[Storage: 40 ± 2°C for 8 weeks, relative humidity: 50 ± 15%, 50ml PP squeeze flask]	
Storage stability test – **long term storage at ambient temperature**	CIPAC MT 75.3 CIPAC MT 191 OECD 109 OECD 114 [using HPLC-UV, as validated in section 2.2.5]	10.23 Insect Repellent Lotion IR3535® 10%	- No change in overall appearance of the test item: white liquid with characteristic odour. - No change in the packaging material: container and lid showed no cracking, fogging discoloration or distortion or significant change in weight. There is no seepage through the container walls or lid. - Change in pH (at 20 ± 1 °C): T0: 7.0 (1% dilution) – 6.4 undiluted T6m: 6.8 (1% dilution) – 6.1 undiluted T12m: 6.8 (1% dilution) – 5.9 undiluted T18m: 6.0 (1% dilution) – 5.5 undiluted T24m: 5.4 (1% dilution) – 5.2 undiluted - Change in density (kg/m3, at 20 ± 1 °C): T0: 1008.2 T6m: 988.5 T12m: 1002.8 T18m: 999.3 T24m: 998.9	Report no. 98321204, Fieseler, A. 2018

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
			- Change in viscosity (20 ± 0.3 °C; min-max; in mPa.s): T0: 534 - 1462 T6m: 535 - 1338 T12m: 490 - 1376 T18m: 424 - 1064 T24m: 434 - 1051 - Change in viscosity (40 ± 0.5 °C; min-max; in mPa.s): T0: 238 - 597 T6m: 230 - 521 T12m: 217 - 547 T18m: 201 - 488 T24m:203 - 498 - Change in IR3535® (w/w %): T0: 10.1 T6m: 9.8 (= 97% T0) T12m: 9.6 (= 94% T0) T18m(*): 9.0 (= 88% T0) T24m 9.0 (= 89% T0) - Change in IR3535® free acid (w/w %): T0: 0.1 T6m: 0.5 T12m: 0.8 T18m(*): 1.0 T24m 1.1 [Storage: 20 ± 2°C, relative humidity: 50 ± 25%, intervals: X ± 2 weeks, 50ml PP squeeze flask]	

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
			(*) Measurement identified as outlier do to experimental error, refer to test report and IUCLID Executive summary for more information	
	OPPTS 830.6317	9.7 EU Lotion Formulation	Another study, on a 9.7 % sample with slightly deviating composition (no buffer but containing preservatives (1 % w/w in total)), gives acceptable results for up to 12 months storage: 7.2 % variation (9.0 versus 9.7 % w/w, respectively T12m versus T0).	Report no. 245-005, Meinerling, M. 2009
Storage stability test – **low temperature stability test for liquids**	CIPAC MT 39.3	10.4 EU Lotion Formulation	A study on a sample with slightly deviating composition (no buffer but containing preservatives (1 % w/w in total)) was introduced, and gives acceptable results: - Appearance of the test item: T0: homogenous, white liquid with characteristic odour. No separated material. T7d: homogenous, white solid with characteristic odour. No separated material. T7d + 24h at RT: homogenous, white liquid with characteristic odour. No separated material after one inversion. [Storage: 0 ± 1°C for 7 days, 100ml PP centrifuge tube]	Report no. 63194204, Meinerling, M. 2011

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
Effects on content of the active substance and technical characteristics of the biocidal product - **ligh**t	Waived	/	The product is intended to be placed on the market in lightproof plastic packaging, so that the effect of light can be excluded.	/
Effects on content of the active substance and technical characteristics of the biocidal product – **temperature and humidity**	Waived	/	- Since the product is tightly closed there are no effects due to humidity. - Effects of temperature have been studied during the storage stability tests (see above). The product should not be stored for prolonged times at temperatures >40°C.	/
Effects on content of the active substance and technical characteristics of the biocidal product - reactivity towards container material	Organoleptic	10.23 Insect Repellent Lotion IR3535® 10% 9.7 EU Lotion Formulation	No reactivity towards container material was observed during accelerated storage at 40 °C and during long term storage at ambient temperature. Refer to storage stability tests (see above)	Report no. 98322204, Fieseler, A. 2015 Report no. 245-005, Meinerling, M. 2009
Wettability	Waived	/	Not applicable, product is not a solid.	/
Suspensibility, spontaneity and dispersion stability	Waived	/	Not applicable, product is ready for use and not intended to be diluted.	/
Wet sieve analysis and dry sieve test	Waived	/	Not applicable, product is ready for use and not intended to be diluted.	/
Emulsifiability, re-emulsifiability and emulsion stability	Waived	/	Whereas the lotion is an emulsion (oil in water), a test for emulsifiability seems not relevant. The lotion formulation is a ready-to-use product and will not need to be diluted, nor emulsified by	/

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
			consumers. In addition, the storage stability trials have shown that the emulsion is stable and no phase-separation has been observed.	
Disintegration time	Waived	/	Not applicable, product is not a tablet.	/
Particle size distribution, content of dust/fines, attrition, friability	Waived	/	Not applicable, product is not a powder/granule.	/
Persistent foaming	Waived	/	Not applicable, product is ready for use and not intended to be diluted.	/
Flowability/Pourability/Dustability	Waived	/	Not applicable since biocidal product is not granular/a suspension.	/
Burning rate — smoke generators	Waived	/	Not applicable, product is not a smoke generator.	/
Burning completeness — smoke generators	Waived	/	Not applicable, product is not a smoke generator.	/
Composition of smoke — smoke generators	Waived	/	Not applicable, product is not a smoke generator.	/
Spraying pattern — aerosols	Waived	/	Not applicable, product is not an aerosol.	/
Physical compatibility	Waived	/	Lotion is not intended for use together with other products.	/
Chemical compatibility	Waived	/	Lotion is not intended for use together with other products.	/
Degree of dissolution and dilution stability	Waived	/	Not applicable, product is ready for use and not intended to be diluted, and is not a tablet.	/
Surface tension	OECD 115	10 Insect Repellent Lotion IR3535® 10%	29.9 nN/m (20 °C ± 0.5 °C)	Project no. 6442, Zur Lage, J. 2016
Viscosity	OECD 114	10.23 Insect Repellent Lotion IR3535® 10%	(Measured using a rotary viscometer at different shear rates (20 – 100 s^{-1}))	Report no. 98322204, Fieseler, A. 2015

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
			534-1462 mPa.s. (20 °C ± 0.5 °C) 238-597 mPa.s. (40 °C ± 0.5 °C) Lotion is not a Newtonian solution since the shear rates influence the viscosity results.	

Conclusion on the physical, chemical and technical properties of the product
The Insect Repellent Lotion IR3535® 10%, as manufactured, is a white liquid with a mild characteristic smell. The relative density of the product is 1.008 at 20 °C. At 20 °C and a concentration between 1.0 vol% and 100 vol%, the pH value is between 6.3 and 7.0. The accelerated stability test indicates that the formulation is stable for two years. Based on the long term stability test at ambient temperature and the IUCLID Executive summary (incl. the proposed linear regression), a stability of 18 months was accepted by the eCA and a majority of the commenting MS during the RCOM. Nonetheless, the applicant must provide the eCA with a new long term stability test at ambient temperature which supports this approach within a 2 year period post-approval. The product has been shown to be stable under cold temperature storage conditions. The product should not be stored for prolonged times at temperatures >40°C. Light influence is avoided by using a lightproof plastic packaging. There are no humidity effects expected in the closed package. The surface tension is 29.9 nN/m and the viscosity – measured at different shear rates – ranges between 534 and 1462 mPa.s. at 20°C, and 238 and 597 mPa.s. at 40°C. The lotion is a non-Newtonian solution. Physical and chemical compatibility with other products are not relevant.

2.2.4 Physical hazards and respective characteristics

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
Explosives	Waived	/	Based on the properties of the ingredients the product is not considered to be explosive.	/
Flammable gases	/	/	/	/
Flammable aerosols	/	/	/	/
Oxidising gases	/	/	/	/

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
Gases under pressure	/	/	/	/
Flammable liquids	EU A9 OPPTS 830.6315 ISO 2719	10 EU Lotion Formulation	No flash point could be determined up to 200 °C using a sample with slightly deviating composition (no buffer but containing preservatives (1 % w/w in total)).	Report no. 242-007, Fieseler, A. 2011
Flammable solids	/	/	/	/
Self-reactive substances and mixtures	Waived	/	The mixture does not contain any substances known to self-react or with chemical groups present in their molecules that are associated with explosive or self-reactive properties. So for the mixture no self reaction must be expected either.	Long-year experience with this and similar mixtures.
Pyrophoric liquids	Waived	/	The mixture does not contain any substances known to react with air so the mixture is no pyrophoric liquid.	Long-year experience with this and similar mixtures.
Pyrophoric solids	/	/	/	/
Self-heating substances and mixtures	Waived	/	The mixture is not self-heating since it is a liquid at room temperature. Since the liquid will also not be absorbed onto powder particles thus generating a large surface, no self-heating must be considered.	/
Substances and mixtures which in contact with water emit flammable gases	/	/	/	/
Oxidising liquids	Waived	/	Based on the properties of the ingredients the product	/

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
			is not considered to be oxidising.	
Oxidising solids	/	/	/	/
Organic peroxides	/	/	/	/
Corrosive to metals			None of the ingredients in the mixture is classified as corrosive or suspected from a chemical point of view to be able to react with metals and thus the mixture is also not corrosive to metal.	Long-year experience with this and similar mixtures.
Auto-ignition temperatures of products (liquids and gases)	EU A15	10.4 EU Lotion Formulation	The auto-ignition temperature was determined to be 480 °C using a sample with slightly deviating composition (no buffer but containing preservatives (1 % w/w in total)).	Report no. 20110105.01, Dornhagen, J. 2011
Relative self-ignition temperature for solids	/	/	/	/
Dust explosion hazard	/	/	/	/

Conclusion on the physical hazards and respective characteristics of the product

The auto-ignition temperature of the solution is 480 °C and the flashpoint of the solution is higher than 200 °C. The product has no self-reacting properties, does not react with air and is not self-heating since it is a liquid at room temperature. It is not able to react with metals and is not corrosive.

The product is not oxidizing nor explosive.

2.2.5 Methods for detection and identification

Analytical methods for the analysis of the product as such including the active substance, impurities and residues										
Analyte (type of analyte e.g. active substance)	**Analytical method**	**Fortification range / Number of measurements**	**Linearity**	**Specificity**		**Recovery rate (%)**			**Limit of quantification (LOQ) or other limits**	**Reference**
						Range	Mean	RSD		
IR3535®	HPLC-UV - No extraction - No clean up - LiChropher RP18 (250*4 mm) column - UV-Vis/DAD at 220 nm	1% / 10 5% / 5 10% / 5 30% / 5	Regression Coefficient (r2): > 0.9992 y = 21706x – 141584 Range (n=9): 25 – 1750 mg/l	No interference substances observed. The retention time of the analyte IR3535 in the sample solutions did not differ by more than 1 % from that for the standard solution.	1	88-114	101	12.5	LOQ: 5 % w/w (=250 mg/L) LOD: 7 mg/L	Report no. 31211101, Meinerling, M. 2007
					5	98-101	99	1.3		
					10	96-100	99	1.8		
					30	96-98	98	0.9		
IR3535® free acid - hydrolysis product	HPLC-UV - No extraction - No clean up - LiChropher RP18 (250*4 mm) column - UV-Vis/DAD at 220 nm	5% / 10 (for 1% IR3535) 5% / 5 (for 5% IR3535) 1% / 5 (for 10% IR3535) 5% / 5 (for 30% IR3535)	Regression Coefficient (r2): > 0.9991 y = 23988x – 67471 Range (n=9): 25 – 300 mg/l	No interference substances observed. The retention time of the analytes IR3535 and its hydrolysis product in the sample solutions did not differ by more than 1 % from that for the standard solution.	5	97-105	101	2.8	LOQ: 0.1% w/w (=5 mg/L) LOD: 3 mg/L	Report no. 31211101, Meinerling, M. 2007
					5	98-100	99	0.9		
					1	100-103	102	1.7		
					5	102-108	104	2.0		
		2 levels (80 & 120%) 5 replicates	Regression Coefficient (r2): > 0.9999 y = 23995x – 280		80	95-108	101	5.1		Report no. 98322204, Fieseler, A. 2015
					80	99-101	100	0.9		
					120	100-101	100	0.5		
					120	100-102	101	0.9		

			Range (n=7): 1 – 50 mg/l							

Analytical methods for monitoring									
Analyte (type of analyte e.g. active substance)	**Analytical method**	**Fortification range / Number of measurements**	**Linearity**	**Specificity**	**Recovery rate (%)**			**Limit of quantification (LOQ) or other limits**	**Reference**
					Range	Mean	RSD		
See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535

Analytical methods for soil									
Analyte (type of analyte e.g. active substance)	**Analytical method**	**Fortification range / Number of measurements**	**Linearity**	**Specificity**	**Recovery rate (%)**			**Limit of quantification (LOQ) or other limits**	**Reference**
					Range	Mean	RSD		
See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535

Analytical methods for air									
Analyte (type of analyte e.g. active substance)	**Analytical method**	**Fortification range / Number of measurements**	**Linearity**	**Specificity**	**Recovery rate (%)**			**Limit of quantification (LOQ) or other limits**	**Reference**
					Range	Mean	RSD		
See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535

Analytical methods for water									
Analyte (type of analyte e.g. active substance)	**Analytical method**	**Fortification range / Number of measurements**	**Linearity**	**Specificity**	**Recovery rate (%)**			**Limit of quantification (LOQ) or other limits**	**Reference**
					Range	Mean	RSD		
See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535

Analytical methods for animal and human body fluids and tissues									
Analyte (type of analyte e.g. active substance)	**Analytical method**	**Fortification range / Number of measurements**	**Linearity**	**Specificity**	**Recovery rate (%)**			**Limit of quantification (LOQ) or other limits**	**Reference**
					Range	Mean	RSD		
See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535

Analytical methods for monitoring of active substances and residues in food and feeding stuff									
Analyte (type of analyte e.g. active substance)	**Analytical method**	**Fortification range / Number of measurements**	**Linearity**	**Specificity**	**Recovery rate (%)**			**Limit of quantification (LOQ) or other limits**	**Reference**
					Range	Mean	RSD		
See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535	See AR IR3535

Conclusion on the methods for detection and identification of the product
IR3535® and its metabolite IR3535® free acid (hydrolysis product) can both be determined in the lotion product with an HPLC-Diode Array Detector/UV-VIS detector (at 220nm) and a RP18 (250*4 mm) column. The identity of the analyte is confirmed by comparison of the retention times. The standard regression is linear. The method is repeatable. The mean recovery rates at each spiking level are in the range of 88 – 114% for IR3535® and 95 – 108 % for its metabolite IR3535® free

acid (hydrolysis product). The limit of quantification (LOQ) is 5% for IR3535® corresponding to 250 mg/L and the limit of detection (LOD) is 7 mg/L for IR3535®. The limit of quantification (LOQ) is 0.1% for IR3535® free acid corresponding to 5 mg/L and the limit of detection (LOD) is 3 mg/L for IR3535® free acid. The overall mean recovery rate for IR3535® and IR3535® free acid was in the range of 98 - 101% and 99 - 104%, respectively.

2.2.6 Efficacy against target organisms

2.2.6.1 Function and field of use

Main Group 03 : Pest Control

Product Type 19 : Repellents and attractants

According to a "concept" label submitted by Merck (please note that Merck does not market these products):

The product ***Insect Repellent Lotion IR3535® 10%*** is presented as a ready-to-use lotion to be applied on dry, exposed human skin (to face, arms, hands and legs only), at a rate of a walnut-sized amount per application, with up to 8-hour protection.

The product is intended to be used by general public in temperate areas. An adult should apply this product to children under 12 years of age.

Please note that many warnings will be mentioned on the label such as :

- Do not apply sun care products or cosmetic formulations after repellent use, the repellent can't protect you anymore.
- Use product for infants only when disease vectors are present.
- Do not apply over cuts, wounds, freshly shaven or irritated skin.
- Mechanical protection (clothing, mosquito nets) is to be preferred.

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

According to the use claimed by the Applicant :

- The product ***Insect Repellent Lotion IR3535® 10%*** is intended to be used to repel arthropods on skin.

- The target organisms to be control are mosquitoes and ticks.

- The product ***Insect Repellent Lotion IR3535® 10%*** is used as an insect repellent and is applied evenly over dry, exposed skin. Contact with cuts, wounds, freshly shaved or irritated skin should be avoided.

The organisms to be protected are humans.

2.2.6.3 Effects on target organisms, including unacceptable suffering

In total the Applicant submitted 12 studies. Please see the summary (and comments) of all the studies submitted in the table section #2.2.6.5.

