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 Aerosol IR3535® 30%

Product type 19

Ethyl butylacetylaminopropionate
(Further referred to as IR3535®)

Case Number in R4BP: BC-HQ013914-29

Evaluating Competent Authority: Belgium

Date: 05/2019

TABLE OF CONTENTS

Overview of applications

Overview regarding all relevant applications

Application type	refMS	Case number in the refMS	Decision date	Assessment carried out
NA-APP	BE	BC-HQ013914-29	17/05/2017	First authorisation
NA-AAT	BE	BC-UF044420-48	26/10/2018	Amendment by CA (dissemination)
NA-AAT	BE	BC-XG051392-35	10/05/2019	Amendment by eCA*

* COMMISSION IMPLEMENTING DECISION (EU) 2018/1477 of 2 October 2018: product authorization for Insect Repellent Aerosol IR3535 30% (Asset nr: BE-0012317-0000) is amended to eliminate discrepancy for application rates used for efficacy, human health and environmental risk assessment. The final PAR contains revised terms and conditions of the authorization after re-evaluation.

Within two years of the publication by the European Chemicals Agency of Union guidance on how to generate efficacy data for insect repellents at the recommended application rates, the authorisation holder shall submit data to confirm the minimum effective application rate. Those data shall be submitted in the form of an application for a change of the authorisation in accordance with Commission Implementing Regulation (EU) No 354/2013.

1 CONCLUSION

Insect Repellent Aerosol IR3535® 30% cannot be authorised according to Art.19(1) of Regulation (EU) No 528/2012. Following assessment, the product shows unacceptable risks for humans following topical application.

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 Aerosol IR3535® 30%	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	BE-0012317-0000	
Date of the authorisation	16/05/2017	
Expiry date of the authorisation	16/05/2027	

2.1.1.3 Manufacturer(s) of the product

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

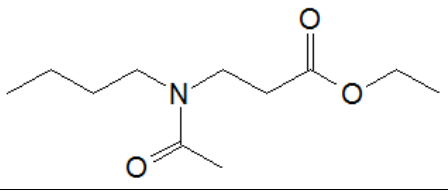
NB: the full composition of the product according to Annex III Title 1 should be provided in the confidential annex.

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	20 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

Not applicable

2.1.2.6 Type of formulation

AE – Aerosol dispenser

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	Flammable aerosol cat 2 Eye irritation cat.2
Hazard statement	H223: Flammable aerosol H229: Pressurised container: may burst if heated H319: Causes serious eye irritation
Labelling	
Signal words	Warning
Hazard statements	H223: Flammable aerosol H229: Pressurised container: may burst if heated H319: Causes serious eye irritation
Precautionary statements	P101 If medical advice is needed, have product container or label at hand P102 Keep out of reach of children. P210 Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking P251 Pressurised container – do not pierce or burn, even after use P264 Wash hands thoroughly after handling P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P410+P412 Protect from sunlight. Do not expose to temperatures exceeding 50 °C/122 °F
Note	

2.1.4 Authorised use(s)

None

2.1.5 General directions for use

N/A

2.1.6 Other information

N/A

2.1.7 Packaging of the biocidal product

N/A

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>
<tr><th colspan="2">Table 1. Use # 1 – application to skin</th></tr>
<tr><td>Product Type</td><td>PT19 - Repellents and attractants (Pest control)</td></tr>
<tr><td>Where relevant, an exact description of the authorised use</td><td>Insect Repellent Aerosol IR3535® 30 % is a ready to use product. The repellent is sprayed onto the skin. 3 g solution 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, spray the repellent solution onto the palm of the hand and distribute the solution 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).</td></tr>
<tr><td>Target organism (including development stage)</td><td>
<table>
<tr><th>Scientific name</th><th>Common name</th><th>Development stage</th></tr>
<tr><td>Cullidae</td><td>Mosquitoes</td><td>Adults</td></tr>
<tr><td>Ixodidae</td><td>Ticks</td><td>Nymphs</td></tr>
<tr><td>Ixodidae</td><td>Ticks</td><td>Adults</td></tr>
</table>
</td></tr>
<tr><td>Field of use</td><td>Other</td></tr>
<tr><td>Application method(s)</td><td>Spraying</td></tr>
<tr><td>Application rate(s) and frequency</td><td>Dose: 3.0 gram
Dilution: 100%
Insect Repellent Aerosol IR3535® 30 % is intended to be used in summer when insects are frequent. It is usually applied once a day depending on outdoor activities, weather and presence of insects. Reapply only when effectiveness diminishes. The aerosol spray can be applied up to 2 times per day for adults and maximally 1 time per day for children below 10 years of age. Product can be used for children older than 1 year.</td></tr>
<tr><td>Category(ies) of users</td><td>General public</td></tr>
<tr><td>Pack sizes and packaging material</td><td>
<table>
<tr><th>Type</th><th>Material</th><th>Size</th></tr>
<tr><td>Aerosol can</td><td>Metal</td><td>>=25.0 - <=250.0 mL</td></tr>
</table>
</td></tr>
</table>

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 Aerosol IR3535® 30% are described, whereas the full composition of the test materials is provided in the confidential part of the PAR.

- **Aerosol solution without propellant:** The IR3535® concentration in the aerosol solution without propellant is 30.7%, whereas the IR3535® concentration in the full composition of the aerosol (including propellant) is 20%.
- **Aerosol solution without propellant and Bitrex:** The IR3535® concentration in the aerosol solution without propellant is 30.7%, whereas the IR3535 concentration in the full composition of the aerosol (including propellant) is 20%. No Bitrex was present and the water content was adjusted to compensate for the slight difference in composition.
- **US Aerosol Formulation:** In the US EPA formulation, ethanol denatured with Bitrex and tertbutanol (final concentrations 0.0001% and 0.026 %, respectively) is used, whereas in the EU formulation (Insect Repellent Aerosol IR3535® 30%) a final concentration of 0.0007% Bitrex is present in the aerosol containing propellant. Other components are identical in both formulations and only the water content is adjusted to compensate for the slight differences in composition. The IR3535® concentration in the aerosol solution without propellant is 30.7%, whereas the IR3535® concentration in the full composition of the aerosol (including propellant) is 20%. Several studies have been conducted with the aerosol solution instead of the final aerosol due to the fact that the propellant is not miscible with the solution and evaporates upon spraying.
- **US Pump Spray Formulation:** The composition of the test material is similar to the solution of the Insect Repellent Aerosol IR3535® 30% (after evaporation of the propellant). Whereas the concentration of IR3535® is lower (20% versus 30%) in the pump spray, the content of water and ethanol is quite similar. The major difference is the presence of propylene glycol in the aerosol instead of polyethylene glycols and polysorbate in the pump spray.
- **TMT-003** (test against Aedes albopictus)**:** The IR3535® concentration on the skin is lower than for the aerosol (20% vs. 30%) and the formulation is more complex than the aerosol formulation once dried on the skin. The major difference is the presence of propylene glycol in the aerosol instead of butanediol, polyethylene glycols and polysorbate in TMT-003.