2.2.6.4 Mode of action, including time delay

The mode of action of IR3535® is not a passive masking of an attracting odour of a victim, but an active repellent effect as insects avoid entering regions with IR3535® vapours. The exact biochemical mode of action of IR3535® on insects is not well known yet, but it is most self-evident to assume that IR3535® has an olfactory-based effect.

2.2.6.5 Efficacy data

Experimental data on the efficacy of the biocidal product against target organism(s)							
Function	**Field of use envisaged**	**Test substance**	**Test organism(s)**	**Test method**	**Test system / concentrations applied / exposure time**	**Test results: effects**	**Reference**
Initial dossier (2015)							
TICKS							
PT19 Repellent	- RTU Lotion - Applied on uncovered human skin - For consumers	Insect Repellent Lotion IR3535 10% (liquid, 10% IR3535) With composition of the formulation provided at the end of the efficacy test report.	***TICKS*** *Ixodes scapularis* (US deer ticks) nymphs Given the information provided by DE eCA (Büchel et al. - 2015 - "Repellent efficacy of DEET, Icaridin, and EBAAP against Ixodes ricinus and Ixodes scapularis nymphs (Acari, Ixodidae).") during the commenting phase about the Pump Spray 20% IR3535, no significant differences in repellent efficacy were found between the two species tested (when compared the repellent efficacy of 10% EBAAP =IR3535)."	Lab test	- with 10 volunteers - 0.00115 g BP/cm^2 on the lower arm - Exposure started 15 minutes after application - 3 min exposure time, every 15 min until 14 hours - "normal" climatic conditions for temperate areas (+19-26°C ; 31-52% H_R)	The product used at 0.00115 g BP/cm^2 (with d = 0.989 => 0.00115 mL BP/cm^2 or 0.000115 mL A.I./cm^2) is efficacious to repel ticks up to 9h.	**Carroll S.P. (2006)** **Document B5_10_(01)_336-1916** "Test of Personal Insect Repellents: Study EMD-003.1 - Replacement for MRID 46979001 - Volume 11" **R.2 Key study**
MOSQUITOES							
PT19 Repellent	- RTU Lotion - Applied on uncovered human skin - For consumers	Insect Repellent Lotion IR3535 10% (liquid, 10% IR3535)	**MOSQUITOES** *Aedes melanimon* (predominant species), *Culex erythrothorax*, *Culex tarsalis, Culiseta incidens*, *Anopheles*	Field test on 2 different sites (grassland; wooded picnic area)	- with 10 volunteers - 0.00115 g/cm^2 on legs - Exposure started 15 min (grassland) or 3h15 (wooded	The product used at 0.00115 g BP/cm^2 (with d = 0.989 => 0.00115 mL BP/cm^2 or 0.000115 mL A.I./cm^2) is efficacious to repel mosquitoes up to 8h.	**Carroll S.P. (2006)** **Document B5_10_(02)_336-1917** "Test of Personal

			freeborni and *Aedes vexans*		picnic area) after application - 1 min exposure time, every 15 min until 14 hours - "normal" climatic conditions for temperate areas (+19-25°C ; 24 - 39% H_R)		Insect Repellents: Study EMD 004.1 - Replacement for MRID 4699003 - Volume 12" **R.1 Key study**
Resubmission (06/2018)							
PT19 Repellent	- RTU Lotion - Applied on uncovered human skin	Insect Repellent Lotion IR3535 10% (liquid, 10% IR3535) With composition of the formulation provided at the end of the efficacy test report.	**TICKS** *Ixodes ricinus* (EU sheep ticks) nymphs	Lab study performed according to the EPA guideline OPPTS 810.3700	- with 10 volunteers - Application rate : 1µL BP/cm^2 - 5 min exposure time until 8 hours - "normal" climatic conditions for temperate areas (+22.8°C ; 48.3% H_R)	Repellence over time : 0h Application 1h 100% 2h 100% 3h 100% 4h 97% 5h 95% 6h 97% 7h 92% 8h 88% The product used at 1µL BP/cm^2 (0.001 mL BP/cm^2 or 0.0001 mL A.I./cm^2) is efficacious to repel ticks up to 7 h*	**Büchel K. (2017)** **IUCLID Document "ede87fed-55aa-4327-bf68-f884ee68fb3d"** **Report N° ME_IR_0117a_01 Lotion** "Evaluation of the repellent efficacy of Insect Repellent Lotion IR3535 10% (1.0 µl/cm^2) against the European Sheep Tick *Ixodes ricinus* on

							human volunteers" **R.1 Key study**
PT19 Repellent	- RTU Lotion - Applied on uncovered human skin	Insect Repellent Lotion IR3535 10% (liquid, 10% IR3535) With composition of the formulation provided at the end of the efficacy test report.	**TICKS** *Ixodes ricinus* (EU sheep ticks) nymphs	Lab study performed according to the EPA guideline OPPTS 810.3700	- with 10 volunteers - Application rate : 0.72µL BP/cm^2 - 5 min exposure time until 8 hours - "normal" climatic conditions for temperate areas (+22.8°C ; 48.3% H_R)	Repellence over time : 0h Application 1h 100% 2h 98% 3h 93% 4h 95% 5h 88% 6h 88% 7h 93% 8h 78% The product used at 0.72 µL BP/cm^2 (0.00072 mL BP/cm^2 or 0.000072 mL A.I./cm^2) is efficacious to repel ticks up to 4h. The efficacy assessed was 4 hours, 5 hours or 7 hours for 3 volunteers and ≥ 8 hours for the other 7 volunteers. Thus, the results are not clear enough to give a higher protection time.	**Büchel K. (2017)** **Document "c48bb01c-a30f-4f50-88dd-5d72d811460f"** **Report N° ME_IR_0117b_01 Lotion** "Evaluation of the repellent efficacy of Insect Repellent Lotion IR3535 10% (0.72 µl/cm^2) against the European Sheep Tick *Ixodes ricinus* on human volunteers" **R.2**
Submission 08/2018							
PT19 Repellent	- RTU Lotion	Insect Repellent Lotion IR3535	**MOSQUITOES** *Aedes aegypti* (female)	Arm-in-Cage simulated-use test	- with 12 volunteers (10 + 2 control)	The product used at 1g BP/600 cm^2 (0.00166 g BP/ cm^2 & with d = 0.989	**P. H. Herculano, & G. P.**

	- Applied on uncovered human skin	10% (liquid, 10% IR3535) With composition of the formulation provided in the efficacy test report.		according to the EPA guideline OPPTS 810.3700	- Application rate : 1 g BP/600 cm^2 - in a netted cage : V = 64.000 cm^3 With 55 mosquitoes (*as described in the OPPTS 810.3700 methodology, July 7th, 2010 & within the range recommended by the WHO guidelines p.6*) - 5 min exposure time until 7 hours - "normal" climatic conditions for temperate areas (+25.0 ± +2°C ; between 50 & 70 % H_R; photoperiod 12/12)	=> 0.00166 mL BP/cm^2 or 0.000166 mL A.I./cm^2) is 100% efficacious to repel female *Aedes aegypti* mosquitoes up to 6 h.	**Machado (2017)** **Document "RMQAA-039843.R1 (Inglês)"** **Report N° RMQAA - 039843.R1** "EFFICACY TESTS IN A REPELLENT PRODUCT FOR MOSQUITOES Aedes aegypti (DIPTERA: CULICIDAE)" **R.1 Key study**
PT19 Repellent	- RTU Lotion - Applied on uncovered human skin	Insect Repellent Lotion IR3535 10% (liquid, 10% IR3535) With composition of the formulation provided in the efficacy test report.	**MOSQUITOES** *Aedes albopictus* (female)	Arm-in-Cage simulated-use test according to the EPA guideline OPPTS 810.3700	- with 12 volunteers (10 + 2 control) - Application rate : 1 g BP/600 cm^2 - in a netted cage : V = 64.000 cm^3 With 55 mosquitoes (*as described in the OPPTS 810.3700 methodology, July 7th, 2010 & within the range recommended by*	The product used at 1g BP/600 cm^2 (0.00166 g BP/cm^2 & with d = 0.989 => 0.00166 mL BP/cm^2 or 0.000166 mL A.I./cm^2) is 100% efficacious to repel female *Aedes albopictus* mosquitoes up to 8 h, according to the requirements (i.e. ≈ 100% repellence) mentioned in the ECHA PT19 guidance.	**P. H. Herculano, & G. P. Machado (2017)** **Document "RMQAA-039843.R1 (Inglês)"** **Report N° RMQAAL - 039843.R1**

					the WHO guidelines p.6) - 5 min exposure time until 9 hours - "normal" climatic conditions for temperate areas (+25.0 ± +2°C ; between 50 & 70 % H_R; photoperiod 12/12)		"EFFICACY TESTS IN A REPELLENT PRODUCT FOR MOSQUITOES Aedes albopictus (DIPTERA: CULICIDAE)" **R.1 Key study**
PT19 Repellent	- RTU Lotion - Applied on uncovered human skin	Insect Repellent Lotion IR3535 10% (liquid, 10% IR3535) With composition of the formulation provided in the efficacy test report.	**MOSQUITOES** *Anopheles aquasalis* (female)	Arm-in-Cage simulated-use test according to the EPA guideline OPPTS 810.3700	- with 12 volunteers (10 + 2 control) - Application rate : 1 g BP/600 cm^2 - in a netted cage : V = 64.000 cm^3 With 55 mosquitoes (*as described in the OPPTS 810.3700 methodology, July 7th, 2010 & within the range recommended by the WHO guidelines p.6*) - 5 min exposure time until 8 hours - "normal" climatic conditions for temperate areas (+25.0 ± +2°C ; between 50 & 70 % H_R; photoperiod 12/12)	The product used at 1g BP/600 cm^2 (0.00166 g BP/cm^2 & with d = 0.989 => 0.00166 mL BP/cm^2 or 0.000166 mL A.I./cm^2) is 100% efficacious to repel female *Anopheles aquasalis* mosquitoes up to 7 h.	**P. H. Herculano, & G. P. Machado (2017)** **Document "RMQANE-039843.R1 (Inglês)"** **Report N° RMQANE-039843.R1** "EFFICACY TESTS IN A REPELLENT PRODUCT FOR MOSQUITOES *Anopheles aquasalis* (DIPTERA: CULICIDAE)" **R.1 Key study**

PT19 Repellent	- RTU Lotion - Applied on uncovered human skin	Insect Repellent Lotion IR3535 10% (liquid, 10% IR3535) With composition of the formulation provided in the efficacy test report.	**MOSQUITOES** *Culex quinquefasciatus* (female)	Arm-in-Cage simulated-use test according to the EPA guideline OPPTS 810.3700	- with 12 volunteers (10 + 2 control) - Application rate : 1 g BP/600 cm^2 - in a netted cage : V = 64.000 cm^3 With 55 mosquitoes (*as described in the OPPTS 810.3700 methodology, July 7th, 2010 & within the range recommended by the WHO guidelines p.6*) - 5 min exposure time until 8 hours - "normal" climatic conditions for temperate areas (+25.0 ± +2°C ; between 50 & 70 % H_R; photoperiod 12/12)	The product used at 1g BP/600 cm^2 (0.00166 g BP/cm^2 & with d = 0.989 => 0.00166 mL BP/cm^2 or 0.000166 mL A.I./cm^2) is 100% efficacious to repel female *Culex quinquefasciatus* mosquitoes up to 7 h.	**P. H. Herculano, & G. P. Machado (2017)** **Document "RMQCQ-039843.R1 (Inglês)"** **Report N° RMQCQ-039843.R1** "EFFICACY TESTS IN A REPELLENT PRODUCT FOR MOSQUITOES *Culex quinquefasciatus* (DIPTERA: CULICIDAE)" **R.1 Key study**
PT19 Repellent	- RTU Lotion - Applied on uncovered human skin	Insect Repellent Lotion IR3535 10% (liquid, 10% IR3535) With composition of the formulation provided in the efficacy test report.	**MOSQUITOES** *Aedes aegypti* (female)	Arm-in-Cage simulated-use test according to the EPA guideline OPPTS 810.3700	- with 12 volunteers (10 + 2 control) - Application rate : 2 g BP/600 cm^2 - in a netted cage : V = 64.000 cm^3 With 55 mosquitoes (*as described in the OPPTS 810.3700*	The product used at 2g BP/600 cm^2 (0.00333 g BP/cm^2 & with d = 0.989 => 0.00333 mL BP/cm^2 or 0.000333 mL A.I./cm^2) is 100% efficacious to repel female *Aedes aegypti* mosquitoes up to 8 h.	**P. H. Herculano, & G. P. Machado (2017)** **Document "039843 R - RMQAA_ing »**

					methodology, July 7th, 2010 & within the range recommended by the WHO guidelines p.6) - 5 min exposure time until 9 hours - "normal" climatic conditions for temperate areas (+25.0 ± +2°C ; between 50 & 70 % H_R; photoperiod 12/12)		**Report N° RMQAA – 039843.R** "EFFICACY TESTS IN A REPELLENT PRODUCT FOR MOSQUITOES Aedes aegypti (DIPTERA: CULICIDAE)" **R.1 Key study**
PT19 Repellent	- RTU Lotion - Applied on uncovered human skin	Insect Repellent Lotion IR3535 10% (liquid, 10% IR3535) With composition of the formulation provided in the efficacy test report.	**MOSQUITOES** *Aedes albopictus* (female)	Arm-in-Cage simulated-use test according to the EPA guideline OPPTS 810.3700	- with 12 volunteers (10 + 2 control) - Application rate : 2 g BP/600 cm^2 - in a netted cage : V = 64.000 cm^3 With 55 mosquitoes (*as described in the OPPTS 810.3700 methodology, July 7th, 2010 & within the range recommended by the WHO guidelines p.6*) - 5 min exposure time until 9 hours - "normal" climatic conditions for temperate areas (+25.0 ± +2°C ;	The product used at 2g BP/600 cm^2 (0.00333 g BP/cm^2 & with d = 0.989 => 0.00333 mL BP/cm^2 or 0.000333 mL A.I./cm^2) is 100% efficacious to repel female *Aedes albopictus* mosquitoes up to 8 h.	**P. H. Herculano, & G. P. Machado (2017)** **Document "039843 R - RMQAAL_ing"** **Report N° 039843 R - RMQAAL_ing** "EFFICACY TESTS IN A REPELLENT PRODUCT FOR MOSQUITOES Aedes albopictus

					between 50 & 70 % H_R; photoperiod 12/12)		(DIPTERA: CULICIDAE)" **R.1 Key study**
PT19 Repellent	- RTU Lotion - Applied on uncovered human skin	Insect Repellent Lotion IR3535 10% (liquid, 10% IR3535) With composition of the formulation provided in the efficacy test report.	**MOSQUITOES** *Anopheles aquasalis* (female)	Arm-in-Cage simulated-use test according to the EPA guideline OPPTS 810.3700	- with 12 volunteers (10 + 2 control) - Application rate : 2 g BP/600 cm^2 - in a netted cage : V = 64.000 cm^3 With 55 mosquitoes (*as described in the OPPTS 810.3700 methodology, July 7th, 2010 & within the range recommended by the WHO guidelines p.6*) - 5 min exposure time until 9 hours - "normal" climatic conditions for temperate areas (+25.0 ± +2°C ; between 50 & 70 % H_R; photoperiod 12/12)	The product used at 2g BP/600 cm^2 (0.00333 g BP/cm^2 & with d = 0.989 => 0.00333 mL BP/cm^2 or 0.000333 mL A.I./cm^2) is 100% efficacious to repel female *Anopheles aquasalis* mosquitoes up to 8 h.	**P. H. Herculano, & G. P. Machado (2017)** **Document "039843.R - RMQANE_in g »** **Report N° RMQANE – 039843.R** "EFFICACY TESTS IN A REPELLENT PRODUCT FOR MOSQUITOES *Anopheles aquasalis* (DIPTERA: CULICIDAE)" **R.1 Key study**
PT19 Repellent	- RTU Lotion - Applied on uncovered human skin	Insect Repellent Lotion IR3535 10% (liquid, 10% IR3535) With composition of the formulation	**MOSQUITOES** *Culex quinquefasciatus* (female)	Arm-in-Cage simulated-use test according to the EPA guideline OPPTS 810.3700	- with 12 volunteers (10 + 2 control) - Application rate : 2 g BP/600 cm^2 - in a netted cage : V = 64.000 cm^3	The product used at 2g BP/600 cm^2 (0.00333 g BP/cm^2 & with d = 0.989 => 0.00333 mL BP/cm^2 or 0.000333 mL A.I./cm^2) is 100% efficacious to repel female *Culex*	**P. H. Herculano, & G. P. Machado (2017)** **Document "039843.R -**

		provided in the efficacy test report.			With 55 mosquitoes (*as described in the OPPTS 810.3700 methodology, July 7th, 2010 & within the range recommended by the WHO guidelines p.6*) - 5 min exposure time until 8 hours - "normal" climatic conditions for temperate areas (+25.0 ± +2°C ; between 50 & 70 % H_R; photoperiod 12/12)	*quinquefasciatus* mosquitoes up to 9 h.	**RMQCQ_ing »** **Report N° RMQCQ – 039843.R** "EFFICACY TESTS IN A REPELLENT PRODUCT FOR MOSQUITOES *Culex quinquefasciatus* (DIPTERA: CULICIDAE)" **R.1 Key study**

DISCUSSION & CONCLUSIONS :

Repellence efficacy of the product ***Insect Repellent Lotion IR3535 10%*** (liquid, 10% IR3535) against mosquitoes:

Simulated-use tests (Arm-in-Cage tests according to WHO or OPPTS 810.3700 method) and a field test were submitted to support this claim. We're of the opinion that this test performed in real-use conditions gives more realistic results compared to Arm-in-Cage tests. Since the field test has been considered as a reliable and acceptable test according to the comments received about the IR3535 Pump Spray/Aerosol products, the results of the field test submitted here are used to draw a conclusion about the repellence efficacy of the product ***Insect Repellent Lotion IR3535 10%*** against mosquitoes. Then, with this field test, the results show 100% repellence efficacy of the product ***Insect Repellent Lotion IR3535 10%*** when applied on uncovered human skin up to 8 h at the dose of 0.00115 g BP/cm² against mosquito's genus *Aedes, Culex* and *Anopheles* found in temperate areas, which is also supported by the Arm-in-Cage tests

Repellence efficacy of the product ***Insect Repellent Lotion IR3535 10%*** (liquid, 10% IR3535) against ticks :

Laboratory choice tests (according to OPPTS 810.3700 method) were submitted to support this claim.

- The lab test performed with *Ixodes scapularis (similar to I. ricinus according to the scientific paper provided by the DE eCA* Büchel *& al.* (2015) "*Repellent efficacy of DEET, Icaridin, and EBAAP against Ixodes ricinus and Ixodes scapularis nymphs (Acari, Ixodidae)*" showing that no significant differences in repellent efficacy were found between the two species tested (when compared the repellent efficacy of 10% IR3535)*) & 3 min exposure (exposure time* acceptable according to the comments received about the IR3535 Pump Spray/Aerosol products) shows the 100% repellence efficacy of the product ***Insect Repellent Lotion IR3535 10%*** when applied on uncovered human skin up to 9 h at the dose of 0.00115 g BP/cm^2.
- The lab test performed with *Ixodes ricinus* & 5 min exposure shows the 90 % repellence efficacy of the product ***Insect Repellent Lotion IR3535 10%*** when applied on uncovered human skin up to 7 h at the dose of 0.001 g BP/cm^2.
- Since the test performed with *I. ricinus* European ticks & 5 min exposure time is more in line with the TNsG PT18-19 2012 guidance about tick strain & exposure time, we are of the opinion to conclude that the product ***Insect Repellent Lotion IR3535 10%*** when applied on uncovered human skin up to 7 h at the dose of 0.001 g BP/cm2 is 100% effective to repel ticks in temperate areas.

Conclusion on the efficacy of the product
The product ***Insect Repellent Lotion IR3535® 10%*** (liquid, 10% IR3535®) when applied on uncovered human skin **at the dose of 0.00115 g/cm^2** provides up to 8 hours protection time against mosquitoes found in temperate areas. The product ***Insect Repellent Lotion IR3535® 10%*** (liquid, 10% IR3535®) when applied on uncovered human skin **at the dose of 0.001 g BP/cm^2** provides up to 7 hours protection time against ticks found in temperate areas.

2.2.6.6 Occurrence of resistance and resistance management

As the active substance IR3535® is a repellent (no killing action) and does not give rise to selection pressure, no resistance is expected to be developed. However, given the importance of vector control, the registration holder will collect informationregistered by end users to monitor potential resistance phenomena, and report to relevand eCA every 5 years if needed. The following Risk Mitigation Measure is implemented in the SPC:

- The users should inform if the treatment is ineffective and report straightforward to the registration holder.

2.2.6.7 Known limitations

- As stated by the applicant, the product is intended to be used in tropical areas. But, due to the absence of efficacy tests on tropical species (at more than +30°C), the use of this product in tropical areas hasn't be authorized.

2.2.6.8 Evaluation of the label claims

According to a "concept" label, ***Insect Repellent Lotion IR3535® 10%*** (liquid, 10% IR3535®) does provide a good protection against ticks and mosquitoes for 8 hours in temperate areas.

Based on the efficacy tests submitted and validated, the product ***Insect Repellent Lotion IR3535® 10%*** (liquid, 10% IR3535®) can be granted with the following use conditions:

When used at 0.00115 g/cm^2 in temperate areas only, the product ***Insect Repellent Lotion IR3535® 10%*** (liquid, 10% IR3535®) does provide a good protection against ticks and mosquitoes up to 7h.

For products claiming only protection against mosquitoes, the protection time against mosquitoes found in temperate areas would be of 8h when used at 0.00115 g/cm^2, based on the efficacy tests submitted and validated.

For products claiming only protection against ticks, the protection time against ticks found in temperate areas would be 7h when used at 0.001 g/cm^2, based on the efficacy tests submitted and validated.

- It's necessary to inform the user to in an easily understandable form how much of the biocidal product he should use. Then, please add the following sentence on the label " *Place a limited amount of lotion on the palm of the hand and distribute the lotion sparingly over the exposed skin. ONLY apply to uncovered parts of the body, limited to the face, hands, arms, legs and feet.*
- References related to intended uses under tropical conditions must be removed from the label
- References related to intended uses on clothes must be removed from the label
- All references related to target organisms other than mosquitoes & ticks must be removed from the label.
- All the warnings such as "Do not apply sun care products or cosmetic formulations after repellent use, the repellent can't protect you anymore", "Do not apply over cuts, wounds, freshly shaven or irritated skin" and "Mechanical protection (clothing, mosquito nets) is to be preferred" must be mentioned on the label.

2.2.6.9 Relevant information if the product is intended to be authorised for use with other biocidal product(s)

Not relevant.

2.2.7 Risk assessment for human health

For acute dermal toxicity, skin and eye irritation and skin sensitisation, a read-across from studies performed with US Lotion formulation has been performed. As the composition of the BP under evaluation is very similar to the reference formulation, read-across is considered appropriate. (see Confidential Annex section 2.1)

2.2.7.1 Assessment of effects on Human Health

(I) Skin corrosion and irritation

New data for this section are due to differences in product composition.

Summary table of animal studies on skin corrosion /irritation					
Method, Guideline, GLP status, Reliability	**Species, Strain, Sex, No/group**	**Test substance, Vehicle, Dose levels, Duration of exposure**	**Results** ***Average score (24, 48, 72h)/ observations and time point of onset, reversibility; other adverse local / systemic effects, histopathological findings***	**Remarks** ***(e.g. major deviations)***	**Reference**
OPPTS 870.2500 OECD 404 EU 92/69 Annex V, B4 GLP=yes Rel=1	Albino rabbit New Zealand White 2♂, 1♀ 1 test group, 3 animals	US Lotion Formulation No vehicle 0.5 ml/2.5 cm x 2.5 cm 4h	Erythema: Animal 1: 1.0 Animal 2: 1.0 Animal 3: 1.0 Edema: Animal 1: 0.33 Animal 2: 0.0 Animal 3: 0.33 Max score erythema 1, earliest onset 0.5-1h; max score edema 1, earliest onset 0.5-1h. Very slight erythema	Identity of test material slightly different from BP: buffers added (1% in total) and omission of preservatives (1% in total)	[redacted] 2006 (a)

			and/or desquamation persisted through study termination (day 14) for 2 animals. No deaths, no remarkable bw changes		

Individual and mean dermal scores for erythema and edema ([redacted] 2006 (a))

Animal	Sex	Site	Erythema							Edema						
			0.5 – 1 h	24 h	48 h	72 h	4 d	7 d	14 d	0.5 – 1 h	24 h	48 h	72 h	4 d	7 d	14 d
45165	M	D	1	1	1	1	1	1	1	1	1	0	0	0	0	0
45168	M	B	1	1	1	1	1	1	0	0	0	0	0	0	0	0
45183	F	C	0	1	1	1	1	1d	1d	0	1	0	0	0	0	0
Means 24-72 hours (individual animals)																
45165			1.0							0.33						
45168			1.0							0.0						
45183			1.0							0.33						
Mean 24-72 hours (all animals)																
			1.0							0.22						

There were no deaths or remarkable body weight changes noted during the study. Dermal findings consisted of very slight erythema and/or edema for all animals. Desquamation was noted for one female rabbit on study day 7 and day 14. Very slight erythema and/or desquamation persisted through study termination (day 14).

The mean scores determined for erythema (1.0) and edema (0.22) do not require a classification according to the EU and GHS classification and labelling system.

Although erythema grade 1 (very slight erythema, barely perceptible, area of edges not well defined) persisted in two out of three animals with one animal therefrom showing desquamation until the end of the 14-day post-observation period, a classification as a potential skin irritant is not required. According to EU Directive 2001/59/EC or Regulation (EC) No. 1272/2008 (CLP), a classification as a skin irritant should be considered when hyperplasia, hyperkeratosis, scaling, discoloration, fissures, scabs or alopecia persist in two or more animals at the end of the observation period which has not been observed in the skin irritation study with the US Lotion Formulation.

Note: Though the conclusions drawn from this test report were questioned during the RCOM phase for the BP under evaluation, it was agreed that the non-classification of the BP could be maintained. Please see the confidential annex section 2.4 for details.

No *in vitro* or human data are available for skin corrosion/irritation.

Conclusion used in Risk Assessment – Skin corrosion and irritation	
Value/conclusion	Biocidal product not classified for skin corrosion/irritation according to (EU) nr. 1272/2008
Justification for the value/conclusion	Mean scores for erythema and edema do not trigger a classification. Severity of skin reactions that persisted to the end of the observation period was limited (erythema grade 1). BP under evaluation does not include skin irritating co-formulants. According to the calculation method the biocidal product is not classified as skin irritating.
Classification of the product according to CLP and DSD	none

(II) Eye Irritation

New data for this section are due to differences in product composition.

Summary table of animal studies on serious eye damage and eye irritation					
Method, Guideline, GLP status, Reliability	**Species, Strain, Sex, No/group**	**Test substance,Dose levels, Duration of exposure**	**Results** ***Average score (24, 48, 72h)/ observations and time point of onset, reversibility***	**Remarks** ***(e.g. major deviations)***	**Reference**
OPPTS 870.2400 OECD 405 EU 92/69 Annex V, B5 GLP=yes Rel=1	Albino rabbit New Zealand White 3♂ 1 test group, 3 animals	US Lotion Formulation No vehicle 0.1ml 1 single unwashed exposure	- Conjunctival chemosis score Animal 1 :1.0 Animal 2 : 1.0 Animal 3 : 1.0 - Conjunctival redness score Animal 1 :2.33 Animal 2 : 1.0 Animal 3 : 1.0 - Iris score Animal 1 :0.0 Animal 2 : 0.0 Animal 3 : 0.0	Identity of test material slightly different from BP: buffers added (1% in total) and omission of preservatives (1% in total)	[redacted] (2006) (b)

			- Cornea score Animal 1 :1.67 Animal 2 : 0.0 Animal 3 : 0.0 Reversibility: Yes Earliest onset for all symptoms: 1h Max scores: cornea 2, conjunctiva, redness 3, conjunctiva, chemosis 3 Reversible at d17		

Individual Total Scores and for Ocular Irritation ([redacted] 2006 (b))

Rabbit No/sex	No. 45157/male				No. 45160/male				No. 45161/male			
Time after treatment [hours]	1	24	48	72	1	24	48	72	1	24	48	72
Cornea												
Opacity	1	2	2	1	0	0	0	0	0	0	0	0
Area involved	1	3	3	1	0	0	0	0	0	0	0	0
Iris	0	0	0	0	0	0	0	0	0	0	0	0
Conjunctivae												
Redness	3	3	2	2	1	1	1	1	2	1	1	1
Chemosis	3	1	1	1	1	1	1	1	2	1	1	1
Discharge	2	0	0	0	1	0	0	0	3	0	0	0
Mean of 24-72-hour Readings: individual animals	Opacity: 1.67 Iris: 0 Redness: 2.33 Chemosis: 1.0				Opacity: 0 Iris: 0 Redness: 1.0 Chemosis: 1.0				Opacity: 0 Iris: 0 Redness: 1.0 Chemosis: 1.0			
Mean of 24-72-hour Readings: all animals	Opacity: 0.55 Iris: 0 Redness: 1.44 Chemosis: 1.0											
Classification	Non-irritant (EU: -; GHS: -)											

The primary eye irritation potential of the US lotion formulation was investigated in 3 NZW rabbits according to OECD TG 405 and under GLP. There were no deaths or remarkable body weight changes noted during the study. Positive corneal and conjunctival irritations were noted for two animals. Corneal irritation subsided by study day 7 and conjunctival irritation subsided by study termination (study day 17). The left (control) eyes were free of evidence of ocular irritation and other findings for the duration of the study. According to EU and CLP criteria, the mean scores for corneal reactions, iritis, conjunctival redness and chemosis were 0.55, 0, 1.44 and 1.0, respectively. Based on the mean scores obtained, a classification as an eye irritant is not required.

No in vitro or human data are available for eye corrosion/irritation.

Conclusion used in Risk Assessment – Eye irritation	
Value/conclusion	Biocidal product not classified for eye corrosion/irritation according to (EU) nr. 1272/2008

Justification for the value/conclusion	Mean scores for corneal reactions, iritis, conjunctival redness and chemosis do not trigger a classification.
Classification of the product according to CLP and DSD	none

(III) Respiratory tract irritation

Conclusion used in the Risk Assessment – Respiratory tract irritation	
Justification for the conclusion	Neither the active ingredient nor one of the other relevant ingredients of the biocidal product are classified with respect to respiratory tract irritation. Insect Repellent Lotion IR3535® 10 % does not pose a respiratory tract irritation hazard.
Classification of the product according to CLP and DSD	There is no indication that a classification with respect to respiratory tract irritation is necessary for Insect Repellent Lotion IR3535® 10 %.

(IV) Skin sensitization

Summary table of animal studies on skin sensitisation					
Method, Guideline, GLP status, . Reliability	**Species, Strain, Sex, No/group**	**Test substance, Vehicle, Dose levels, duration of exposure Route of exposure *(topical/intradermal, if relevant)***	**Results *(EC3-value or amount of sensitised animals at induction dose); evidence for local or systemic toxicity (time course of onset)***	**Remarks *(e.g. major deviations)***	**Reference**
OECD 406 OPPTS 870.2600 EU 92/69 Annex V, B6 GLP=yes Rel=1	Guinea pig Hartley [Crl: HA] 10 ♂ and 10 ♀/ test group 5 ♂ and 5 ♀/ naïve control group	US Lotion Formulation No vehicle Undiluted 0.3 ml/site 6h exposure Epicutaneous, occlusive	No positive dermal reactions in the test or the naive control groups No deaths, no test article related clinical findings, no remarkable bw changes	Identity of test material slightly different from BP: buffers added (1% in total) and omission of preservatives (1% in total)	[redacted] (2006) (c)

Dermal Observations and Severity Indices ([redacted] 2006 (c))

Dermal Scores													
Group	**Material**	**24 hour**					**48 hour**					**Severity Index**		**Incidence Index**
		0	+/-	1	2	3	0	+/-	1	2	3	24 h	48 h	
Test		20	0	0	0	0	20	0	0	0	0	0.0	0.0	0 %
Naive Control-I		10	0	0	0	0	10	0	0	0	0	0.0	0.0	NA

TA = Test Article
NA = Not Applicable

The sensitisation potential of the US lotion formulation was evaluated using the modified Buehler test method.

There were no deaths, test article-related clinical findings or remarkable body weight changes during the study period. Following challenge dosing with the US lotion formulation, there were no positive dermal reactions (score ≥ 1) in the test or the naive control groups. The Incidence Index for the test group with a score ≥ 1 was 0 % (0/20) following challenge dosing.

In the positive control experiments which were performed as a separate study, the positive control substance HCA was a sensitizer when administered as both a 10 % concentration in 70/30 (v/v) in acetone/PEG 400 and a 20 % concentration in 70/30 (v/v) in acetone/PEG 400 under the conditions of the study, thereby demonstrating the reliability of the experimental design. The mean incidence indices for the positive controls were 20 % and 60 % at a concentration of 10 % and 20 %, respectively. This confirms the reliability of the test system as indicated by the dose-response relationship.