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	OPPTS 830.6317/ organoleptic	US Aerosol Formulation	liquid	Meinerling, M. EUS26-16 Insect repellent aerosol – Determination of the storage stability at ambient temperatures. 2009
Colour at 20 °C and 101.3 kPa	OPPTS 830.6317/ organoleptic	US Aerosol Formulation	colourless	Meinerling, M. EUS26-16 Insect repellent

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
				aerosol – Determination of the storage stability at ambient temperatures. 2009
Odour at 20 °C and 101.3 kPa	OPPTS 830.6317/ organoleptic	US Aerosol Formulation	mild characteristic, slight alcoholic	Meinerling, M. EUS26-16 Insect repellent aerosol – Determination of the storage stability at ambient temperatures. 2009
Acidity / alkalinity	CIPAC MT 75	US Aerosol Formulation	≥3.8-≤4.6 (20.0°C ca 1.0 vol%) ≥4.2-≤4.8 (20.0°C ca 100.0 vol%)	Meinerling, M. EUS26-16 Insect repellent aerosol – Determination of the storage stability at ambient temperatures. 2009
Relative density / bulk density	OECD guideline 109	Aerosol solution without propellant and Bitrex	0.949 g/l (20°C)	Fieseler, A. Determination of the relative density of Aerosol solution (without propellant) containing 30% IR 3535®. 2011
Storage stability test – accelerated storage	CIPAC MT 46.3 and OPPTS 830.6317	US Aerosol Formulation without propellent	12 weeks at 35±1°C. Humidity 75%. Packaging: commercial packaging: white metal flask with white pump stopper and green cap - No change in colour, odour, or clarity.	Meinerling, M. EUS26-16 Insect repellent aerosol – Determination of the storage stability at ambient temperatures. 2009

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
			- No change in packaging appearance. -pH values (20°C): Undiluted formulation: 4.8 at the beginning of the test; 4.3 at the end of the test 1% dilution; 4.6 at the beginning of the test; 4.2 at the end of the test -Active substance content: - 29.7% to 30.3%: this corresponds to a variation of 2.0% of active substance content - Free acid content: <0.3 % w/w before and after storage.	
Storage stability test – long term storage at ambient temperature	OPPTS 830.6317	US Aerosol Formulation without propellant	Packaging: commercial packaging: white metal flask with white pump stopper and green cap - No change in the appearance of the tested item. - No change in packaging appearance: no indication of corrosion or decomposition, no alteration of label -pH values (20°C): Undiluted formulation: 5.0 at the beginning of the test; 4.0 at the end of the test 1% dilution; 4.6 at the beginning of the test; 3.8 at the end of the test	Meinerling, M. EUS26-16 Insect repellent aerosol – Determination of the storage stability at ambient temperatures. 2009

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
			-Active substance content: 24 months at 25° : 29.7% to 28.6%: this corresponds to a variation of 3.7% of active substance content → results acceptable for storage of 2 years. -Free acid content: At the beginning 0.2 % w/w; after 24 months of storage: 1.8% w/w	
Storage stability test – low temperature stability test for liquids	CIPAC MT 39.3	Aerosol solution without propellant and Bitrex	0°C during 1 week: colourless clear homogenous liquid with a slight alcoholic odour before and after.	Meinerling, M. and Hermman, S. Determination of the low temperature stability of Aerosol solution (without propellant) containing 30 % IR 3535®. 2011
Effects on content of the active substance and technical characteristics of the biocidal product - light	Waived	-	The product is intended to be placed on the market in lightproof aluminium packaging (aerosol spray can), 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. The product should not be stored for prolonged times at temperature > 35°C	-
Effects on content of the active substance and technical characteristics of the biocidal product - reactivity towards container material	Organoleptic	US Aerosol Formulation	No indication of corrosion or decomposition was observed (during 8 years).	Justification from applicant (July 2016)

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
		Product in original packing (aerosol aluminium cans)		
Wettability	Waived	-	the product is an aerosol	-
Suspensibility, spontaneity and dispersion stability	Waived	-	the product is not intended to be diluted	-
Wet sieve analysis and dry sieve test	Waived	-	the product is not intended to be diluted and the product is an aerosol	-
Emulsifiability, re-emulsifiability and emulsion stability	Waived	-	the product is not intended to be diluted and is not an emulsion	-
Disintegration time	Waived	-	the product is not a tablet to be disintegrated	-
Particle size distribution, content of dust/fines, attrition, friability	Waived	-	the product is not a powder nor a granule	-
Persistent foaming	Waived	-	the product is not intended to be diluted	-
Flowability/Pourability/Dustability	Waived	-	the product is not a powder, a granule nor an emulsion	-
Burning rate — smoke generators	Waived	-	the product is not a smoke generator	-
Burning completeness — smoke generators	Waived	-	the product is not a smoke generator	-
Composition of smoke — smoke generators	Waived	-	the product is not a smoke generator	-
Spraying pattern — aerosols	FEA-method 644	US Aerosol Formulation	The different batches provide slightly different mean spray diameters of 17,15 cm and 14 cm respectively, whereas they all provide a clear transparent solution with circular shape. All of the spray patterns appear to be homogeneous on visual inspection.	Rodriguez, N. Mo5329 - Determination of spray pattern of insect repellent Skinsmart. 2015.
	Sprayability WHO and FAO pesticide specifications	US Aerosol Formulation	No clogging of valves was observed. The discharge rate was 2.2 g/s at the start of the test	Meinerling, M. EUS26-16 Insect repellent aerosol – Determination of the

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
			and 1.5 g/s after 12 weeks storage at elevated temperatures.	accelerated storage stability. 2007
	Aerosol particle size determinations was conducted using an 8-stage Andersen impactor (model 20-801, Andersen instruments inc. Atlanta, GA) in line with the requirements for inhalation studies.	US Aerosol Formulation	0.38 % had a particle size less than 10 microns, with 99.62 % of the test article aerosol having a particle size of greater than or equal to 10 microns	Kirkpatrick, D.T. Doc 214-002. An aerosol particle size study of IR3535 aerosol spray insect repellent: A study to determine proportions of respirable and non-respirable aerosol. 2007
Physical compatibility	Waived	-	the product is not intended to be used in combination with other products	-
Chemical compatibility	Waived	-	the product is not intended to be used in combination with other products	-
Degree of dissolution and dilution stability	Waived	-	the product is not a tablet and is not intended to be diluted	-
Surface tension	OECD test guideline 115: sample aerosol without propellant.	Aerosol solution without propellant	29.9 mN/m (20°C ± 0.5 °C)	zur Lage, J. EUS26-16 Lab Investigation 009093-PM-PFC-RT, Project no.: 6442. 2016
Viscosity	Viscosity based on OECD test guideline 114: sample aerosol without propellant. An adapter with Expert L and a spindle LCP at 60 rpm were used.	Aerosol solution without propellant	5.13 mPa.s (20°C ± 0.2°C) 3.04 mPa.s (40°C ± 0.2°C) The liquid has Newtonian behaviour	zur Lage, J. EUS26-16 Lab Investigation 009093-PM-PFC-RT, Project no.: 6442. 2016

Conclusion on the physical, chemical and technical properties of the product
The insect repellent aerosol as manufactured is a clear colourless liquid with a mild characteristic, slight alcoholic smell. The relative density of the product without propellant is 0.949 g/l at 20 °C. At 20°C and a concentration between 1.0 vol% and 100 vol%, the pH value

is between 3.8 and 4.8. The product has a long term stability and is stable under cold and accelerated storage conditions. The shelf life of the product is 2 years. Light influence is avoided by using a lightproof aluminium packaging. There are no humidity effects expected in that closed package. The product should not be stored for prolonged times (more than 12 weeks) at temperatures >35°C. All of the spray patterns appear to be homogeneous. The discharge rate of the spray is 2.2 g/s at the start of the product use. More than 99% of the aerosol has a particle size greater than or equal to 10 microns. The surface tension of the product without propellant is 29.9 mN/m and the viscosity 5.13 mPa.s. 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
Explosiviness	Waived	-	none of ingredients are classified as explosive substances	-
Flammability	EPA OPPTS 830.6315 Repeated test after emptying and recharging until three successive determinations agreed within the limits specified for repeatability (2 °C).	Aerosol solution without propellant and Bitrex	The flash point of the aerosol solution without propellant was determined to be 29.6°C	Fieseler, A. Doc 242-006 Determination of the flash point of Aerosol solution (without Propellant) containing 30% IR 3535®, 2011
Flammable gases	Waived	-	the product is an aerosol	-
Flammable aerosols	UNECE Section 31	US Aerosol Formulation	The product is placed on the market filled in aerosol dispensers with extremely flammable propellants under pressure (35% w/w per spray can). The product with propellant has to be classified as flammable aerosol, category 2. Ignition distance = 30 cm	Report R150394 : Ignition Distance Determination per UNECE Section 31 (23/07/2015)
Oxidising gases	Waived	-	Based on the properties of the ingredients the product is not considered to be oxidising.	-
Gases under pressure	Waived	-	the product is an aerosol	-
Flammable liquids	Waived	-	the product is an aerosol	-
Flammable solids	Waived	-	the product is an aerosol	-
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.