The US lotion formulation induced no skin sensitisation reactions in albino guinea pigs when using the modified Buehler test method. A classification with respect to skin sensitisation is not required.

No *in vitro* or human data are available for skin sensitisation.

Conclusion used in Risk Assessment – Skin sensitisation	
Value/conclusion	Biocidal product not classified for skin sensitisation according to (EU) nr. 1272/2008
Justification for the value/conclusion	Following challenge dosing with the US lotion formulation, there were no positive dermal reactions (score ≥ 1) in the test or the naive control groups. The Incidence Index for the test group with a score ≥ 1 was 0 % (0/20) following challenge dosing.
Classification of the product according to CLP and DSD	none

(V) Respiratory sensitization (ADS)

Conclusion used in Risk Assessment – Respiratory sensitisation	
Value/conclusion	
Justification for the value/conclusion	None of the ingredients of the product are known to be sensitizing to the respiratory tract. Moreover, from tests in guinea pigs the product was proven not to exert any skin sensitizing properties. In addition, the active ingredient IR3535® did not show a sensitizing or photosensitizing potential from tests in guinea pigs. Finally, IR3535® products are on the market for more than 40 years and there are no indications for any sensitizing potential neither to the skin nor to the respiratory tract. Based on all these data it is thus concluded that the product is not sensitizing to the respiratory tract.

Classification of the product according to CLP and DSD	none

(VI) Acute toxicity

a. Acute toxicity by oral route

Value used in the Risk Assessment – Acute oral toxicity	
Value	Biocidal product not classified for acute oral toxicity according to (EU) nr. 1272/2008
Justification for the selected value	Neither the active ingredient nor one of the components of the product are classified with respect to acute oral toxicity. Thus, Insect Repellent Lotion IR3535® 10 % has no potential for an acute oral toxicity hazard and no classification with respect to acute oral toxicity is required. No human data are available for acute oral toxicity.
Classification of the product according to CLP and DSD	none

Data waiving	
Information requirement	Acute oral toxicity: Study scientifically unjustified
Justification	Since the acute oral toxicity of Insect Repellent Lotion IR3535® 10% can be assessed on the basis of the properties of the ingredients, the performance of an acute oral toxicity study with the biocidal product is scientifically not justified. See IUCLID data point 8.5.1 Endpoint study record: Acute toxicity: oral.001 and confidential PAR section 1.2. There are valid data available on each of the components in the mixture sufficient to allow classification of the mixture according to the rules laid down in Regulation (EC) No 1272/2008 (CLP), and synergistic effects between any of the components are not expected.

b. Acute toxicity by inhalation

No human data are available for acute inhalation toxicity.

Value used in the Risk Assessment – Acute inhalation toxicity	
Value	Biocidal product not classified for acute toxicity (inhalation) according to (EU) nr. 1272/2008
Justification for the selected value	None of the relevant components of the biocide are classified for acute inhalation toxicity according to (EU) nr. 1272/2008.
Classification of the product according to CLP and DSD	none

Data waiving	
Information requirement	Acute inhalation toxicity: Study scientifically unjustified
Justification	Since the acute inhalation toxicity of Insect Repellent Lotion IR3535® 10% can be assessed on the basis of the properties of the ingredients, the performance of an acute inhalation toxicity study with the biocidal product is scientifically not justified. See IUCLID data point 8.5.2 Endpoint study record: Acute toxicity: inhalation.001 and confidential PAR section 1.2. There are valid data available on each of the components in the mixture sufficient to allow classification of the mixture according to the rules laid down in Regulation (EC) No 1272/2008 (CLP), and synergistic effects between any of the components are not expected.

c. Acute toxicity by dermal route

Summary table of animal studies on acute dermal toxicity						
Method, Guideline, GLP status, Reliability	**Species, strain, Sex, No/group**	**Test substance, Vehicle, Dose levels, Surface area**	**Signs of toxicity** *(nature, onset, duration, severity, reversibility)*	**LD50**	**Remarks** *(e.g. major deviations)*	**Reference**
OECD 402 EU 92/69 Annex V, B.3 EPA OPPTS 870.1200 GLP=yes Rel=1	Rat Crl:CD(SD) 5♀, 5♂/dose	US Lotion Formulation Undiluted 5000 mg/kg bw 10% of body area Semiocclusive	See below	>5000 mg/kg bw	Identity of test material slightly different from BP: buffers added (1% in total) and omission of preservatives (1% in total)	[redacted] (2006) (d)

There were no deaths, remarkable body weight changes or macroscopic findings at the scheduled necropsy. Clinical findings included abnormal excretion, various discoloured areas due to discharges/excretions and hair loss on the forelimbs, and persisted until study termination on day 14. Dermal findings noted during the study consisted of very slight (grade 1) erythema, very slight (grade 1) edema, pinpoint scabbing and yellow discoloration at the dose sites. Very slight erythema (grade 1) persisted to study termination (study at day 14). Macroscopic findings consisted of a dilated pelvis of the right kidney for 1 male, multiple irregularly shaped white areas on the spleen of 1 male, and enlarged medial lymph node for 2 females.

Based on the results of this study, the LD_{50} of the US lotion formulation was greater than 5000 mg/kg bw when administered once for 24 hours to the clipped, unabraded skin of male and female albino rats. A classification of the biocidal product with respect to acute dermal toxicity is not required.

No human data are available for acute dermal toxicity.

Value used in the Risk Assessment – Acute dermal toxicity	
Value	Biocidal product not classified for acute dermal toxicity according to (EU) nr. 1272/2008
Justification for the selected value	In an acute dermal toxicity study, the LD_{50} of the US lotion formulation was greater than 5000 mg/kg bw.
Classification of the product according to CLP and DSD	none

(VII)Information on dermal absorption

A dermal penetration study has not been performed with Insect Repellent Lotion IR3535® 10%. However, there is other data available that can be used.

In a dermal toxicokinetics/metabolism study with 5 male and 5 female human volunteers, the dermal absorption of the active substance IR3535® from a pump spray containing 20 % IR3535® has been determined in parallel. In this study, approx. 3 grams of the formulation were applied once to hands, arms, legs, feet, face and neck of each volunteer (ca. 50 % of total body area). The total amount of IR3535® and its metabolite IR3535®-free acid excreted with the urine over a period of 48 hours presented 13.3% of the dermal dose of IR3535® applied. Since IR3535® is rapidly and extensively metabolized and as IR3535®-free acid has a low molecular weight and high water solubility, it is expected that urinary excretion of IR3535®-free acid and IR3535® represents the total extent of absorption of IR3535® in humans and a distribution to organs and tissues is considered to be negligible.

The results of this study have been summarized in in the active substance dossier and were assessed for the approval of IR3535®.

The assessment of this study resulted in an overall dermal penetration of 14% IR3535®.

In contrast to Insect Repellent Pump Spray IR3535® 20% which contains a large amount of ethanol, Tween 20 and polyethylene glycols, all of which are known to enhance the skin penetration of substance, Insect Repellent Lotion IR3535® 10 contains only a few ingredients which might slightly influence the penetration of substances; the concentration of these skin penetration enhancing compounds is much lower compared to the concentration in the Pump Spray. The use of a skin absorption of 14% as derived from the dermal toxicokinetics/metabolism study performed with the pump spray represents, thus, a worst case for Insect Repellent Lotion IR3535® 10 and will be used in the human exposure assessments for the intended use of the biocidal product.

See IUCLID datapoint 8.6 Dermal absorption Endpoint study record: Dermal absorption.001.

Note: During the RCOM it became apparent that there was a divergence in opinions between cMS on the correct value to be used in the risk assessment. BE decided to use the highest of the 2 values discussed, which is the 14% value proposed above. We refer to the confidential annex section 2.6 for a comparison between the BP under evaluation and the formula from which the 14% value was derived.

Value(s) used in the Risk Assessment – Dermal absorption			
Substance	IR3535® in Insect Repellent Pump Spray IR3535® 20%		
Value(s)*	14% dermal absorption		
Justification for the selected value(s)	Read-across from human volunteer study on a water/ethanol-based 20 % IR3535® formulation (Dekant, 2010)		

Data waiving	
Information requirement	Skin absorption study
Justification	Read-across from human volunteer study on a water/ethanol-based 20% IR3535® formulation

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

There are valid data available on each of the components in the mixture sufficient to allow classification of the mixture according to the rules laid down in Directive 1999/45/EC and Regulation (EC) No 1272/2008 (CLP), and synergistic effects between any of the components are not expected.

For endpoints beyond acute toxicity, irritation and sensitization, we refer to the confidential PAR, section 1.2, which includes a breakdown of the formula under evaluation indicating the classification of each component in the formula.

For an overview of the formula and the potential presence of substances of concern, we refer to section 2.5 of the confidential PAR.

(IX) Available toxicological data relating to a mixture

Available toxicological data relating to a mixture that a substance(s) of concern is a component of

There are valid data available on each of the components in the mixture sufficient to allow classification of the mixture according to the rules laid down in Directive 1999/45/EC and Regulation (EC) No 1272/2008 (CLP), and synergistic effects between any of the components are not expected.

(X) Other

Not applicable.

2.2.7.2 Exposure assessment

The composition of the representative product from the CAR for IR3535® is not identical to that of Insect Repellent Lotion IR3535® 10%. The representative product from the CAR contains 20% of active substance while Insect Repellent Lotion contains 10%. It does not contain substances of toxicological concern apart IR3535®.

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

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

This product exposure assessment is based on the recommendation 11 of the BPC Ad hoc Working Group on Human Exposure : Proposal for harmonising the assessment of human exposure to repellents (PT19) – Version 2.1 agreed at WGV 2017 and on the assessment report of the active substance.

For primary exposure, the most relevant route of exposure is the dermal route. Applying a lotion would not give significant inhalative exposure. Direct oral exposure is not considered to be relevant because of the repellent taste (bad palatability) of the active substance and because the biocidal product is not intended to be applied by children younger than 12 years.

For secondary exposure, dermal exposure is possible for adults treating or handling children. However this scenario is fully covered by primary adult dermal exposure. Hand to mouth transfer is also possible for adults and children; nonetheless, the biocidal product is not intended to be applied on children's hands which reduces potential oral uptake of the dermally applied active substance. For inhalative exposure, the inhalation of volatilized residues after application is also relevant.

(I) General information

General default values for exposure assessment

Default value considering age groups[1]			
Age groups	**Body weight [kg]**	**Respiration rate [m³/air/hour]**	**Total body surface area [cm²]**
ADULT irrespective of gender (based on female 30 to <40 years old)	60	1.25	16600
CHILD 6 to < 12 years old irrespective of gender (based on female 6 to <11 years old)	23.9	1.32	9200
CHILD 2 to < 6 years old irrespective of gender (based on data from female 2 to <6 years old)	15.6	1.26	6800
TODDLER 1 to <2 years old irrespective of gender (based on female 1 to <2 years old)	10	1.26	4800
INFANT < 1 year old irrespective of gender (based on female 6 to <12 months old)	8	0.84	4100

[1] Recommendation no. 14 of the BPC Ad hoc Working Group on Human Exposure Default human factor values for use in exposure assessments for biocidal products (revision of HEEG opinion 17 agreed at the Human Health Working Group III on 12 June 2017)

Treated surface, applied amount of biocidal product and number of application per day:

Treated surface:

The treated surface is assumed to be the uncovered parts of the body. According Recommendation no. 11 of the BPC Ad hoc Working Group on Human Exposure : Proposal for harmonising the assessment of human exposure to repellents (PT19) (Version 2.1 agreed at Human Health Working Group V on 22 November 2017), the uncovered body surface area corresponds to **55**% of the total body surface.

Amount of biocidal product:

Following the efficacy assessment for this product, the efficacious application rate is : 0.001 g biocidal product/cm² of skin against ticks and 0.00115 g/cm² against mosquitoes.

Number of application per day:

The applicant proposed : "Insect Repellent Lotion IR3535® 10% is intended to be used in Europe in summer when insects are frequent. It is usually applied once a day depending on outdoor activities, weather and presence of insects. The product can be applied (face, hands, arms and legs) up to 7 times per day for adults, up to 4 times for children < 10 years and maximally 2 times per day for smaller children and infants. The frequency must be reduced if more body parts are treated."

The age categories proposed in Recommendation no. 14 of the BPC Ad hoc Working Group on Human Exposure were used, this differ from the intended uses proposed by the applicant.

Summary : Amount of product used per application for the different age groups, treated surface and number of application per day				
Age groups	**Amount of product used per application [g]** **Mosquitoes (1.15 mg/cm²)**	**Amount of product used per application [g]** **Ticks (1.0 mg/cm²)**	**Treated surface [cm²]**	**Number of applications per day (as initially applied by the applicant. These assumptions do not correspond with the outcome of the risk assessment)**
ADULT irrespective of gender (based on female 30 to <40 years old)	10.4995	9.130	9130	7 applications/day
CHILD 6 to < 12 years old irrespective of gender (based on female 6 to <11 years old)	5.819	5.060	5060	4 applications/day
CHILD 2 to < 6 years old irrespective of gender (based on data from female 2 to <6 years old)	4.301	3.7404	3740	2 applications/day
TODDLER 1 to <2 years old irrespective of gender (based on female 1 to <2 years old)	3.036	2.640	2640	2 application/day
INFANT < 1 year old irrespective of gender (based on female 6 to <12 months old)	2.59325	2.255	2255	2 application/day

Following a referral to the coordination group: it was agreed by consensus on 16 September 2019 that the application rate for the non-professional uses will be expressed as ml per application since the product packaging size is expressed in ml. Considering the density of the product (d= 1.008), the following application amount are calculated:

Age groups	**Amount of product used per application [mL]** **Mosquitoes (1.16 µL/cm²)**	**Amount of product used per application [mL]** **Ticks (1.01 µL/cm²)**
ADULT irrespective of gender (based on female 30 to <40 years old)	10.58	9.20
CHILD 6 to < 12 years old irrespective of gender (based on female 6 to <11 years old)	5.87	5.10
CHILD 2 to < 6 years old irrespective of gender (based on data from female 2 to <6 years old)	4.33	3.77
TODDLER 1 to <2 years old irrespective of gender (based on female 1 to <2 years old)	3.06	2.66
INFANT < 1 year old irrespective of gender (based on female 6 to <12 months old)	2.61	2.27

Dermal, inhalatory and oral absorption:

- Inhalatory absorption : 100 %
- Dermal absorption : 14 %
- Oral absorption : 100 %

(II) List of scenarios

Insect Repellent Lotion IR3535® 10 % is used by the general public. The primary route of exposure is dermal.

Oral exposure by hand-to-mouth transfer is not considered to be a significant route of primary exposure, because of the repellent taste (bad palatability) of the active substance, thus, preventing repeated mouthing of IR3535® by children and infants. Furthermore, the biocidal product is not intended to be applied on hands of children which excludes an oral uptake of the dermally applied active substance.

Dermal secondary exposure is possible for adults treating or handling children. However, this scenario is fully covered by primary adult dermal exposure.

Hand to mouth transfer has been developed consistently with the DEET dossier.

Inhalation of volatilized residues after application is relevant. The exposure to volatilised residues indoors was calculated with ConsExpo.

Summary table: scenarios			
Scenario number	**Scenario** (e.g. mixing/ loading)	**Primary or secondary exposure Description of scenario**	**Exposed group** (e.g. professionals, non-professionals, bystanders)
1.	Application phase	Primary exposure: Dermal exposure assessment for adults, children, toddlers and infants.	Non-professionals
2.	Post-application phase	Secondary exposure (indirect exposure as a result of use): Hand-mouth transfer reverse reference scenario (oral exposure)	Non-professionals
3.	Post-application phase	Inhalation of volatilised residues after application (inhalative exposure)	Non-professionals

(III) Industrial exposure

There is no concern about industrial exposure because of the intend of use apart for the production/formulation and disposal of the biocidal product. This exposure is address under a point below.

(IV) Professional exposure

Not relevant since the product Insect Repellent Lotion IR3535® 10% is intended to be used by general public.

(V) Non-professional exposure

USE 1 against mosquitoes – application rate 1.15 mg/cm²

Scenario 1: Primary exposure: Dermal exposure assessment for adults, children, toddlers and infants.

Description of Scenario 1
This scenario is based on the one available in the CAR of IR3535®. It has been updated according the recommendation 11 of the BPC Ad hoc Working Group on Human Exposure : Proposal for harmonising the assessment of human exposure to repellents (PT19) – Version 2.1 agreed at WGV 2017.
Dermal exposure: Number of application/day x amount b.p./application x percent of a.s. in b.p. **Systemic exposure:** Dermal exposure x percent of dermal absorption **Dermal systemic exposure:** Systemic exposure / body weight

	Parameters	**Value**
For All categories	Dermal absorption[1]	14%
	% of active substance in biocidal product[1]	10%
Tier 1- Adult	Number of application / day[1]	7
	Body weight[1]	60 kg
	Amount of biocidal product/ application[1]	10.50 g
Tier 1- Child 6 to < 12 years old	Number of application / day[1]	4
	Body weight[1]	23.9 kg
	Amount of biocidal product/ application[1]	5.82 g
Tier 1- Child 2 to < 6 years old	Number of application / day[1]	2
	Body weight[1]	15.6 kg
	Amount of biocidal product/ application[1]	4.30 g
Tier 1- Toddler	Number of application / day[1]	2
	Body weight[1]	10 kg
	Amount of biocidal product/ application[1]	3.04 g
Tier 1- Infant	Number of application / day[1]	2
	Body weight[1]	8 kg
	Amount of biocidal product/ application[1]	2.59 g
Tier 2- Adult	Number of application / day[2]	6
Tier 2- Child 6 to < 12 years old	Number of application / day[2]	3
Tier 2- Child 2 to < 6 years old	Number of application / day[2]	1
Tier 2- Toddler	Number of application / day[2]	1
Tier 2- Infant	Number of application / day[2]	1
Tier 3- Adult	Number of application / day[3]	2
Tier 3- Child 6 to < 12 years old	Number of application / day[3]	1

[1] General information, see justification above
[2] Limitation of the exposure

[3] Limitation of the exposure (to the maximum safe use)

Calculations for scenario 1

Summary table: estimated exposure for Dermal Primary exposure		
Exposure scenario	**Tier/PPE**	**Estimated dermal uptake**
Scenario 1 – ADULT 7 applications/day	Tier 1 / no PPE	17.15 mg/kg bw/day
Scenario 1 – CHILD (6-12) 4 applications/day	Tier 1 / no PPE	13.63 mg/kg bw/day
Scenario 1 – CHILD (2-6) 2 applications/day	Tier 1 / no PPE	7.72 mg/kg bw/day
Scenario 1 – TODDLER 2 applications/day	Tier 1 / no PPE	8.50 mg/kg bw/day
Scenario 1 – INFANT 2 applications/day	Tier 1 / no PPE	9.08 mg/kg bw/day
Scenario 1 – ADULT 6 applications/day	Tier 2 / no PPE	14.70 mg/kg bw/day
Scenario 1 – CHILD (6-12) 3 applications/day	Tier 2 / no PPE	10.23 mg/kg bw/day
Scenario 1 – CHILD (2-6) 1 application/day	Tier 2 / no PPE	3.86 mg/kg bw/day
Scenario 1 – TODDLER 1 application/day	Tier 2 / no PPE	4.25 mg/kg bw/day
Scenario 1 – INFANT 1 application/day	Tier 2 / no PPE	4.54 mg/kg bw/day
Scenario 1 – ADULT 2 applications/day	Tier 3 / no PPE	4.90 mg/kg bw/day
Scenario 1 – CHILD (6-12) 1 application/day	Tier 3 / no PPE	3.41 mg/kg bw/day

Scenario 2: Secondary exposure (indirect exposure as a result of use): Hand-mouth transfer reverse reference scenario (oral exposure)

Description of Scenario 2

This scenario is based on the one available in the CAR of IR3535®. It has been updated according the recommendation 11 of the BPC Ad hoc Working Group on Human Exposure : Proposal for harmonising the assessment of human exposure to repellents (PT19) – Version 2.1 agreed at WGV 2017.

Hand to mouth transfer might be possible for small children. However this scenario is not considered to be a significant route of exposure because of bad palatability (bitterness) preventing repeated mouthing by small children and you may not apply to children's hand.

At TM IV 2010, it was agreed to develop the scenario "hand-mouth transfer" consistently with the DEET dossier evaluated by SE and to be discussed with HEEG and TM agreed not to sum up the two routes (oral and dermal) in small children.

Reverse reference scenario is included to show how much IR3535® anyone can be exposed to, after oral exposure without exceeding reference dose (AEL for IR3535® is 5 mg/kg bw/d).

External dermal amount of a.s. per application:

Amount of b.p./application x percent of a.s. in b.p. / body weight

Oral systemic exposure via hand-mouth transfer is:

External dermal amount of a.s. per application x Factor for oral intake by hand-mouth transfer x oral absorption

Number of time of application b.p. before exceeding the AEL via hand-mouth transfer :

AEL / Oral systemic exposure via hand-mouth transfer

As a worst case, the scenario has been assessed considering that the whole body is treated.

	Parameters[1]	**Value**
For All categories	Oral absorption[1]	100%
	% of active substance in biocidal product[1]	10%
Tier 1- Adult	Factor for oral intake by hand-mouth transfer[2]	4 %
	Body weight[1]	60 kg
	Amount of biocidal product/ application[1]	10.50 g
Tier 1- Child 6 to < 12 years old	Factor for oral intake by hand-mouth transfer[2]	8 %
	Body weight[1]	23.9 kg
	Amount of biocidal product/ application[1]	5.82 g
Tier 1- Child 2 to < 6 years old	Factor for oral intake by hand-mouth transfer[2]	8 %
	Body weight[1]	15.6 kg
	Amount of biocidal product/ application[1]	4.30 g
Tier 1- Toddler	Factor for oral intake by hand-mouth transfer[2]	8 %
	Body weight[1]	10 kg
	Amount of biocidal product/ application[1]	3.04 g
Tier 1- Infant	Factor for oral intake by hand-mouth transfer[2]	8 %
	Body weight[1]	8 kg
	Amount of biocidal product/ application[1]	2.59 g

[1] General information, see justification above

[2] Recommendation 11 of the BPC Ad hoc Working Group on Human Exposure : Proposal for harmonising the assessment of human exposure to repellents (PT19) – Version 2.1 agreed at WGV 2017.

Calculations for scenario 2

Summary table: estimated exposure for Hand-mouth transfer reverse reference scenario (oral exposure)		
Exposure scenario	**Tier/PPE**	**Calculated exposure to IR3535®**
Scenario 2 – ADULT	Tier 1 / no PPE	Adult up to 7.14 applications
Scenario 2 – CHILD (6-12)	Tier 1 / no PPE	Child (6-12) up to 2.57 applications
Scenario 2 – CHILD (2-6)	Tier 1 / no PPE	Child (2-6) up to 2.27 applications
Scenario 2 – TODDLER	Tier 1 / no PPE	Toddler up to 2.06 applications
Scenario 2 – INFANT	Tier 1 / no PPE	Infant up to 1.93 applications

Scenario 3: Inhalation of volatilised residues after application (inhalative exposure)

Description of Scenario 3

This scenario is not based on the one available in the CAR of IR3535® because it's has been demonstrated that the SVC could exceed 1% in a number of cases. Considering HEEG opinion 13 (Assessment of Inhalation Exposure of Volatilized Biocide Active Substance), the inhalation of volatilised residues after application has to be taken into account for this product.

This scenario is based on the one available in the CAR of IR3535®. It has been updated according the recommendation 11 of the BPC Ad hoc Working Group on Human Exposure : Proposal for harmonising the assessment of human exposure to repellents (PT19) – Version 2.1 agreed at WGV 2017.

Inhalation of volatilized residues after application is relevant considering the HEEG opinion on Assessment of Inhalation Exposure of Volatilized Biocide Active Substance:

$$\frac{0.328 \times 215.29 \times 0.15}{5} = 2.12$$

The result of this equation is superior to 1 which means that the inhalation exposure couldn't be considered as negligible.
So this exposure was assessed using ConsExpo – exposure to vapour – instantaneous release.

General inputs to the model :
Exposure duration: 24 hours (all day)
Product amount: calculated dependant of the amount applied per day and per age categories
Weight fraction compound: 10% (biocidal product information)
Room volume: 20m^3 (default value of ConsExpo)
Ventilation rate: 0.6 /h (default value of ConsExpo)

Vapour pressure: 0.15 Pa (at 20 °C) (active substance information)
Molecular weight: 215.29 g/mol (active substance information)
Temperature : 25°c (ambient temperature)

	Parameters	**Value**
Tier 1- Adult	Product amount[1]	21.0 g
	Body weight[2]	60 kg
	Respiration rate [m^3/air/hour][2]	1.25 m³/h
Tier 1- Child 6 to < 12 years old	Product amount[1]	5.82 g
	Body weight[2]	23.9 kg
	Respiration rate [m^3/air/hour][2]	1.32 m³/h
Tier 1- Child 2 to < 6 years old	Product amount[1]	4.30 g
	Body weight[2]	15.6 kg
	Respiration rate [m^3/air/hour][2]	1.26 m³/h
Tier 1- Toddler	Product amount[1]	3.04 g
	Body weight[2]	10 kg
	Respiration rate [m^3/air/hour][2]	1.26 m³/h
Tier 1- Infant	Product amount[1]	2.59 g
	Body weight[2]	8 kg
	Respiration rate [m^3/air/hour][2]	0.84 m³/h

[1] According the primary exposure, only two applications per day can be authorized for adults and one application per day for the other age categories. Therefore, the product amount corresponds to 2 application/day for adults and 1 application/day for child, toddler and infant.
[2] General information, see justification above

Calculations for scenario 3

Summary table: estimated exposure for inhalation of volatilised residues after application (inhalative exposure)		
Exposure scenario	**Tier / PPE**	**Estimated inhalation uptake of volatilised residues after application**
Scenario 3 – ADULT	Tier 1 / no PPE	3.65 mg/kg bw/day
Scenario 3 – CHILD (6-12)	Tier 1 / no PPE	2.68 mg/kg bw/day
Scenario 2 – CHILD (2-6)	Tier 1 / no PPE	2.89 mg/kg bw/day
Scenario 3 – TODDLER	Tier 1 / no PPE	3.19 mg/kg bw/day
Scenario 3 – INFANT	Tier 1 / no PPE	2.27 mg/kg bw/day

Combined exposure :

Combined exposure is not performed in this case considering the following facts:

- Dermal exposure and inhalation exposure: to addition of the two routes of exposure will result in an unrealistic worst case as it is considered that all the product applied will be available for dermal exposure and for inhalation exposure. A part of the product will either be only absorbed by dermal route or by inhalation route and therefore will not be available for the other route.
  It is not possible to know which route will be the most used. Therefore, it was considered that all the product might be absorbed by one or the other route as a worst case and that it should not be summed up.
- Oral exposure by hand-to-mouth transfer is not considered to be a significant route of primary exposure, because of the repellent taste (bad palatability) of the active substance, thus, preventing repeated mouthing of IR3535® by children and infants. Furthermore, the biocidal product is not intended to **be applied on hands of children** which excludes an oral uptake of the dermally applied active substance. The scenario could be seen as a worst case and therefore should not be added to the total exposure. In addition, a part of it, will not be available anymore for oral uptake since it will be dermally absorbed.

USE 2 against ticks – application rate 1.0 mg/cm²

Scenario 1: Primary exposure: Dermal exposure assessment for adults, children, toddlers and infants.

Description of Scenario 1
This scenario is based on the one available in the CAR of IR3535®. It has been updated according the recommendation 11 of the BPC Ad hoc Working Group on Human Exposure : Proposal for harmonising the assessment of human exposure to repellents (PT19) – Version 2.1 agreed at WGV 2017.
Dermal exposure: Number of application/day x amount b.p./application x percent of a.s. in b.p. **Systemic exposure:** Dermal exposure x percent of dermal absorption **Dermal systemic exposure:** Systemic exposure / body weight

	Parameters	**Value**
For All categories	Dermal absorption[1]	14%
	% of active substance in biocidal product[1]	10%
Tier 1- Adult	Number of application / day[1]	7
	Body weight[1]	60 kg
	Amount of biocidal product/ application[1]	9.13 g
Tier 1- Child 6 to < 12 years old	Number of application / day[1]	4
	Body weight[1]	23.9 kg
	Amount of biocidal product/ application[1]	5.06 g
Tier 1- Child 2 to < 6 years old	Number of application / day[1]	2
	Body weight[1]	15.6 kg
	Amount of biocidal product/ application[1]	3.74 g
Tier 1- Toddler	Number of application / day[1]	2
	Body weight[1]	10 kg
	Amount of biocidal product/ application[1]	2.64 g
Tier 1- Infant	Number of application / day[1]	2
	Body weight[1]	8 kg
	Amount of biocidal product/ application[1]	2.255 g
Tier 2- Adult	Number of application / day[2]	6
Tier 2- Child 6 to < 12 years old	Number of application / day[2]	3
Tier 2- Child 2 to < 6 years old	Number of application / day[2]	1
Tier 2- Toddler	Number of application / day[2]	1
Tier 2- Infant	Number of application / day[2]	1
Tier 3- Adult	Number of application / day[3]	2
Tier 3- Child 6 to < 12 years old	Number of application / day[3]	1

[1] General information, see justification above
[2] Limitation of the exposure
[3] Limitation of the exposure (to the maximum safe use)

2.2.7.2.1.1.1.1 Calculations for scenario 1

Summary table: estimated exposure for Dermal Primary exposure		
Exposure scenario	**Tier/PPE**	**Estimated dermal uptake**
Scenario 1 – ADULT 7 applications/day	Tier 1 / no PPE	14.91 mg/kg bw/day
Scenario 1 – CHILD (6-12) 4 applications/day	Tier 1 / no PPE	11.86 mg/kg bw/day
Scenario 1 – CHILD (2-6) 2 applications/day	Tier 1 / no PPE	6.71 mg/kg bw/day
Scenario 1 – TODDLER 2 applications/day	Tier 1 / no PPE	7.39 mg/kg bw/day
Scenario 1 – INFANT 2 applications/day	Tier 1 / no PPE	7.89 mg/kg bw/day
Scenario 1 – ADULT 6 applications/day	Tier 2 / no PPE	12.78 mg/kg bw/day
Scenario 1 – CHILD (6-12) 3 applications/day	Tier 2 / no PPE	8.89 mg/kg bw/day
Scenario 1 – CHILD (2-6) 1 application/day	Tier 2 / no PPE	3.36 mg/kg bw/day
Scenario 1 – TODDLER 1 application/day	Tier 2 / no PPE	3.70 mg/kg bw/day
Scenario 1 – INFANT 1 application/day	Tier 2 / no PPE	3.95 mg/kg bw/day
Scenario 1 – ADULT 2 applications/day	Tier 3 / no PPE	4.26 mg/kg bw/day
Scenario 1 – CHILD (6-12) 1 application/day	Tier 3 / no PPE	2.96 mg/kg bw/day

Scenario 2: Secondary exposure (indirect exposure as a result of use): Hand-mouth transfer reverse reference scenario (oral exposure)

Description of Scenario 2

This scenario is based on the one available in the CAR of IR3535®. It has been updated according the recommendation 11 of the BPC Ad hoc Working Group on Human Exposure : Proposal for harmonising the assessment of human exposure to repellents (PT19) – Version 2.1 agreed at WGV 2017.

Hand to mouth transfer might be possible for small children. However this scenario is not considered to be a significant route of exposure because of bad palatability (bitterness) preventing repeated mouthing by small children and you may not apply to children's hand.

At TM IV 2010, it was agreed to develop the scenario "hand-mouth transfer" consistently with the DEET dossier evaluated by SE and to be discussed with HEEG and TM agreed not to sum up the two routes (oral and dermal) in small children.

Reverse reference scenario is included to show how much IR3535® anyone can be exposed to, after oral exposure without exceeding reference dose (AEL for IR3535® is 5 mg/kg bw/d).

External dermal amount of a.s. per application:

Amount of b.p./application x percent of a.s. in b.p. / body weight

Oral systemic exposure via hand-mouth transfer is:

External dermal amount of a.s. per application x Factor for oral intake by hand-mouth transfer x oral absorption

Number of time of application b.p. before exceeding the AEL via hand-mouth transfer :

AEL / Oral systemic exposure via hand-mouth transfer

As a worst case, the scenario has been assessed considering that the whole body is treated.