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
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	Waived	-	the product is an aerosol	-
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	Waived	-	none of ingredients are classified as able to emit flammable gases in contact with water	-
Oxidising liquids	Waived	-	none of ingredients are classified as oxidising substances	-
Oxidising solids	Waived	-	the product is an aerosol	-
Organic peroxides	Waived	-	none of ingredients are classified as organic peroxides	-
Corrosive to metals	Waived	-	none of ingredients are classified as corrosive to metals	Long-year experience with this and similar mixtures.
Auto-ignition temperatures of products (liquids and gases)	EC Method A.15	Aerosol solution without propellant and Bitrex	425°C.	Dornhagen, J. Doc 242-003 Aerosol Solution (without Propellant) containing 30 % IR 3535® - Batch No.: SM-0-1-2/090211 - Auto-Ignition Temperature (Liquids and gases) A.15. 2011
Relative self-ignition temperature for solids	Waived	-	the product is an aerosol	-
Dust explosion hazard	Waived	-	the product is an aerosol	-

Conclusion on the physical hazards and respective characteristics of the product

The auto-ignition temperature of the solution without propellant is 425°C and the flashpoint of the solution without propellant is 29.6°C. The product has no self-reacting properties and 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 but based on the results of the ignition distance test must be classified as flammable aerosol category 2

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 (IR) 3-[N-n-butyl-n-acetyl]aminopropionic acid in aerosol.	HPLC-UV - No extraction - No clean up - LiChropher RP18 (250*4 mm) column - UV-Vis/DAD at 220 nm	1%/10 5%/10 10%/10 30%/15	Regression Coefficient (r2): > 0.9992; y = 21706x - 141584 Concentration range = from 51 to 1571 mg/L, Number of calibration points = 9	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.	1% 92-98 5 %10% 30%	94 100 100 97	1.6 1.9 1.1 1.3	LOQ: 250 mg/l LOD: 7 mg/l	Meinerling, M. DOC421-001. IR3535® - Validation of an analytical method for the determination of ir3535® and its hydrolysis product in different formulations. 2007 1st Final Report Amendement from 14th of June 2016
IR3535 free acid – hydrolysis product	HPLC-UV - No extraction - No clean up	5%/10 (for 1%IR3535) 5%/10 (5%IR3535) 1%/10	Regression Coefficient (r2): > 0.9991; y = 23988x - 67471	No interference substances observed. The retention time of the analytes IR3535 and its hydrolysis	5% 5 % 1% 1%	100% 101% 102% 102%	1.5 2.7 1.7 2.0	LOQ: 50 mg/l LOD: 3 mg/l	Meinerling, M. DOC421-001. IR3535® - Validation of an analytical method for the

	- LiChropher RP18 (250*4 mm) column - UV-Vis/DAD at 220 nm	(10%IR3535) 1%/15 (30%IR3535) Validated concentration range 0.1 – 5% hydrolysis product. The lowest concentration comes from report 98322204 with 10% IR3535 solution (READ ACROSS from IR3535 Lotion)	Concentration range = from 50 to 250 mg/L, Number of calibration points = 9	product in the sample solutions did not differ by more than 1 % from that for the standard solution.					determination of ir3535® and its hydrolysis product in different formulations. 2007 Statement Ibacon, 2016 Study no 98322204, Fieseler,2015

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 aerosol 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 94 – 102%. Repeated injection of the aerosol samples resulted in a coefficient of variation which was less than 2.7 %. 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 ≥ 94%.

For other analytical methods refer to the CAR of active substance.

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 the label submitted by the applicant :

The product ***Insect Repellent Aerosol IR3535® 30%*** is presented as a ready-to-use pump spray to be applied on uncovered human skin (to face, arms, hands, legs and feet only) and on clothes.

The product is intended to be used by general public (children from 1 year old and adults) in temperate and tropical areas. An adult should apply this product to children under 10 years of age.

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

- Applying sun care products or cosmetic formulations after repellent use will decrease the efficacy of the repellent considerably
- 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.

IMPORTANT NOTE : The overall aerosol product, used in some if the efficacy tests, does contain 20 % IR3535®. However, when the product is applied, the propellant is lost through evaporation, leaving only the liquid phase. This liquid phase then contains 30 % IR3535®, which is in fact the concentration to which the skin is exposed. Hence the name given to the product.

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 Aerosol IR3535® 30%*** is intended to be used to repel arthropods on skin and clothes.

- The target organisms to be control are mainly mosquitoes and ticks. This product is also intended to repel biting flies (stable flies, black flies, sand flies), deer flies, biting midges, house flies, wasps and bees from treated skin and clothing preventing respective consequences.

- The organisms to be protected are humans.

2.2.6.3 Effects on target organisms, including unacceptable suffering

Important Note **:** The formulation does contain 20 % IR3535 and 35 % w/w of propellant which is lost after evaporation from the spray resulting in an applied concentration of 30 % IR3535 on skin.

The applicant submitted 4 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**
PT19 Repellent	- Aerosol - Applied on uncovered human skin - For consumers - In temperate and tropical areas	Insect Repellent Aerosol IR3535® *Product without propellant EUS26-16-9N (lot # M17347) containing 30.4% IR3535®* according to the certificate of analysis joined to the efficacy report. But the test-product with propellant (aerosol) is equivalent to the US Aerosol Formulation	**TICKS** *Ixodes scapularis* (US deer ticks) nymphs	Lab test	- with 10 volunteers - 0.00134 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 (+19-23°C ; 41-51% rH)	11 hours complete protection	Doc N° 336-1914/2007 Reliability 2
PT19 Repellent	- Aerosol - Applied on uncovered human skin - For consumers - In temperate and tropical areas	Insect Repellent Aerosol IR3535® Aerosol with hydroalcoholic solution, 30% IR3535 *Product without propellant EUS26-16-9N (lot # M17347) containing 30.4% IR3535®* according to the certificate of analysis joined to the efficacy report. But the test-product with propellant (aerosol) is equivalent to the US Aerosol Formulation	**MOSQUITOES** *Aedes melanimon* (predominant species), *Culex erythrothorax, Culex tarsalis, Culiseta incidens, Anopheles freeborni* and *Aedes vexans* With very high mosquito pressure	Field test on 2 different sites (Forest and Marsh/Pasture)	- with 10 volunteers in each of the two habitats - 0.000987 g/cm^2. - Exposure started 2h (grassland) or 3h (wooded picnic area) after application - 1 min exposure time, every 15 min until 14 hours - "normal" climatic conditions for temperate areas (+13-20°C ; 57-91% rH)	10 hours complete protection	Doc N° 336-1915/2007 Reliability 1

PT19 Repellent	- RTU lotion/spray - Applied on uncovered human skin - For consumers - In temperate and tropical areas	Insect Repellent Lotion/Pump spray (15% IR3535)	**TICKS** *Ixodes ricinus* (EU sheep ticks) nymphs	Lab test	- with 11 volunteers - 1 g BP/600 cm^2 on the forearm - Exposure started immediately after application - 5 min exposure time, every 15 min - "normal" climatic conditions for temperate areas (+23.2-25.4°C ; 24.2±3.7% rH)	8 hours complete protection	Doc N° 336-1921/2006 Supportive study
PT19 Repellent	- RTU spray - Applied on uncovered human skin - For consumers - In temperate and tropical areas	The composition of the product tested is not reported **TMT-003**	**MOSQUITOES** *Aedes albopictus*	"Arm-in-cage" simulated-use test	-	-	Doc N° 336-1922/2006 Reliability 4

Conclusion on the efficacy of the product
The product ***Insect Repellent Aerosol IR3535®*** (aerosol with hydroalcoholic solution, 30% IR3535) when used at a dose of 0.00134 g/cm^2 provides up to 11 hours complete protection time against ticks found in temperate areas. The product ***Insect Repellent Aerosol IR3535®*** (aerosol with hydroalcoholic solution, 30% IR3535) when used at a dose of 0.000987 g/cm^2 provides up to 10 hours complete protection time against mosquitoes found in temperate areas.