	Parameters[1]	**Value**
For All categories	Oral absorption[1]	100%
	% of active substance in biocidal product[1]	10%
Tier 1- Adult	Factor for oral intake by hand-mouth transfer[2]	4 %
	Body weight[1]	60 kg
	Amount of biocidal product/ application[1]	9.13 g
Tier 1- Child 6 to < 12 years old	Factor for oral intake by hand-mouth transfer[2]	8 %
	Body weight[1]	23.9 kg
	Amount of biocidal product/ application[1]	5.06 g
Tier 1- Child 2 to < 6 years old	Factor for oral intake by hand-mouth transfer[2]	8 %
	Body weight[1]	15.6 kg
	Amount of biocidal product/ application[1]	3.74 g
Tier 1- Toddler	Factor for oral intake by hand-mouth transfer[2]	8 %
	Body weight[1]	10 kg
	Amount of biocidal product/ application[1]	2.64 g
Tier 1- Infant	Factor for oral intake by hand-mouth transfer[2]	8 %
	Body weight[1]	8 kg
	Amount of biocidal product/ application[1]	2.255 g

[1] General information, see justification above

[2] Recommendation 11 of the BPC Ad hoc Working Group on Human Exposure : Proposal for harmonising the assessment of human exposure to repellents (PT19) – Version 2.1 agreed at WGV 2017.

2.2.7.2.1.1.1.2 Calculations for scenario 2

Summary table: estimated exposure for Hand-mouth transfer reverse reference scenario (oral exposure)		
Exposure scenario	**Tier/PPE**	**Calculated exposure to IR3535®**
Scenario 2 – ADULT	Tier 1 / no PPE	Adult up to 8.21 applications
Scenario 2 – CHILD (6-12)	Tier 1 / no PPE	Child (6-12) up to 2.95 applications
Scenario 2 – CHILD (2-6)	Tier 1 / no PPE	Child (2-6) up to 2.61 applications
Scenario 2 – TODDLER	Tier 1 / no PPE	Toddler up to 2.37 applications
Scenario 2 – INFANT	Tier 1 / no PPE	Infant up to 2.22 applications

Scenario 3: Inhalation of volatilised residues after application (inhalative exposure)

Description of Scenario 3

This scenario is not based on the one available in the CAR of IR3535® because it's has been demonstrated that the SVC could exceed 1% in a number of cases. Considering HEEG opinion 13 (Assessment of Inhalation Exposure of Volatilized Biocide Active Substance), the inhalation of volatilised residues after application has to be taken into account for this product.

This scenario is based on the one available in the CAR of IR3535®. It has been updated according the recommendation 11 of the BPC Ad hoc Working Group on Human Exposure : Proposal for harmonising the assessment of human exposure to repellents (PT19) – Version 2.1 agreed at WGV 2017.

Inhalation of volatilized residues after application is relevant considering the HEEG opinion on Assessment of Inhalation Exposure of Volatilized Biocide Active Substance:

$$\frac{0.328 \times 215.29 \times 0.15}{5} = 2.12$$

The result of this equation is superior to 1 which means that the inhalation exposure couldn't be considered as negligible.
So this exposure was assessed using ConsExpo – exposure to vapour – instantaneous release.

General inputs to the model :
Exposure duration: 24 hours (all day)
Product amount: calculated dependant of the amount applied per day and per age categories
Weight fraction compound: 10% (biocidal product information)
Room volume: 20m^3 (default value of ConsExpo)
Ventilation rate: 0.6 /h (default value of ConsExpo)

Vapour pressure: 0.15 Pa (at 20 °C) (active substance information)
Molecular weight: 215.29 g/mol (active substance information)
Temperature : 25°c (ambient temperature)

	Parameters	**Value**
Tier 1- Adult	Product amount[1]	18.26 g
	Body weight[2]	60 kg
	Respiration rate [m^3/air/hour][2]	1.25 m³/h
Tier 1- Child 6 to < 12 years old	Product amount[1]	5.06 g
	Body weight[2]	23.9 kg
	Respiration rate [m^3/air/hour][2]	1.32 m³/h
Tier 1- Child 2 to < 6 years old	Product amount[1]	3.74 g
	Body weight[2]	15.6 kg
	Respiration rate [m^3/air/hour][2]	1.26 m³/h
Tier 1- Toddler	Product amount[1]	2.64 g
	Body weight[2]	10 kg
	Respiration rate [m^3/air/hour][2]	1.26 m³/h
Tier 1- Infant	Product amount[1]	2.255 g
	Body weight[2]	8 kg
	Respiration rate [m^3/air/hour][2]	0.84 m³/h

[1] According the primary exposure, only two applications per day can be authorized for adults and one application per day for the other age categories. Therefore, the product amount corresponds to 2 application/day for adults and 1 application/day for child, toddler and infant.
[2] General information, see justification above

2.2.7.2.1.1.1.3 Calculations for scenario 3

Summary table: estimated exposure for inhalation of volatilised residues after application (inhalative exposure)		
Exposure scenario	**Tier / PPE**	**Estimated inhalation uptake of volatilised residues after application**
Scenario 3 – ADULT	Tier 1 / no PPE	3.17 mg/kg bw/day
Scenario 3 – CHILD (6-12)	Tier 1 / no PPE	2.33 mg/kg bw/day
Scenario 2 – CHILD (2-6)	Tier 1 / no PPE	2.52 mg/kg bw/day
Scenario 3 – TODDLER	Tier 1 / no PPE	2.77 mg/kg bw/day
Scenario 3 – INFANT	Tier 1 / no PPE	1.97 mg/kg bw/day

Combined exposure :

Combined exposure is not performed in this case considering the following facts:

- Dermal exposure and inhalation exposure: to addition of the two routes of exposure will result in an unrealistic worst case as it is considered that all the product applied will be available for dermal exposure and for inhalation exposure. A part of the product will either be only absorbed by dermal route or by inhalation route and therefore will not be available for the other route.
  It is not possible to know which route will be the most used. Therefore, it was considered that all the product might be absorbed by one or the other route as a worst case and that it should not be summed up.
- Oral exposure by hand-to-mouth transfer is not considered to be a significant route of primary exposure, because of the repellent taste (bad palatability) of the active substance, thus, preventing repeated mouthing of IR3535® by children and infants. Furthermore, the biocidal product is not intended to **be applied on hands of children** which excludes an oral uptake of the dermally applied active substance. The scenario could be seen as a worst case and therefore should not be added to the total exposure. In addition, a part of it, will not be available anymore for oral uptake since it will be dermally absorbed.

(VI) Exposure of the general public

Exposure of the general public is covered by the secondary exposure of non-professional.

(VII)Monitoring data

Not applicable.

(VIII) Dietary exposure

Considering the scenario 2 (hand to mouth transfer), considering that the amount in scenario 2 will be superior to the amount on the fingers of the hands (possible contact surface for transfer of residue to food) and finally considering that the biocidal product is not

used for and/or during food production, or in rooms where food is produced processed or stored, the dietary risk would be covered by the scenario 2.

However, Belgium is of advice that the risk mitigation measures ("Wash hands before handling food. Do not apply directly on or near food, feed or drinks, or on surfaces or utensils likely to be in direct contact with food, feed, drinks. To prevent contamination of food, avoid contact of treated skin with food" and do not use on children's hands) must be present to avoid any misuse of the product.

The above RMM should be sufficient to minimize the risk of a transfer of residues of IR3535 from hand to food.

(IX) Exposure associated with production, formulation and disposal of the biocidal product

Occupational exposure during production and formulation of biocidal product is not covered by the BPR. It is expected that production and formulation are performed in conformity with European and national worker protection legislation.

(X) Aggregated exposure

Not applicable.

(XI) Summary of exposure assessment

USE 1 against mosquitoes – application rate 1.15 mg/cm^2

Scenarios and values to be used in risk assessment			
Scenario number	**Exposed group (e.g. professionals, non-professionals, bystanders)**	**Tier/PPE**	**Estimated total uptake**
1.	Non-professionals, adult	Tier 1, no PPE, dermal, 7 applications/day	17.15 mg/kg bw/day
	Non-professionals, child (6-12)	Tier 1, no PPE, dermal, 4 applications/day	13.63 mg/kg bw/day
	Non-professionals, child (2-6)	Tier 1, no PPE, dermal, 2 applications/day	7.72 mg/kg bw/day
	Non-professionals, toddler	Tier 1, no PPE, dermal, 2 applications/day	8.50 mg/kg bw/day
	Non-professionals, infant	Tier 1, no PPE, dermal, 2 applications/day	9.08 mg/kg bw/day
	Non-professionals, adult	Tier 2, no PPE, dermal, 6 applications/day	14.70 mg/kg bw/day
	Non-professionals, child (6-12)	Tier 2, no PPE, dermal, 3 applications/day	10.23 mg/kg bw/day
	Non-professionals, child (2-6)	Tier 2, no PPE, dermal, 1 application/day	3.86 mg/kg bw/day
	Non-professionals, toddler	Tier 2, no PPE, dermal, 1 application/day	4.25 mg/kg bw/day
	Non-professionals, infant	Tier 2, no PPE, dermal, 1 application/day	4.54 mg/kg bw/day
	Non-professionals, adult	Tier 3, no PPE, dermal, 2 applications/day	4.90 mg/kg bw/day
	Non-professionals, child (6-12)	Tier 3, no PPE, dermal, 1 application/day	3.41 mg/kg bw/day
2.	Non-professionals, adult	Tier 1, no PPE, Hand-mouth transfer reverse reference scenario, oral	Up to 7.14 applications
	Non-professionals, child (6-12)	Tier 1, no PPE, Hand-mouth transfer reverse reference scenario, oral	Up to 2.57 applications
	Non-professionals, child (2-6)	Tier 1, no PPE, Hand-mouth transfer reverse reference scenario, oral	Up to 2.27 applications
	Non-professionals, toddler	Tier 1, no PPE, Hand-mouth transfer reverse reference scenario, oral	Up to 2.06 applications
	Non-professionals, infant	Tier 1, no PPE, Hand-mouth transfer reverse reference scenario, oral	Up to 1.93 applications
3.	Non-professionals, adult	Tier 1 / no PPE	3.65 mg/kg bw/day
	Non-professionals, child (6-12)	Tier 1 / no PPE	2.68 mg/kg bw/day
	Non-professionals, child (2-6)	Tier 1 / no PPE	2.89 mg/kg bw/day
	Non-professionals, toddler	Tier 1 / no PPE	3.19 mg/kg bw/day
	Non-professionals, infant	Tier 1 / no PPE	2.27 mg/kg bw/day

USE 2 against ticks – application rate 1.0 mg/cm²

Scenarios and values to be used in risk assessment			
Scenario number	**Exposed group (e.g. professionals, non-professionals, bystanders)**	**Tier/PPE**	**Estimated total uptake**
1.	Non-professionals, adult	Tier 1, no PPE, dermal, 7 applications/day	14.91 mg/kg bw/day
	Non-professionals, child (6-12)	Tier 1, no PPE, dermal, 4 applications/day	11.86 mg/kg bw/day
	Non-professionals, child (2-6)	Tier 1, no PPE, dermal, 2 applications/day	6.71 mg/kg bw/day
	Non-professionals, toddler	Tier 1, no PPE, dermal, 2 applications/day	7.39 mg/kg bw/day
	Non-professionals, infant	Tier 1, no PPE, dermal, 2 applications/day	7.89 mg/kg bw/day
	Non-professionals, adult	Tier 2, no PPE, dermal, 6 applications/day	12.78 mg/kg bw/day
	Non-professionals, child (6-12)	Tier 2, no PPE, dermal, 3 applications/day	8.89 mg/kg bw/day
	Non-professionals, child (2-6)	Tier 2, no PPE, dermal, 1 application/day	3.36 mg/kg bw/day
	Non-professionals, toddler	Tier 2, no PPE, dermal, 1 application/day	3.70 mg/kg bw/day
	Non-professionals, infant	Tier 2, no PPE, dermal, 1 application/day	3.95 mg/kg bw/day
	Non-professionals, adult	Tier 3, no PPE, dermal, 2 applications/day	4.26 mg/kg bw/day
	Non-professionals, child (6-12)	Tier 3, no PPE, dermal, 1 application/day	2.96 mg/kg bw/day
2.	Non-professionals, adult	Tier 1, no PPE, Hand-mouth transfer reverse reference scenario, oral	Up to 8.21 applications
	Non-professionals, child (6-12)	Tier 1, no PPE, Hand-mouth transfer reverse reference scenario, oral	Up to 2.95 applications
	Non-professionals, child (2-6)	Tier 1, no PPE, Hand-mouth transfer reverse reference scenario, oral	Up to 2.61 applications
	Non-professionals, toddler	Tier 1, no PPE, Hand-mouth transfer reverse reference scenario, oral	Up to 2.37 applications
	Non-professionals, infant	Tier 1, no PPE, Hand-mouth transfer reverse reference scenario, oral	Up to 2.22 applications
3.	Non-professionals, adult	Tier 1 / no PPE	3.17 mg/kg bw/day
	Non-professionals, child (6-12)	Tier 1 / no PPE	2.33 mg/kg bw/day
	Non-professionals, child (2-6)	Tier 1 / no PPE	2.52 mg/kg bw/day
	Non-professionals, toddler	Tier 1 / no PPE	2.77 mg/kg bw/day
	Non-professionals, infant	Tier 1 / no PPE	1.97 mg/kg bw/day

2.2.7.3 Risk characterisation for human health

Reference values to be used in Risk Characterisation

Reference	Study	NOAEL (LOAEL)	AF[1]	Correction for oral absorption	Value
AELshort-term	Rabbit, oral, 28-days toxicity study Rabbit, oral, developmental study	500 (1500) mg/kg bw/d 300 (600) mg/kg bw/d	100	100%	5 mg/kg bw/d
AELmedium-term	Rabbit, oral, 28-days toxicity study Rabbit, oral, developmental study	500 (1500) mg/kg bw/d 300 (600) mg/kg bw/d	100	100%	5 mg/kg bw/d
AELlong-term	Rabbit, oral, 28-days toxicity study Rabbit, oral, developmental study	500 (1500) mg/kg bw/d 300 (600) mg/kg bw/d	100	100%	5 mg/kg bw/d (not applicable here, maximum number of applications is 28 days per year)
ARfD	n.a.	n.a.			not applicable, no residues in food or feed occur
ADI	n.a.	n.a.			not applicable, no residues in food or feed occur

[1] reason for assessment factor: factor 10 for both intra-species and interspecies differences. No extrapolation factor for duration is needed, as the overall NOAEL is derived from a repeated 28d-oral toxicity study and a teratogenicity study.

(I) Risk for industrial users

Not relevant since the product Insect Repellent Lotion IR3535® 10% is not intended to be used by industrial users.

(II) Risk for professional users

Not relevant since the product Insect Repellent Lotion IR3535® 10% is not intended for professional use.