2.2.6.6 Occurrence of resistance and resistance management

There are no reported cases of resistance developing in the literature so far.

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 been authorized.

- As stated by the applicant, the product is intended to be used on skin against black flies, horse-flies, wasps and bees. But, due to the absence of relevant efficacy tests, these uses of the product haven't been authorized.

- As stated by the applicant, the product is intended to be used on clothes. But, due to the absence of efficacy tests and good results on clothes, this use of the product hasn't been authorized.

2.2.6.8 Evaluation of the label claims

According to the label, the product ***Insect Repellent Aerosol IR3535®*** (aerosol with hydroalcoholic solution, 30% IR3535) does provide a good protection against ticks and mosquitoes during 8 hours in temperate and tropical areas.

Based on the efficacy tests submitted and validated, this claim is partially supported i.e. only for a use in temperate areas.

For products claiming protection against mosquitoes & ticks such as the product ***Insect Repellent Aerosol IR3535®*** (aerosol with hydroalcoholic solution, 30% IR3535), the protection time against mosquitoes & ticks found in temperate areas would be up to 8h (protection time claimed by the Applicant) when used at 0.00134 g/cm2, based on the efficacy tests submitted and validated.

For products claiming protection against mosquitoes only, the protection time against mosquitoes found in temperate areas would be up to 11h when used at 0.00134 g/cm2 based on the efficacy tests submitted and validated.

For products claiming protection against ticks only, the protection time against ticks found in temperate areas would be of 10h when used at 0.000987 g/cm2, based on the efficacy tests submitted and validated.

The overall protection time of 8h mentioned on the label for this product against ticks and mosquitoes can be therefore granted.

Remark : Mentioning on the label application rate (such as 0.00167 g product/cm^2) is not easy to observe and useless for the consumer. Therefore, the efficacy expert is of the opinion to put on the label more friendly consumer use instructions such as "Apply sparingly to uniformly cover uncovered parts of the body (face, hands, arms, legs and feet only)"

- 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 ticks and mosquitoes 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)

N.D.

2.2.7 Risk assessment for human health

2.2.7.1 Assessment of effects on Human Health

Skin and eye irritation and sensitising properties were assessed using formula EUS26-16 Insect Repellent Aerosol (US Aerosol Formulation). The test substance can be regarded as representative for the product under evaluation. The main difference between the 2 formulas is the presence (EUS26-16) / absence (product under evaluation) of a small amount of denaturant, and a slightly higher concentration of Bitrex in the product under evaluation. Classifications of the substances in question indicate that they will not affect the results of the properties tested. For details, see section 2.2.2 and confidential part of the PAR.

(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 1♂, 2♀ 1 test group, 3 animals	EUS26-16 Insect Repellent Aerosol No vehicle 0.5 ml / 2.5 cm x 2.5 cm 4h	Erythema: 24h: 1.0 48h: 1.0 72h: 1.0 Edema: 24h: 0.6 48h: 0.3 72h: 0.3 Reversibility: yes Very slight erythema and/or edema for all animals. Max score erythema 1, earliest onset 0.5-1h; max score edema 1, earliest onset 24h. At d7, 1♀ showed desquamation. All irritation subsided by d14. No deaths, no remarkable bw changes	US Aerosol Formulation	[redacted] 2006 (a)

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
45172	M	B	1	1	1	1	1	1	0	0	1	0	0	0	0	0
45185	F	A	0	1	1	1	1	1	0	0	1	1	1	1	1	0
45187	F	D	0	1	1	1	1	1d	0	0	0	0	0	0	0	0

Means 24-72 hours (individual animals)		
45172	1.0	0.33
45185	1.0	1.0
45187	1.0	0.0
Mean 24-72 hours (all animals)		
	1.0	0.44

d = Desquamation

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. All irritation subsided by study termination (day 14). Based on the evaluation according to EU criteria, the mean scores at 24-72 hours for erythema and edema were calculated to be 1.0 and 0.44, respectively.

The mean scores determined for erythema (1.0) and edema (0.44) do not trigger a classification according to the EU and GHS classification and labelling system taking also into account that skin reactions were shown to have returned to normal by the end of the post-observation period. The biocidal product is not classified for skin corrosion/irritation according to (EU) nr. 1272/2008.

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; skin reactions were shown to have returned to normal by the end of the post-observation period.
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 1♂, 2♀ 1 test group, 3 animals	EUS26-16 Insect Repellent Aerosol No vehicle 1 animal: 0.3g 2 animals: 1.2g 1 single unwashed exposure	Cornea: 24h: 1.3 48h: 1.3 72h: 1.0 Iris: 24h: 0.0 48h: 0.0 72h: 0.0 Conjunctiva; redness: 24h: 2.0 48h: 1.6 72h: 1.6 Conjunctiva; chemosis: 24h: 1.6 48h: 1.6 72h: 1.3 Reversibility: Yes Earliest onset for all symptoms: 1h Max scores: cornea 2, conjunctiva, redness 3, conjunctiva, chemosis 3 Reversible at d14 2 out of 3 animals: average corneal opacity ≥1, average conjunctival redness ≥2	US Aerosol Formulation	[redacted] (2006) (b)

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

Rabbit No/sex	No. 45159/male				No. 45179/female				No. 45180/female			
Time after treatment [hours]	1	24	48	72	1	24	48	72	1	24	48	72
Cornea												
Opacity	0	0	0	0	1	2	2	2	1	2	2	1
Area involved	0	0	0	0	1	3	2	2	1	2	2	1
Iris	0	0	0	0	0	0	0	0	0	0	0	0
Conjunctivae												
Redness	2	1	1	1	3	3	2	2	3	2	2	2
Chemosis	1	1	1	1	3	2	2	1	3	2	2	2
Discharge	1	0	0	0	3	2	1	0	3	1	1	1
Mean of 24-72-hour Readings: individual animals	Opacity: 0 Iris: 0 Redness: 1 Chemosis: 1				Opacity: 2 Iris: 0 Redness: 2.33 Chemosis: 1.67				Opacity: 1.67 Iris: 0 Redness: 2 Chemosis: 2			
Mean of 24-72-hour Readings: all animals	Opacity: 1.22 Iris: 0 Redness: 1.78 Chemosis: 1.55											
Classification	Irritant (EU: --; GHS: Eye Irrit. 2, H319)											

The primary eye irritation potential of EUS26-16 Insect Repellent Aerosol was investigated in 3 NZW rabbits according to OECD TG 405 and under GLP.

Initially, a single animal was dosed to evaluate the ocular irritative potential of the test article; no severe ocular damage was observed. Two additional rabbits each received a single unwashed exposure of the test article. The single animal was administered 0.3 g of the test article and the two additional animals were administered a combined total of 2.4 g of the test article.

There were no deaths or remarkable body weight changes noted during the study. Positive corneal and conjunctival irritations were noted for all animals. Corneal and conjunctival irritation subsided by study termination (study day 14). According to CLP criteria, the mean scores for corneal reactions, iritis, conjunctival redness and chemosis were 1.22, 0, 1.78 and 1.55, respectively. Since the average score was ≥ 1 for corneal opacity and ≥ 2 for conjunctival redness in animals 45179 and 45180, the biocidal product has to be classified as a potential eye irritant according to GHS criteria (Eye Irrit. 2, H319).

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

Conclusion used in Risk Assessment – Eye irritation	
Value/conclusion	the biocidal product has to be classified as a potential eye irritant according to (EU) nr. 1272/2008 (Eye Irrit. 2, H319)
Justification for the value/conclusion	average score was ≥ 1 for corneal opacity and ≥ 2 for conjunctival redness in 2 out of 3 animals
Classification of the product according to CLP and DSD	Eye damage/irritation cat 2, H319

(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 Aerosol IR3535® 30 % 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 Aerosol IR3535® 30 %.