(III) Risk for non-professional users

Systemic effects

USE 1 against mosquitoes – application rate 1.15 mg/cm²

Task/ Scenario	Tier	Systemic NOAEL mg/kg bw/d	AEL mg/kg bw/d	Estimated uptake mg/kg bw/d	Estimated uptake/ AEL (%)	Acceptable (yes/no)
Scenario 1, dermal, adult	1	500	5	17.15	342.98	No
Scenario 1, dermal, child (6-12)	1	500	5	13.63	272.69	No
Scenario 1, dermal, child (2-6)	1	500	5	7.72	154.39	No
Scenario 1, dermal, toddler	1	500	5	8.50	170.02	No
Scenario 1, dermal, infant	1	500	5	9.08	181.53	No
Scenario 1, dermal, adult	2	500	5	14.70	293.99	No
Scenario 1, dermal, child (6-12)	2	500	5	10.23	204.52	No
Scenario 1, dermal, child (2-6)	2	500	5	3.86	77.20	Yes
Scenario 1, dermal, toddler	2	500	5	4.25	85.01	Yes
Scenario 1, dermal, infant	2	500	5	4.54	90.76	Yes
Scenario 1, dermal, adult	3	500	5	4.90	97.995	Yes
Scenario 1, dermal, child (6-12)	3	500	5	3.41	68.17	Yes
Scenario 2, hand-mouth transfer, adult	1	500	5	Up to 7.14 applications	n.a.	Reverse reference scenario
Scenario 2, hand-mouth transfer, child (6-12)	1	500	5	Up to 2.57 applications	n.a.	Reverse reference scenario
Scenario 2, hand-mouth transfer, child (2-6)	1	500	5	Up to 2.27 applications	n.a.	Reverse reference scenario
Scenario 2, hand-mouth transfer, toddler	1	500	5	Up to 2.06 applications	n.a.	Reverse reference scenario

Scenario 2, hand-mouth transfer, infant	1	500	5	Up to 1.93 applications	n.a.	Reverse reference scenario
Scenario 3, inhal, adult	1	500	5	3.65	73	Yes
Scenario 3, inhal, child	1	500	5	2.68	53.6	Yes
Scenario 3, inhal, child	1	500	5	2.89	57.8	Yes
Scenario 3, inhal, toddler	1	500	5	3.19	63.8	Yes
Scenario 3, inhal, infant	1	500	5	2.27	45.4	Yes

USE 2 against ticks – application rate 1.0 mg/cm²

Task/ Scenario	**Tier**	**Systemic NOAEL mg/kg bw/d**	**AEL mg/kg bw/d**	**Estimated uptake mg/kg bw/d**	**Estimated uptake/ AEL (%)**	**Acceptable (yes/no)**
Scenario 1, dermal, adult	1	500	5	14.91	298.25	No
Scenario 1, dermal, child (6-12)	1	500	5	11.86	237.12	No
Scenario 1, dermal, child (2-6)	1	500	5	6.71	134.26	No
Scenario 1, dermal, toddler	1	500	5	7.39	147.84	No
Scenario 1, dermal, infant	1	500	5	7.89	157.85	No
Scenario 1, dermal, adult	2	500	5	12.78	255.64	No
Scenario 1, dermal, child (6-12)	2	500	5	8.89	177.84	No
Scenario 1, dermal, child (2-6)	2	500	5	3.36	67.13	Yes
Scenario 1, dermal, toddler	2	500	5	3.70	73.92	Yes
Scenario 1, dermal, infant	2	500	5	3.95	78.925	Yes
Scenario 1, dermal, adult	3	500	5	4.26	85.21	Yes
Scenario 1, dermal, child (6-12)	3	500	5	2.96	59.28	Yes
Scenario 2, hand-mouth transfer, adult	1	500	5	Up to 8.21 applications	n.a.	Reverse reference scenario
Scenario 2, hand-mouth transfer, child (6-12)	1	500	5	Up to 2.95 applications	n.a.	Reverse reference scenario
Scenario 2, hand-mouth transfer, child (2-6)	1	500	5	Up to 2.61 applications	n.a.	Reverse reference scenario
Scenario 2, hand-mouth transfer, toddler	1	500	5	Up to 2.37 applications	n.a.	Reverse reference scenario

Scenario 2, hand-mouth transfer, infant	1	500	5	Up to 2.22 applications	n.a.	Reverse reference scenario
Scenario 3, inhal, adult	1	500	5	3.17	63.4	Yes
Scenario 3, inhal, child	1	500	5	2.33	46.6	Yes
Scenario 3, inhal, child	1	500	5	2.52	50.4	Yes
Scenario 3, inhal, toddler	1	500	5	2.77	55.4	Yes
Scenario 3, inhal, infant	1	500	5	1.97	39.4	Yes

Combined scenarios

Scenarios combined	Tier	Systemic NOAEL [mg/kg bw/d]	AEL [mg/kg bw/d]	Estimated uptake [mg/kg bw]	Estimated uptake/ AEL (%)	Acceptable (yes/no)
n.a.						

Local effects

The biocidal product is not classified for any local effect. Consequently, there is no need to consider local effects separately.

Conclusion

Safe uses are identified for this product, Insect Repellent Lotion IR3535® 10% :

- For **adult and child above 12 years** when the product is applied **twice per day** on uncovered body parts: head, neck, lower arms, lower legs, feet and 70% of upper arms and thighs.
- For **child under 12 years (including infant)** when the product is applied **once per day** on uncovered body parts: head, neck, lower arms, lower legs, feet and 70% of upper arms and thighs.

There is no concern for indirect secondary exposure for adults, children and infants from the use of the biocidal product as a Repellent Subtype PT19.01. as this is expected to be lower and covered by the assessment of primary exposure. Exposure via hand-to-mouth transfer is of minor concern when the product is used as intended (not to be applied to children's hands), and inhalation of volatilized residues after application is limited.

Proper use, i.e. use in compliance with correct and complete conditions on the label, of Insect Repellent Lotion IR3535® 10% is considered safe for adults and children.

The following RMM are required:

- ONLY apply to uncovered parts of the body, limited to the face, arms, legs and feet.
- Do not use on children's hands. An adult should apply the product to children below 12 years of age and wash his hands after application.
- Wash hands before handling food. Do not apply directly on or near food, feed or drinks, or on surfaces or utensils likely to be in direct contact with food, feed, drinks. To prevent contamination of food, avoid contact of treated skin with food.
- Only apply outdoor or in well ventilated area.

(IV) Risk for the general public

Risk for the general public is covered by the secondary exposure of non-professional.

(V) Risk for consumers via residues in food

Not applicable

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

Not applicable

2.2.8 Risk assessment for animal health

Not applicable. The product is not intended to be used on animal.

2.2.9 Assessment of ED properties

A stepwise approach based on CA-March18.Doc.7.b-final was followed to assess the ED properties of the substances in Insect Repellent Lotion IR3535® 10%:

2.2.9.1 Assessment of the ED properties of the active substances in Insect Repellent Lotion IR3535® 10%:

- According to section 2.1.1 of the final CA document, the assessment of ED properties of the active substances that have already been evaluated and approved will be coordinated at EU level. Hence, the rMS should not evaluate the ED properties of these substances nor request additional data on the ED properties in the context of product authorisation procedures. As ethyl 3-[N-acetyl-N-butyl] aminopropionate (IR3535) is not part of the list of approved active substances identified as having potential ED properties, it is for the moment not triggered for an early review.
- Therefore, BE eCA considers that there are no concerns regarding ED properties of ethyl 3-[N-acetyl-N-butyl] aminopropionate (IR3535).

2.2.9.2 Assessment of the ED properties of non-active substances (co-formulants) in Insect Repellent Lotion IR3535® 10%:

- After reviewing the potential ED properties of co-formulants (please refer to the Confidential Annex - ED assessment), none of the co-formulants has been identified as having ED properties or are subject to an on-going evaluation or a decision regarding their ED properties. Based on the available information, BE eCA considers that there is no concern regarding the ED properties of these co-formulants.

2.2.9.3 Overall conclusion on the biocidal product/family regarding ED properties:

Based on the existing knowledge and the data provided by the applicant, there is no indication of concern regarding the ED properties of the substances used in the biocidal product Insect Repellent Lotion IR3535® 10%.

If one or several components are identified as having ED properties in the future, the conditions for granting the biocidal product authorisation will be revised according to CA-March18.Doc.7.b-final, section 2.3 (47).

2.2.10 Risk assessment for the environment

For the product Insect Repellent Lotion IR3535® 10 % no new studies or additional information for the environment have been provided. The active substance contained in this product is the same as evaluated in the CAR for IR3535® and therefore no new data/information on the active substance is required.

2.2.10.1 Effects assessment on the environment

All data used for the effect assessment of Insect Repellent Lotion IR3535® 10% is based on the available information on the active substance IR3535®, such as it is presented in its respective CAR.

No new data relevant for the environmental evaluation, nor on the product, nor on the active substance, have been submitted. Apart from the active substance, the product does not contain any formulants that are of ecotoxicological concern.
An overview of the environmental fate and behaviour for the active substance, taken from the EU CAR, is presented in the first two titles below.

Environmental fate and behavior of the active substance

IR3535® is used in insect repellents (PT19) that are applied on uncovered human skin. Products containing IR3535® will be used indoors and outdoors. However the main emission pathway to the environment is assumed to be indirect due to bathing and showering of treated people. Based on the physico-chemical properties it is expected that the emissions primarily will affect the aquatic compartment.

IR3535® is not ready biodegradable according to two screening tests, but in a Sewage Treatment Plant (STP) simulation test 99 % elimination was measured. In an aerobic water/sediment degradation study, IR3535® was shown to remain mainly in the water phase. There it was first rapidly degraded to its free acid, after which this metabolite ultimately degraded after a lag phase.

No photolysis was observed in water and hydrolysis only occurred slowly under alkaline conditions (DT_{50} = 176.5 h at 25 °C and pH 9 or 866.13 h at 12 °C). Under acidic and neutral conditions IR3535® is hydrolytically stable.

The vapour pressure of IR3535® is low (0.15 Pa at 20 °C) which results in low exposure to the atmosphere. The half-life of IR3535® in air was calculated to be about 0.5482 days or 13.16 hours due to reaction with OH-radicals (24-hr day). Thus, accumulation of IR3535® in air and long range transport is unlikely.

IR3535® is a liquid at room temperature and the solubility in water is 70 g/L (at 20 °C). The log P_{ow} is 1.7 (at 23-24 °C) indicating that IR3535® has a low potential for bioaccumulation.

Based on the adsorption/desorption test a mean (arithmetic) K_{oc} form 475.25 L/kg was registered.

Effect assessment of the active substance

No toxic effects where observed during the acute toxicity studies on fish (*Brachydanio rerio*), *Daphnia magna* and algae (*Desmodesmus subspicatus*) (LC_{50} >100 mg/L). Therefore IR3535® is considered as not toxic for the aquatic environment.

The effect on aerobic biological sewage treatment processes was assessed by determining inhibition of respiration of the micro-organisms present in activated sludge following 3 hours contact. No inhibitory effect on aquatic microbial activity was registered for IR3535® (EC_{50} > 1000 mg/L).

Long term aquatic tests were not required because no acute toxicity was observed for the aquatic environment and the substance is primarily emitted to the STP before reaching the aquatic environment. Besides the Sewage Treatment Plant (STP) simulation test showed an elimination of 99 % in the STP.

No marine species were tested based on the presence of studies performed on freshwater species, all suggesting low toxicity and because no major emissions to the marine environment are expected.

In the absence of any long-term toxicity endpoints and marine data, the TGD on Risk Assessment prescribes an assessment factor of 1000 for the freshwater environment and 10000 for the marine environment.

For the sediment compartment, there are also no toxicity data available. The $PNEC_{sediment}$ was calculated based on equilibrium partitioning method and $PNEC_{water}$.

No terrestrial toxicity tests were performed for IR3535®. Due to the method of application directly on the skin only limited and very local emissions to the soil are expected. IR3535® is not likely to become accumulated in the soil in large amounts. $PNEC_{soil}$ has been calculated based on the equilibrium partitioning method.

The physicochemical properties of IR3535® do not suggest that this substance will pose a risk to the atmospheric environment. Therefore no PNECs where calculated for this compartment.

The low BCF values suggest that IR3535® has a low bioaccumulation potential. Therefore the risk of secondary poisoning via ingestion of contaminated food (eg. earthworms or fish) by birds or mammals is also low and no avian dietary tests were required.

Summary of PNEC values for the active substance	
Compartment	**PNEC value**
$PNEC_{aquatic}$	> 0.1 mg/l
$PNEC_{sediment}$	> 1.11 mg/kg wwt
$PNEC_{micro\text{-}organisms\ (STP)}$	100 mg/l
$PNEC_{soil}$	> 0.85 mg/kg wwt
$PNEC_{saltwater}$	> 0.01 mg/l
$PNEC_{marine\text{-}sediment}$	> 0.111 mg/kg wwt

(I) Information relating to the ecotoxicity of the biocidal product which is sufficient to enable a decision to be made concerning the classification of the product is required

The product does not contain any substance at such a concentration that it has an effect on the environmental classification of the product. No additional information on the biocidal product is required.

Conclusion on the environmental classification and labelling of the product
Insect Repellent Lotion IR3535® 10% does not require any environmental classification or labelling.

(II) Further Ecotoxicological studies

The assessment of the active substance in the CAR showed that there is no concern for the aquatic and terrestrial environment and thus no further ecotoxicological studies are required according to the CAR.

For this particular product, there is no direct exposure to the environment and the product does not contain formulants other than the active substance that could be of ecotoxicological concern, thus the data on the active substance are sufficient for the evaluation of the ecotoxicological effects of the biocidal product.

(III) Effects on any other specific, non-target organisms (flora and fauna) believed to be at risk (ADS)

No further data is available.

(IV) Supervised trials to assess risks to non-target organisms under field conditions

The product is not in the form of bait or granules, so nonesuch data is required.

(V) Studies on acceptance by ingestion of the biocidal product by any non-target organisms thought to be at risk

The product is not in the form of bait or granules, so nonesuch data is required.

(VI) Secondary ecological effect e.g. when a large proportion of a specific habitat type is treated (ADS)

Not relevant.

(VII) Foreseeable routes of entry into the environment on the basis of the use envisaged

The foreseeable routes of entry into the environment have been described in the CAR for the active substance and are also valid for this product.

Direct release to soil is not considered relevant, whereas direct release to surface water (swimming lake scenario) is considered relevant and is assessed in this PAR, but was not yet assessed in the CAR due to the lack of an endorsed scenario. The emission to swimming water is an important emission route.

Secondary release via wastewater and STP through showering and bathing is also a relevant route of emission.

(VIII) Further studies on fate and behaviour in the environment (ADS)

No new data was submitted or is required. Information on the active substance suffices for the environmental risk assessment of the product. Moreover, the product does not contain any other substances relevant for the environment apart from the active substance.

(IX) Leaching behaviour (ADS)

Not relevant.

(X) Testing for distribution and dissipation in soil (ADS)

Since there is no direct release to soil and the soil compartment is not envisioned as a compartment of interest in the evaluation of this product, none such additional data is submitted or required.

(XI) Testing for distribution and dissipation in water and sediment (ADS)

No new data was submitted or is required.

(XII) Testing for distribution and dissipation in air (ADS)

No new data was submitted or is required.

(XIII) If the biocidal product is to be sprayed near to surface waters then an overspray study may be required to assess risks to aquatic organisms or plants under field conditions (ADS)

No new data was submitted or is required.

(XIV) If the biocidal product is to be sprayed outside or if potential for large scale formation of dust is given then data on overspray behaviour may be required to assess risks to bees and non-target arthropods under field conditions (ADS)

No new data was submitted or is required.

2.2.10.2 Exposure assessment

(I) General information

Assessed PT	PT 19
Assessed scenarios	Scenario 1: Removal via showering and bathing of humans (ESD PT19, May 2015, §3.1.4.1) Scenario 2: Release to surface water bodies via swimming (ESD PT19, May 2015, §3.1.4.2)
ESD(s) used	Emission Scenario Document for Product Type 19: Repellents and attractants, May 2015 (ECHA-15-B-10-EN)
Approach	Scenario 1: Average consumption Scenario 2: Average consumption
Distribution in the environment	Calculated based on Guidance on BPR Vol.IV B+C
Groundwater simulation	Not applicable
Confidential Annexes	None
Life cycle steps assessed	Scenario 1: Showering & bathing • Production: No • Formulation: No • Use: Yes • Service life: No Scenario 2: Swimming • Production: No • Formulation: No • Use: Yes • Service life: No
Remarks	Evaluation done taking into account WGV2018 agreement on treated skin surface: TAB ENV v2.0 entry **ENV 172** - Refinement of risk assessment PT19: reduction of treated skin surface area and taking into account dermal adsorption The WG agreed to apply the new value of the HEAdoc recommendation of January 2018 for the treated skin area, i.e. 55% of 16600 cm^2 (= 9130 cm^2), since this could be considered as a mean value taking into account the different skin areas for women, men and children.

(II) Emission estimation

Scenario 1: Removal via showering and bathing

Consumption based scenario

For estimating the emission for products applied on human skin following showering or bathing one could either use a tonnage based scenario or a consumption based scenario.

Tonnage based approaches are mostly only appropriate for assessing an active substance for approval and not so much for the authorisation of biocidal products. Therefore only the consumption based approach is assessed here.

However, the tonnage based approach was calculated in the IR3535 CAR and can be consulted in the confidential annex of said CAR. Anyway when considering the break-even tonnage, the consumption based scenario is deemed to be the most appropriate scenario.

Amount of product per application ($Qform_{appl}$)

The most important input parameter for the consumption based scenario is the amount of product that will be used per application ($Qform_{appl}$). As a default value in the ESD 0.6 mg product/cm² skin is proposed.

However, the ESD also mentions that the value for $Qform_{appl}$ must coincide with the efficacy of the product and must be adapted accordingly.

The validated efficacious dose for the product 'Insect Repellent Lotion IR3535 10%' is 1.15 mg product per cm² of skin. This value will be considered in the environmental risk assessment instead of the default value from the ESD.

$Qform_{appl}$ = 1.15 mg product/cm² skin

Number of applications per day (N_{appl})

Another important parameter is the number of applications per day (N_{appl}), which the ESD also links to the efficacy of the product.

The conclusion for efficacy of 'Insect Repellent Lotion IR3535 10%' is that the product will remain efficacious for 8 hours against mosquitoes, when used at the application rate of 1.15 mg/cm². Following the ESD Table 3-2, 2 applications per day will be used in the further assessment.

N_{appl} = 2 d^{-1}

Treated area of human skin ($AREA_{skin}$)

Following the agreement of the ENV WG-V-2018 to harmonise the value for the treated skin area with that of the Human Health assessment, a value of 55% of the total body surface area will be applied.

$AREA_{skin}$ = 9130 cm²

Input parameters for calculating the local emission				
Input	**Nomenclature**	**Value**	**Unit**	**Remarks**
Scenario: Release of repellents used on human skin based on the average consumption				
Number of inhabitants feeding one STP	Nlocal	10 000	cap	D
Active substance in product	(B) Cformweight	100	g/kg	(10 %)
Consumption per application	(D2) Qformappl	1.15	mg/cm²	(see above)
Number of applications per day	Nappl	2	d^{-1}	(see above)
Treated area of human skin	$AREA_{skin}$	9130	cm²	(see above)
Fraction realeased to air	Fair	0	[-]	D
Fraction dermally absorbed	Fskin	0	[-]	D

Fraction released to wastewater	Fwater	1	[-]	D
Fraction of inhabitants using a repellent product	Finh	0.2	[-]	D
Market share of repellent	Fpenetr	0.5	[-]	D
Specific density of the product	RHOform	1000	kg/m³	D

Calculations for Scenario 1

→ B and D2

$$Elocal_{wastewater} = Nlocal \times N_{appl} \times Qform_{appl} \times AREA_{skin} \times Cform_{weight} \times F_{inh} \times F_{water} \times Fpenetr \times 10^{-9}$$

Resulting local emission to relevant environmental compartments		
Compartment	**Local emission ($Elocal_{compartment}$) [kg/d]**	**Remarks**
Waste water	2.10	/

Scenario 2: Release to surface water bodies via swimming

In the assessment report for IR3535®, in the paragraph on the elements to be taken into account when authorising products, it is mentioned that direct emissions to surface water by swimmers should be kept in mind and assessed. With this new scenario for the ESD for PT19, this requisite is taken into account.

Amount of product per application ($Qform_{appl}$)

Similarly as with scenario 1, the most important input parameter for this scenario is the amount of product that will be used per application ($Qform_{appl}$).

The same notes and thoughts can be applied as with scenario 1. Therefore, also here it is decided that the ESD default value will not be applied.

$Qform_{appl}$ = 1.15 mg product/cm² skin

Treated area of human skin ($AREA_{skin}$)

Concerning the body surface to which the product is applied ($AREA_{skin}$), according to the applicant the product should only be applied to the face, arms, hands and legs. However, when repellent products are used when swimming, one could assume the swimmer would apply it also to their feet and trunk. Therefore, for a worst case calculation, it is assumed the product is applied to the full body surface.

$AREA_{skin}$ = 16600 cm²

Input parameters for calculating the local emission				
Input	**Nomenclature**	**Value**	**Unit**	**Remarks**
Scenario: Release of repellents used on human skin due to swimming activities in surface water bodies				
Daily number of swimmers	$N_{swimmer}$	1500	[-]	D
Fraction of swimmers using the repellent product	F_{swim}	0.1	[-]	P worstcase
Number of applications per day	N_{appl}	1	d^{-1}	D
Fraction released to surface water body	$F_{waterbody}$	1	[-]	D
Active substance in the product	(B) $C_{formweight}$	100	g/kg	(10%)
Consumption per application	(D2) $Qform_{appl}$	1.15	mg/cm²	(see above)
Treated area of human skin	$AREA_{skin}$	16600	cm²	(see above)
Specific density of product	RHOform	1000	kg/m³	D

Intermediate calculation for Scenario 2

→ B and D2

$$Elocal_{water} = N_{swimmer} \times N_{appl} \times Qform_{appl} \times AREA_{skin} \times Cform_{weight} \times F_{swim} \times F_{waterbody} \times 10^{-9}$$

Resulting local emission to relevant environmental compartments		
Compartment	**Local emission ($Elocal_{compartment}$) [kg/d]**	**Remarks**
Local water	$2.86x10^{-1}$	/

Final calculation for scenario 2

In the intermediate calculation a local daily emission to the surface water body due to swimmers treated with the repellent, was calculated. In order to assess the impact of this emission on the aquatic life in this waterbody, the actual concentration in active substance in this waterbody should be calculated.

As a first TIER evaluation concentrations are calculated for emission periods of 1 day and 91 days, without taking into account possible degradation progresses, which represents the worst-case.

Input parameters for calculating surface water concentration				
Input	**Nomenclature**	**Value**	**Unit**	**Remarks**
Scenario: Release of repellents used on human skin due to swimming activities in surface water bodies				
Local emission to surface water body	$Elocal_{water}$	$2.86x10^{-1}$	kg/d	O (Intermediate calculation)
Volume of water body	$V_{waterbody}$	435 000	m³	D
Number of emission days TIER 1	$T_{emission,\ 1d}$	1	D	D
Number of emission days TIER 2	$T_{emission,\ 91d}$	91	D	D
Number of emission events	$N_{emission,\ 91d}$	91	[-]	D

$$Clocal_{water,1d} = \frac{Elocal_{water} \times T_{emission,1d}}{V_{waterbody}}$$

$$Clocal_{water,91d} = \frac{Elocal_{water} \times T_{emission,91d}}{V_{waterbody}}$$

Resulting local concentrations in the waterbody		
Compartment	**Local concentration ($Clocal_{compartment}$) [kg/m³]**	**Remarks**
Surface water – after 1 day	$6.58x10^{-7}$	/
Surface water – after 91 days	$5.99x10^{-5}$	(without considering possible degradation)

(III) Fate and distribution in exposed environmental compartments

Scenario 1:

Applied product is removed from the body through showering or bathing. The wastewater from washing is then removed to the municipal waste water treatment plant, after which the effluent is emitted to the surface water where it can expose both fresh water and fresh water sediments.

Exposure to other compartments is not considered relevant.

Scenario 2:

Applied product is removed from the body directly to the surface water through swimming, where it can expose both fresh water and fresh water sediments.

Exposure to other compartments is not considered relevant.

Identification of relevant receiving compartments based on the exposure pathway									
	Fresh-water	**Freshwater sediment**	**Sea-water**	**Seawater sediment**	**STP**	**Air**	**Soil**	**Ground-water**	**Other**
Scenario 1	yes	Yes	no	no	yes	no	no	no	no
Scenario 2	yes	Yes	no	no	no	no	no	no	no

Input parameters (only set values) for calculating the fate and distribution in the environment			
Input	**Value**	**Unit**	**Remarks**
Molecular weight	215.29		
Melting point	-90	°C	
Boiling point	300	°C	
Vapour pressure (at 20 °C)	0.15	Pa	
Water solubility (at 20 °C)	70 000	mg/l	
Log Octanol/water partition coefficient	1.7	Log 10	
Organic carbon/water partition coefficient (Koc)	475.25	l/kg	
Henry's Law Constant (at 20 °C)	$4.613x10^{-4}$	$Pa/m^3/mol$	
Biodegradability	Inherently biodegradable		

In the CAR for IR3535®, calculations according to EUSES are available for the distribution in the STP, which in this case is only relevant for scenario 1. As a worst-case assessment the distribution presented in the CAR is taken over for the assumption that there is no degradation. As a TIER 2 evaluation, 99% degradation in STP is taken into consideration.

Calculated fate and distribution in the STP				
Compartment	**Percentage [%]**			**Remarks**
	Scenario 1 TIER 1	**Scenario 1 TIER 2**	**Scenario 2**	
Air	0.000547	0	Not relevant	
Water	99	1		
Sludge	1	0		
Degraded in STP	1.000547	99		

(IV) Calculated PEC values

Neither for scenario 1, nor for scenario 2, calculations were made for the sediment, since the $PNEC_{sediment}$ was determined through the EPM-method. This means that the risk assessment for water is applicable for the sediment as well.

As mentioned before, for the scenario 2, possible degradation in surface water is not taken into account as a worst-case evaluation.

Summary table on calculated PEC values			
		PEC_{STP}	**PEC_{water}**
		[mg/m^3]	[mg/l]
Scenario 1	TIER 1	1.04	$1.04x10^{-1}$
	TIER 2	$1.05x10^{-2}$	$1.05x10^{-3}$
Scenario 2	Day 1	n/a	$6.58x10^{-4}$
	Day 91	n/a	$5.99x10^{-2}$

(V) Primary and secondary poisoning

a) Primary poisoning

Not applicable, since this product is a repellent and has no intention of killing.

b) Secondary poisoning

Not relevant, since no bioaccumulation is expected.

2.2.10.3 Risk characterisation

(I) Atmosphere

Conclusion:

Only negligible exposure to the atmosphere is expected and no threat to the atmosphere is expected.

(II) Sewage treatment plant (STP)

Summary table on calculated PEC/PNEC values		
		$PEC/PNEC_{STP}$
Scenario 1	TIER 1	$1.04x10^{-2}$
	TIER 2	$1.05x10^{-4}$
Scenario 2	Day 1	Not relevant
	Day 91	Not relevant

Conclusion:

No adverse effect for the STP is expected. The 99% degradation in the STP (tier 2) is observed in an OECD 303A simulation study which is included in the Final CAR IR3535 (September 2013).

(III) Aquatic compartment

Neither for scenario 1, nor for scenario 2, calculations were made for the sediment, since the $PNEC_{sediment}$ was determined through the EPM-method. This means that the risk assessment for water is applicable for the sediment as well.

For the scenario 2, possible degradation in surface water is not taken into account as a worst-case evaluation.

Summary table on calculated PEC/PNEC values		
		$PEC/PNEC_{water}$
Scenario 1	TIER 1	**1.04**
	TIER 2	$1.05x10^{-2}$
Scenario 2	Day 1	$6.58x10^{-3}$
	Day 91	$5.99x10^{-1}$

For the scenario 1, when considering the worst-case assessment where no elimination from the STP is taken into account, then an adverse effect for the surface water is calculated. However when considering the TIER 2, where 99 % elimination from the STP is considered, no adverse effects are calculated.

For the scenario 2, no adverse effects are expected, neither at day 1 nor at day 91, without considering degradation in the surface water.

Conclusion:

No adverse effect for the aquatic compartment is expected

(IV) Terrestrial compartment

The soil could be exposed through sludge application (according to simple treat V4, up to 6% emission would be directed to sludge), but following the STP-distribution detailed in the second table below, sorption to sewage sludge is unlikely since IR3535 is almost completely degraded. Therefore, emission to soils via sewage sludge is considered negligible.

(V) Groundwater

Not relevant.

(VI) Primary and secondary poisoning

Since the product is a repellant and has no intention to kill, primary poisoning is not applicable.
Secondary poisoning is not relevant, since no bioaccumulation is expected.

(VII)Mixture toxicity

Not relevant.

Overall conclusion on the risk assessment for the environment of the product
No adverse effect for the environment is expected.

2.2.11 Measures to protect man, animals and the environment

Please see §2.1.4 and §2.1.5 above.

2.2.12 Assessment of a combination of biocidal products

Not applicable.

2.2.13 Comparative assessment

Not applicable.

3 ANNEXES

3.1 LIST OF STUDIES FOR THE BIOCIDAL PRODUCT

Author(s)	Year	Title	Report No.	Owner Company	Report date
Fieseler, A.	2015	MDA-A-197-01 Verum 1: Accelerated Storage Stability	98322204	Merck KGaA	2015-08-04
Meinerling. M.	2011	Determination of the Low Temperature Stability of Lotion IR 3535® 10 %	63194204	Merck KGaA	2011-06-27
zur Lage, J.	2016	IR3535_Ref Formulations Surface tension Viscosity_Reg.Aff	6442	Merck KGaA	2016-07-04
Fieseler, A.	2011	Determination of the Flash Point of Lotion IR 3535® 10 %	63191189	Merck KGaA	2011-07-11
Fieseler, A.	2018	MDA-A-197-01 Verum 1: Longterm Storage Stability at 20°C	98321204	Merck KGaA	2018-05-22
Dornhagen, J.	2011	FINAL REPORT (1st Original of 3) Lotion IR 3535® 10 % Batch No.: SM-0-1-3/090211 AUTO-IGNITION TEMPERATURE (LIQUIDS AND GASES) A.15.	20110105.01	Merck KGaA	2011-07-04
Meinerling. M.	2007	IR3535® - VALIDATION OF AN ANALYTICAL METHOD FOR THE DETERMINATION OF IR3535® AND ITS HYDROLYSIS PRODUCT IN DIFFERENT FORMULATIONS	31211101	Merck KGaA	2007-03-19
Meinerling, M.	2009	WV29-01 INSECT REPELLENT LOTION – DETERMINATION OF THE STORAGE STABILITY AT AMBIENT TEMPERATURES	31222204	Merck KGaA	2009-05-30
Carroll, S.P.	2006	Test of Personal Insect Repellents: Study EMD-003.1 - Replacement for MRID 46979001 - Volume 11	336-1916	Merck KGaA	2006-11-08
Carroll, S.P.	2006	Test of Personal Insect Repellents: Study EMD 004.1 - Replacement for MRID 4699003 - Volume 12	336-1917	Merck KGaA	2006-11-06
Büchel K.	2017	"Evaluation of the repellent efficacy of Insect Repellent Lotion IR3535 10% (1.0 µl/cm^2) against the European Sheep Tick *Ixodes ricinus* on human volunteers"	ME_IR_0117a_01 Lotion	Merck KGaA	2017-04-21
Büchel K.	2017	"Evaluation of the repellent efficacy of Insect Repellent Lotion IR3535 10% (0.72 µl/cm^2) against the European Sheep Tick *Ixodes ricinus* on human volunteers"	ME_IR_0117b_01 Lotion	Merck KGaA	2017-05-22
P. H. Herculano, & G. P. Machado	2017	"EFFICACY TESTS IN A REPELLENT PRODUCT FOR MOSQUITOES Aedes aegypti (DIPTERA: CULICIDAE)"	RMQAA - 039843.R1	Merck KGaA	2017-08-28

P. H. Herculano, & G. P. Machado	2017	"EFFICACY TESTS IN A REPELLENT PRODUCT FOR MOSQUITOES Aedes albopictus (DIPTERA: CULICIDAE)"	RMQAAL - 039843.R1	Merck KGaA	2017-08-28
P. H. Herculano, & G. P. Machado	2017	"EFFICACY TESTS IN A REPELLENT PRODUCT FOR MOSQUITOES *Anopheles aquasalis* (DIPTERA: CULICIDAE)"	RMQANE-039843.R1	Merck KGaA	2017-08-28
P. H. Herculano, & G. P. Machado	2017	"EFFICACY TESTS IN A REPELLENT PRODUCT FOR MOSQUITOES *Culex quinquefasciatus* (DIPTERA: CULICIDAE)"	RMQCQ-039843.R1	Merck KGaA	2017-08-28
P. H. Herculano, & G. P. Machado	2017	"EFFICACY TESTS IN A REPELLENT PRODUCT FOR MOSQUITOES Aedes aegypti (DIPTERA: CULICIDAE)"	RMQAA – 039843.R	Merck KGaA	2017-08-28
P. H. Herculano, & G. P. Machado	2017	"EFFICACY TESTS IN A REPELLENT PRODUCT FOR MOSQUITOES Aedes albopictus (DIPTERA: CULICIDAE)"	039843 R - RMQAAL	Merck KGaA	2017-08-28
P. H. Herculano, & G. P. Machado	2017	"EFFICACY TESTS IN A REPELLENT PRODUCT FOR MOSQUITOES *Anopheles aquasalis* (DIPTERA: CULICIDAE)"	RMQANE – 039843.R	Merck KGaA	2017-08-28
P. H. Herculano, & G. P. Machado	2017	"EFFICACY TESTS IN A REPELLENT PRODUCT FOR MOSQUITOES *Culex quinquefasciatus* (DIPTERA: CULICIDAE)"	RMQCQ – 039843.R	Merck KGaA	2017-08-28
[redacted] (a)	2006	Acute dermal irritation study of WV29-01 Insect Repellent Lotion in albino rabbits.	[redacted]	Merck KGaA	2006-09-15
[redacted] (b)	2006	Acute Eye Irritation Study of WV29-01 Insect Repellent Lotion in albino rabbits.	[redacted]	Merck KGaA	2006-09-15
[redacted] (c)	2006	Skin Sensitisation Study of WV29-01 Insect Repellent Lotion in albino guinea pigs (Modified Buehler Method).	[redacted]	Merck KGaA	2006-09-15
[redacted] (d)	2006	Acute dermal toxicity study of WV29-01 Insect Repellent Lotion in albino rats.	[redacted]	Merck KGaA	2006-09-15

3.2 OUTPUT TABLES FROM EXPOSURE ASSESSMENT TOOLS

3.2.1 Human exposure calculations

USE1 - calculation table IR3535 lotion -

USE2 - calculation table IR3535 lotion -

3.3 NEW INFORMATION ON THE ACTIVE SUBSTANCE

Not applicable

3.4 RESIDUE BEHAVIOUR

Not applicable

3.5 SUMMARIES OF THE EFFICACY STUDIES (B.5.10.1-XX)

Not relevant, IUCLID file available.

3.6 CONFIDENTIAL ANNEX

Yes, see seperate document.

3.7 OTHER

Not applicable