(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	Guinea pig Hartley [Crl: HA] 10 ♂ and 10 ♀/ test group 5 ♂ and 5 ♀/ naïve control group	EUS26-16 Insect Repellent Aerosol 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	US Aerosol Formulation	[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		19	1	0	0	0	18	2	0	0	0	0.0	0.1	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 EUS26-16 Insect Repellent Aerosol was evaluated using the modified Buehler test method.

Animal welfare benefits and scientific advantages make the LLNA the preferred test for sensitization. However, existing data of good quality derived from a Buehler test should be acceptable as they preclude the need for further in vivo testing. As none of the cosmetic ingredients in the formulation have a sensitizing potential and as the active substance is not considered as sensitizing (Buehler test and Photoallergenicity maximisation test), the Buehler test was regarded as acceptable.

There were no deaths, test article-related clinical findings or remarkable body weight changes during the study period. Following challenge dosing with EUS26-16 Insect Repellent Aerosol, 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.

EUS26-16 Insect Repellent Aerosol 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 EUS26-16 Insect Repellent Aerosol, 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 is 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 this 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 toxicity (oral) according to (EU) nr. 1272/2008
Justification for the selected value	Neither the active ingredient nor one of the other relevant ingredients of the biocidal product are classified with respect to acute oral toxicity. Thus, Insect Repellent Aerosol IR3535® 30 % 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 Aerosol IR3535® 30 % 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. 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 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 Aerosol IR3535® 30 % 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. 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

Neither the active substance nor one of the ingredients of the biocidal product are classified with respect to acute dermal toxicity. Therefore, the biocidal product Insect Repellent Aerosol IR3535® 30 % has not been classified with respect to acute dermal toxicity.

The absence for an acute dermal toxicity hazard is confirmed by the availability of a OECD TG 402 compliant acute dermal toxicity study performed with EUS26-15 US Pump Spray Formulation, containing 20% IR3535®. The tested pump spray formulation did not contain propylene glycol (dermal LD50 neat substance > 2.0 g/kg bw) as is present in the aerosol formulation. Read-across of the dermal toxicity study is possible on the basis of the data for the pump spray (20% IR3535, dermal LD50 > 5.0 g/kg bw) and data for the active substance IR3535® (dermal LD50 > 10.0 g/kg bw).

The results of the acute dermal toxicity with EUS26-15 demonstrated an acute dermal toxicity of > 5000 mg/kg bw which does not require a classification and labelling with respect to acute dermal toxicity. Moreover, data for the active substance (dermal LD50 > 10.0 g/kg bw) support that the higher active substance concentration in the aerosol solution applied to the skin does not influence the results of the test. It can, therefore, be concluded that Insect Repellent Aerosol IR3535® 30 % is not acutely toxic after dermal application and a classification with respect to acute dermal toxicity is not required.

Since the acute dermal toxicity potential of Insect Repellent Aerosol IR3535® 30 % is sufficiently characterized by the tested similar biocidal product, the conduct of an acute dermal toxicity study with Insect Repellent Aerosol IR3535® 30 % is scientifically not justified.

No human data are available for acute oral toxicity.

Data for the acute dermal toxicity with Insect Repellent Pump Spray IR3535® 20 %:

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 B.3 EPA OPPTS 870.1200	Rat Crl:CD(SD) 5♀, 5♂/dose	EUS26-15 US Pump Spray Formulation Undiluted 5000 mg/kg bw 10% of body area	At necropsy: no deaths no remarkable bw changes no remarkable macroscopic findings	>5000 mg/kg bw	US Pump Spray Formulation A classification of the biocidal product with respect to acute dermal toxicity is not required.	[redacted] (2006) (d)

		Semiocclusive	Clinical findings: abnormal excretion various discoloured areas due to discharges/excretions persisted until day 1 post-dosing Dermal findings: very slight erythema (grade 1), pinpoint scabbing at the dose sites. Very slight erythema (grade 1) persisted until study termination on day 14.			

Value used in the Risk Assessment – Acute dermal toxicity	
Value	Biocidal product not classified for acute toxicity (dermal) according to (EU) nr. 1272/2008
Justification for the selected value	None of the components of the biocide are classified for acute dermal toxicity according to (EU) nr. 1272/2008. Read-across from EUS26-15 US Pump Spray Formulation, containing 20% IR3535® to Insect Repellent Aerosol IR3535® 30 % .
Classification of the product according to CLP and DSD	none

Data waiving	
Information requirement	Acute dermal toxicity: Study scientifically unjustified
Justification	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. The acute inhalation toxicity of Insect Repellent Aerosol IR3535® 30 % can be assessed on the basis of the properties of the ingredients. Read-across from EUS26-15 US Pump Spray Formulation to Insect Repellent Aerosol IR3535® 30 %.

(VII)Information on dermal absorption

A dermal penetration study has not been performed with Insect Repellent Aerosol IR3535® 30%. Referring to Regulation (EU) No 528/2012, Annex IV, a study can be waived if other data are available and which can be used instead.

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®[1] 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. 64 % 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®.

Since the composition of Insect Repellent Aerosol IR3535® 30 % is very comparable to the product tested in the dermal toxicokinetics/metabolism study, especially as concerns the content of organic solvents which may have an impact on the skin absorption, a separate skin absorption study with the biocidal product can be waived. Instead, the skin absorption of 14% for IR3535® can be applied to Insect Repellent Aerosol IR3535® 30%. A dermal penetration of 14% will be used in the human exposure assessments for the intended use of the biocidal product.

It needs to be noted that following application of the aerosol onto the skin, the content of IR3535® in the biocidal product will be 30% instead of 20% as a consequence of a volatilisation of the propellants contained in the aerosol. As stated in Sanco/222/2000 rev. 7 (19 March 2004), the dermal absorption is inversely correlated to concentration. For this reason, the skin absorption of IR3535® from Insect Repellent Aerosol IR3535® 30% will be very likely lower than 14% and the use of the skin absorption as derived in the dermal toxicokinetics/metabolism study represents a conservative approach.

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

Value(s) used in the Risk Assessment – Dermal absorption			
Substance	Insect Repellent Aerosol IR3535® 30%		
Value(s)*	14%		

[1] identical to US Pump Spray Formulation

Justification for the selected value(s)	Read-across from human volunteer study on a water/ethanol-based 20 % IR3535® formulation[1] ([redacted], 2010)		

Data waiving	
Information requirement	Skin absorption study
Justification	Read-across from human volunteer study on a water/ethanol-based 20 % IR3535® formulation[1]

(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.

(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 active substance contained in the product Insect Repellent Aerosol IR3535® 30 % is the same as evaluated in the CAR for IR3535® and therefore no new data/information on the active substance is required.

The product Insect Repellent Aerosol IR3535® 30 % is a clear solution containing IR3535® at a concentration of 20 % when including the propellant in the formulation. The solution reaching the skin contains 30.77% IR3535®. The propellant will evaporate from the aerosol particles before they reach the skin and thus does not need to be assessed. Therefore, the biocidal product 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.	Yes	n.a.	n.a.	Yes	n.a.
Dermal	yes	n.a.	Yes	n.a.	n.a.	Yes	n.a.
Oral	n.a.	n.a.	n.a.	n.a.	n.a.	Yes	n.a.

For primary exposure, the most relevant route of exposure is the dermal route. During the application phase, inhalation exposure is possible resulting from respiring aerosols after spraying. It was considered that the respirable particles will be absorbed via the lower airways and that the non-respirable particles will precipitate in the upper airways and be taken in orally. 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 11 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 : 0.00134 g product/cm² skin against ticks and 0.000987 g/cm^2 against mosquitoes.

The application rate is considered to be **0.987 mg/cm^2.**

Remark: since no safe use is obtained with the value of 0.987 mg/cm^2 , the higher application rate will also not be acceptable.

Number of application per day:

The applicant proposes : "*For prolonged protection the product can be reapplied by adults after 8 hours or sooner if effectiveness is diminished. The product should not be applied more than two times per day for adults, not more than 1 time per day for children and not at all for infants < 3 months.*"

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)**	**Treated surface (cm2)**	**number of application per day**
ADULT irrespective of gender (based on female 30 to <40 years old)	9.01131 g	9130	2 applications/day
CHILD 6 to < 12 years old irrespective of gender (based on female 6 to <11 years old)	4.99422 g	5060	1 application/day
CHILD 2 to < 6 years old irrespective of gender (based on data from female 2 to <6 years old)	3.69138 g	3740	1 application/day
TODDLER 1 to <2 years old irrespective of gender (based on female 1 to <2 years old)	2.60568 g	2640	1 application/day
INFANT < 1 year old irrespective of gender (based on female 6 to <12 months old)	2.225685 g	2255	1 application/day

Dermal, inhalatory and oral absorption:

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

(II) List of scenarios

Insect Repellent Aerosol IR3535® 30 % 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.

A potential inhalation exposure is only possible during the application phase via aerosols. After application, no inhalation exposure risk is anticipated due to the low vapour pressure of IR3535®. Moreover, it has to be taken into account that the exposure time to the aerosol is extremely short and that it is not recommended to spray directly onto the face.

Dermal secondary exposure is possible for adults treating or handling children. However, this scenario is fully covered by primary adult dermal exposure. A parent applying (spraying) the product on children and herself/himself has been taken into account for inhalative secondary exposure.

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

Inhalation of volatilized residues after application is relevant based on the HEEG opinion on Assessment of Inhalation Exposure of Volatilized Biocide Active Substance. The exposure to volatilised residues indoors was calculated using ConsExpo model.

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.	Application phase	Primary exposure: Inhalation exposure assessment for adults, children, toddlers and infants.	Non-professionals
3.	Post-application phase	Secondary exposure (indirect exposure as a result of use): Hand-mouth transfer reverse reference scenario (oral exposure)	Non-professionals
4.	Post-application phase	Parent treating two children and himself/herself (spraying) (combined inhalative and oral exposure)	Non-professionals
5.	Post-application phase	Inhalation of volatilised residues after application (inhalative exposure)	Non-professionals
6.	Exposure during production	Mixing and Loading model – worst case for the production, formulation and disposal of the biocidal product	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 addressed under a point below (scenario 6).

(IV) Professional exposure

Not relevant since the product Insect Repellent Aerosol IR3535® 30 % is intended to be used by general public.

(V) Non-professional exposure

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 with the document : Biocide Human Health Exposure Methodology (Oct 2015).		
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] (reaching the skin)	30.77%
Tier 1- Adult	Number of application / day[1]	2
	Body weight[1]	60 kg
	Amount of biocidal product/ application[1]	9.01 g
Tier 1- Child 6 to < 12 years old	Number of application / day[1]	1
	Body weight[1]	23.9 kg
	Amount of biocidal product/ application[1]	4.99 g
Tier 1- Child 2 to < 6 years old	Number of application / day[1]	1
	Body weight[1]	15.6 kg
	Amount of biocidal product/ application[1]	3.69 g
Tier 1- Toddler	Number of application / day[1]	1
	Body weight[1]	10 kg
	Amount of biocidal product/ application[1]	2.61 g
Tier 1- Infant	Number of application / day[1]	1
	Body weight[1]	8 kg
	Amount of biocidal product/ application[1]	2.23 g
Tier 2- Adult	Number of application / day[2]	1

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

Calculations for scenario 1

Summary table: estimated exposure for Dermal Primary exposure		
Exposure scenario	**Tier/ PPE**	**Estimated dermal uptake**
Scenario 1 – ADULT 2 applications/day	Tier 1 / no PPE	12.94 mg/kg bw/day
Scenario 1 – CHILD (6-12) 1 application/day	Tier 1 / no PPE	9.00 mg/kg bw/day
Scenario 1 – CHILD (2-6) 1 application/day	Tier 1 / no PPE	10.19 mg/kg bw/day
Scenario 1 – TODDLER 1 application/day	Tier 1 / no PPE	11.22 mg/kg bw/day
Scenario 1 – INFANT 1 application/day	Tier 1 / no PPE	11.98 mg/kg bw/day
Scenario 1 – ADULT 1 application/day	Tier 2 / no PPE	6.47 mg/kg bw/day

Scenario 2: Primary exposure: Inhalation exposure assessment for adults, children, toddlers and infants.

Description of Scenario 2

This scenario is based on the one available in the CAR of IR3535®. It has been adapted with the documents : Biocide Human Health Exposure Methodology (Oct 2015) and Guidance on the biocidal products Regulation (volume III Human Health – Part B Risk Assessment, Oct 2015).

Model used: "Consumer spraying and dusting model 2 – pre-pressurised aerosol spray can" from Biocide Human Health Exposure Methodology, p. 220

Inhaled product =

Inhalation rate x number of application/day x spray duration (min.) / 60 min. x indicative value for inhalation

Inhaled active substance =

inhaled product x percent of a.s. in the b.p.

Particle size distribution will determine the respirable fraction of the product released. Regarding the cut-off value for respirable droplet size, different sources are available. The BPR guidance III part B states that particles below 15 µm may reach the alveolar region of the respiratory tract. According to the Biocides Human Health Exposure Methodology, particles larger than 20 µm are all non-respirable and particles smaller than 5 µm are respirable for about 35%. The draft Proposal for harmonising the assessment of human exposure to repellents (PT19) states that in general, the cut-off for the respirable fraction is 10 µm, and refers to ConsExpo 4.1 for the assessment of inhalation exposure. In ConsExpo 4.1, the default cut-off for the respirable fraction has been set at 15 µm.

For Insect Repellent Aerosol IR3535® 30%, particle size distribution data are incomplete; data are available only for particles smaller than 10 µm. However, all particles are considered to be absorbed, either by inhalation or orally; therefore this data gap will not change the total systemic exposure via inhalation nor the conclusion. Moreover, the product Insect Repellent Aerosol IR3535® 30% is not classified as dangerous for the respiratory tract according to CLP regulation. For this reason, we can accept a cut-off of 10µm for the respirable fraction.

The applicant provided a study to determine proportions of respirable and non-respirable particles. The result of this study shows that 0.38% of the total amount of aerosol released has a size lower to 10µm; 99.62% has a size equal or greater to 10µm. The particles above 10µm are assumed to be taken in orally.

Inhalation systemic exposure:

0.38 % x inhaled a.s. x inhalation absorption / body weight

Oral systemic exposure:

99.62 % x inhaled a.s. x oral absorption / body weight

	Parameters	**Value**
For All categories	Inhalation absorption[1]	100%
	Oral absorption[1]	100%
	% of active substance in biocidal product[1] (reaching the skin)	30.77%
	Indicative value for inhalation[2]	35.9 mg/m^3
	Spray duration[3]	4 minutes
Tier 1- Adult	Number of application / day[1]	2

	Body weight[1]	60 kg
	Respiration rate [m³/air/hour] [1]	1.25 m³/h
Tier 1- Child 6 to < 12 years old	Number of application / day[1]	1
	Body weight[1]	23.9 kg
	Respiration rate [m³/air/hour] [1]	1.32 m³/h
Tier 1- Child 2 to < 6 years old	Number of application / day[1]	1
	Body weight[1]	15.6 kg
	Respiration rate [m³/air/hour] [1]	1.26 m³/h
Tier 1- Toddler	Number of application / day[1]	1
	Body weight[1]	10 kg
	Respiration rate [m³/air/hour] [1]	1.26 m³/h
Tier 1- Infant	Number of application / day[1]	1
	Body weight[1]	8 kg
	Respiration rate [m³/air/hour] [1]	0.84 m³/h
Tier 2- Adult	Number of application / day[4]	1

[1] General information, see justification above

[2] Model used: "Consumer spraying and dusting model 2 – Pre-pressurised aerosol spray can" Biocide Human Health Exposure Methodology, p. 220

[3] CAR of IR3535® (expert judgement)

[4] Limitation of the exposure

Calculations for scenario 2

Summary table: estimated exposure for Inhalation Primary exposure			
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake**	**Estimated oral uptake**
Scenario 2 – ADULT 2 applications/day	Tier 1 / no PPE	0.00012 mg/kg bw	0.0306 mg/kg bw
Scenario 2 – CHILD (6-12) 1 application/day	Tier 1 / no PPE	0.000154 mg/kg bw	0.0405 mg/kg bw
Scenario 2 – CHILD (2-6) 1 application/day	Tier 1 / no PPE	0.000226 mg/kg bw	0.0595 mg/kg bw
Scenario 2 – TODDLER 1 application/day	Tier 1 / no PPE	0.000353 mg/kg bw	0.0924 mg/kg bw
Scenario 2 – INFANT 1 application/day	Tier 1 / no PPE	0.000294 mg/kg bw	0.0770 mg/kg bw
Scenario 2 – ADULT 1 application/day	Tier 2 / no PPE	0.000058 mg/kg bw	0.0153 mg/kg bw

Scenario 3: Secondary exposure (indirect exposure as a result of use): Hand-mouth transfer reverse reference scenario (oral exposure)

Description of Scenario 3
This scenario is based on the one available in the CAR of IR3535®. It has been updated with the document : Biocide Human Health Exposure Methodology (Oct 2015).
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 because it's recommended to no apply the product on 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

	Parameters	**Value**
For All categories	Oral absorption[1]	100%
	% of active substance in biocidal product[1] (reaching the skin)	30.77 %
Tier 1- Adult	Factor for oral intake by hand-mouth transfer[2]	4 %
	Body weight[1]	60 kg
	Amount of biocidal product/ application[1]	9.01 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]	4.99 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]	3.69 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]	2.61 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]	2.23 g

[1] General information, see justification above

[2] 4% is the factor of the total treated body surface (Head, hands, arms, legs and feet) reported to the surface area of the fingers. 8% is the factor of the total treated body surface (Head, hands, arms, legs and feet) reported to the surface area of the hands. They are default values currently discuss for a harmonisation of human exposure scenarios for PT19.

Calculations for scenario 3

Summary table: estimated exposure for Hand-mouth transfer reverse reference scenario (oral exposure)		
Exposure scenario	**Tier/PPE**	**Calculated exposure to IR3535®**
Scenario 3 – ADULT	Tier 1 / no PPE	Adult up to 2.70 applications
Scenario 3 – CHILD (6-12)	Tier 1 / no PPE	Child (6-12) up to 0.97 applications
Scenario 3 – CHILD (2-6)	Tier 1 / no PPE	Child (2-6) up to 0.86 applications
Scenario 3 – TODDLER	Tier 1 / no PPE	Toddler up to 0.78 applications
Scenario 3 – INFANT	Tier 1 / no PPE	Infant up to 0.73 applications

Scenario 4: Parent treating two children and himself/herself (combined inhalative and oral exposure)

Description of Scenario 4		
Worst case: a parent applying (spraying) the product on two children and herself/himself **Model used:** it's the same model than the one used to do the scenario 2. Remark: the secondary dermal exposure was not assessed. It is covered by the primary dermal use exposure of the adult. The product would probably be rubbing on the child scalp and the layer on hands will not exceed the amount the adult will put on himself. So, BE has decided to follow the CAR which supposes that the dermal secondary exposure will be covered by the primary dermal exposure. Only inhalation exposure is relevant in this case.		
	Parameters	**Value**
For All categories	Inhalation absorption[1]	100%
	Oral absorption[1]	100%
	% of active substance in biocidal product[1]	30.77%
	Indicative value for inhalation	35.9 mg/m^3
	Body weight[1]	60 kg
	Respiration rate [m^3/air/hour][1]	1.25 m³/h
	Spray duration[3]	4 minutes
Tier 1- Adult	Number of application / day[1]	4 (2 appl/d for Adult himself and 1 appl/d for each of the 2 children)

[1] General information, see justification above

[2] Model used: "Consumer spraying and dusting model 2 – Pre-pressurised aerosol spray can" Biocide Human Health Exposure Methodology, p. 220

[3] CAR of IR3535® (expert judgement)

Calculations for scenario 4

Summary table: estimated exposure for treating two children and himself/herself				
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake**	**Estimated oral uptake**	**Estimated total uptake**
Scenario 4 – ADULT (1 appl/child and 2 appl/himself)	Tier 1 / no PPE	0.000233mg/kg bw	0.0611 mg/kg bw	0.0613 mg/kg bw

Scenario 5: Inhalation of volatilised residues after application (inhalative exposure)

Description of Scenario 5

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.

The scenario is based on ConsExpo : inhalation of vapour, instantaneous release as a worst case and based on the document: Biocide Human Health Exposure Methodology (Oct 2015).

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 scenario 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: 20% (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) = 1.5 x 10^{-3} mbar (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]	9.01 g
	Body weight[2]	60 kg
	Respiration rate [m^3/air/hour][2]	1.25 m^3/h
Tier 1- Child 6 to < 12 years old	Product amount[1]	4.99 g
	Body weight[2]	23.9 kg
	Respiration rate [m^3/air/hour][2]	1.32 m^3/h
Tier 1- Child 2 to < 6 years old	Product amount[1]	3.69 g
	Body weight[2]	15.6 kg
	Respiration rate [m^3/air/hour][2]	1.26 m^3/h
Tier 1- Toddler	Product amount[1]	2.61 g
	Body weight[2]	10 kg
	Respiration rate [m^3/air/hour][2]	1.26 m^3/h
Tier 1- Infant	Product amount[1]	2.23 g
	Body weight[2]	8 kg
	Respiration rate [m^3/air/hour][2]	0.84 m^3/h

[1] According the primary exposure, no application per day can be authorized. Therefore, the product amount corresponds to 1 application/day.
[2] General information, see justification above

Calculations for scenario 5

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 5 – ADULT	Tier 1 / no PPE	4.81 mg/kg bw/day
Scenario 5 – CHILD (6-12)	Tier 1 / no PPE	7.07 mg/kg bw/day
Scenario 5 – CHILD (2-6)	Tier 1 / no PPE	7.65 mg/kg bw/day
Scenario 5 – TODDLER	Tier 1 / no PPE	8.44 mg/kg bw/day
Scenario 5 – INFANT	Tier 1 / no PPE	6.01 mg/kg bw/day

Combined scenarios : Total primary exposure : combination of scenario 1 and 2

Summary table: estimated exposure for combined scenarios 1+2					
Exposure scenario	**Tier / PPE**	**Estimated dermal uptake [mg/kg bw/day]**	**Estimated inhalation uptake [mg/kg bw]**	**Estimated oral uptake [mg/kg bw]**	**Estimated total acute uptake for primary use [mg/kg bw]**
Scenario 1+2 – ADULT 2 applications/day	Tier 1 / no PPE	12.94	0.00012	0.0306	12.97
Scenario 1+2 – CHILD (6-12) 1 application/day	Tier 1 / no PPE	9.00	0.000154	0.0405	9.04
Scenario 1+2 – CHILD (2-6) 1 application/day	Tier 1 / no PPE	10.19	0.000226	0.0595	10.25
Scenario 1+2 – TODDLER 1 application/day	Tier 1 / no PPE	11.22	0.000353	0.0924	11.32
Scenario 1+2 – INFANT 1 application/day	Tier 1 / no PPE	11.98	0.000294	0.0770	12.06
Scenario 1+2 – ADULT 1 application/day	Tier 2 / no PPE	6.47	0.000058	0.0153	6.49

The exposure of inhalation of volatilized residues after application and the combined inhalative and oral exposure of a parent treating two children are negligible compared to primary (dermal) exposure

(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 3 (hand to mouth transfer), considering that the amount in scenario 3 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 3.

However, Belgium is of advice that the restriction measures (Wash hands thoroughly after handling, do not use on children's hands) must stay to avoid any misuse of the product.

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

In modern formulation plants typically automated equipment is used to add the formulation ingredients and to fill the formulated product into the respective vessels (closed systems). The workers (trained professionals) usually wear personal protective equipment (e.g. gloves). Thus the exposure can occur during the mixing and loading and have been calculated as a worst case.

Scenario 6 : Mixing and Loading model – worst case for the production, formulation and disposal of the biocidal product

Description of Scenario 6
For a worst case situation, it was estimated that the more sustainable model for industrial exposure production, formulation and disposal is : RISKOFDERM Dermal model (loading liquid, automated or semi-automated) from HEEG opinion 1 (2008). **Dermal exposure via clothing:** default potential exposure rates on clothing x Purity of the active substance x Duration of task x Number of events per day (x (1-Factor of protection for clothing)) **Dermal exposure via hands:** default potential exposure rates on hands x Purity of the active substance x Duration of task x Number of events per day (x (1-Factor of protection for gloves)) **Dermal systemic exposure:** (Dermal exposure via clothing + Dermal exposure via hands) x percent of dermal absorption / body weight **Inhalation exposure:** Inhalation is no relevant for this model and is not taken into account **Systemic exposure**: Dermal systemic exposure + 0 (inhalation exposure n.r.)

	Parameters[1]	**Value**
Tier 1	Purity of the active substance[1]	99%
	Dermal absorption[1]	50%
	default potential exposure rates on clothing[2]	101 mg/min
	default potential exposure rates on hand[2]	2.02 mg/ min
	default potential exposure rates for inhalation[2]	n.r. mg/m^3 (and the substance has a low vapour pressure)
	Bodyweight[3]	60 kg
	Number of events per day	1/day
	Duration of task	10 min
Tier 2	Factor of protection for Uncoated cotton coverall[3]	75%
Tier 3	Factor of protection for gloves[3]	90%

[1] CAR (doc IIA)
General information, see justification above
[2] RISKOFDERM Dermal model: loading liquid, automated or semi-automated (HEEG opinion 1, 2008)
[3] Biocide Human Health Exposure Methodology (Oct 2015)

Calculations for Scenario 6

Summary table: systemic exposure associated with production, formulation, and disposal					
Exposure scenario	**Tier/ PPE**	**Estimated inhalation uptake**	**Estimated dermal uptake**	**Estimated oral uptake**	**Estimated total uptake**
Scenario 6	Tier 1/ no PPE	n.r.	8.5 mg/kg bw/d	n.r.	8.5 mg/kg bw/d
Scenario 6	Tier 2/ Uncoated cotton coverall	n.r.	2.25 mg/kg bw/d	n.r.	2.25 mg/kg bw/d
Scenario 6	Tier 3/ Uncoated cotton coverall and gloves	n.r.	2.1 mg/kg bw/d	n.r.	2.1 mg/kg bw/d

(X) Aggregated exposure

Not applicable

(XI) Summary of exposure assessment

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, 2 applications/day	12.94 mg/kg bw/day
	Non-professionals, child (6-12)	Tier 1, no PPE, dermal, 1 application/day	9.00 mg/kg bw/day
	Non-professionals, child (2-6)	Tier 1, no PPE, dermal, 1 application/day	10.19 mg/kg bw/day
	Non-professionals, toddler	Tier 1, no PPE, dermal, 1 application/day	11.22 mg/kg bw/day
	Non-professionals, infant	Tier 1, no PPE, dermal, 1 application/day	11.98 mg/kg bw/day
	Non-professionals, adult	Tier 2, no PPE, dermal, 1 application/day	6.47 mg/kg bw/day
2.	Non-professionals, adult	Tier 1, no PPE, inhalation, 2 applications/day	0.03085 mg/kg bw
	Non-professionals, child (6-12)	Tier 1, no PPE, inhalation, 1 application/day	0.04067 mg/kg bw
	Non-professionals, child (2-6)	Tier 1, no PPE, inhalation, 1 application/day	0.05948 mg/kg bw
	Non-professionals, toddler	Tier 1, no PPE, inhalation, 1 application/day	0.09279 mg/kg bw
	Non-professionals, infant	Tier 1, no PPE, inhalation, 1 application/day	0.77325 mg/kg bw
	Non-professionals, adult	Tier 2, no PPE, inhalation, 1 application/day	0.01534 mg/kg bw
3.	Non-professionals, adult	Tier 1, no PPE, Hand-mouth transfer reverse reference scenario, oral	Adult up to 2.70 applications
	Non-professionals, child (6-12)	Tier 1, no PPE, Hand-mouth transfer reverse reference scenario, oral	Child (6-12) up to 0.97 applications
	Non-professionals, child (2-6)	Tier 1, no PPE, Hand-mouth transfer reverse reference scenario, oral	Child (2-6) up to 0.86 applications
	Non-professionals, toddler	Tier 1, no PPE, Hand-mouth transfer reverse reference scenario, oral	Toddler up to 0.78 applications
	Non-professionals, infant	Tier 1, no PPE, Hand-mouth transfer reverse reference scenario, oral	Infant up to 0.73 applications
4.	Non-professionals, adult	Tier 1, no PPE, inhal+oral, 4 appl/d	0.0613 mg/kg bw
5.	Non-professionals, adult	Tier 1 / no PPE	4.81 mg/kg bw/day
	Non-professionals, child (6-12)	Tier 1 / no PPE	7.07 mg/kg bw/day
	Non-professionals, child (2-6)	Tier 1 / no PPE	7.65 mg/kg bw/day
	Non-professionals, toddler	Tier 1 / no PPE	8.44 mg/kg bw/day

	Non-professionals, infant	Tier 1 / no PPE	6.01 mg/kg bw/day
6.	Professionals	Tier 1 / no PPE	8.5 mg/kg bw/d
	Professionals	Tier 2/ Uncoated cotton coverall	2.25 mg/kg bw/d
	Professionals	Tier 3/ Uncoated cotton coverall and gloves	2.1 mg/kg bw/d

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 application 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

Systemic effects

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 6, mixing & loading, professional	1	500 mg/kg bw/d	5 mg/kg bw/d	8.5 mg/kg bw/d	170%	no
Scenario 6, mixing & loading, professional	2	500 mg/kg bw/d	5 mg/kg bw/d	2.25 mg/kg bw/d	45%	yes
Scenario 6, mixing & loading, professional	3	500 mg/kg bw/d	5 mg/kg bw/d	2.1 mg/kg bw/d	42%	yes

Combined scenarios

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

Local effects

The biocidal product is classified as eye damage/irritation cat 2, H319. However, appropriate risk mitigation measures are assumed to be taken by professionals during production, formulation and disposal. Consequently, there is no need to consider local effects separately.

Conclusion

There is no concern for professionals working with Insect Repellent Aerosol IR3535® 30% during production, formulation and disposal when using appropriate PPE (minimum PPE required: uncoated cotton coverall).

(II) Risk for professional users

Systemic effects

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)
n.a.						

Combined scenarios

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

Local effects

n.a.

Conclusion

n.a.

(III) Risk for non-professional users

Systemic effects

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	12.94	258.79	No
Scenario 1, dermal, child (6-12)	1	500	5	9.00	180.03	No
Scenario 1, dermal, child (2-6)	1	500	5	10.19	203.87	No
Scenario 1, dermal, toddler	1	500	5	11.22	224.50	No
Scenario 1, dermal, infant	1	500	5	11.98	239.69	No
Scenario 1, dermal, adult	2	500	5	6.47	129.40	No
Scenario 2, inhal +oral, adult	1	500	5	0.03085	0.61	Yes
Scenario 2, inhal +oral, child (6-12)	1	500	5	0.04067	0.81	Yes
Scenario 2, inhal +oral, child (2-6)	1	500	5	0.05948	1.19	Yes
Scenario 2, inhal +oral, toddler	1	500	5	0.09279	1.86	Yes
Scenario 2, inhal +oral, infant	1	500	5	0.77325	1.55	Yes
Scenario 2, inhal +oral, adult	2	500	5	0.01534	0.31	Yes
Scenario 3, hand-mouth transfer, adult	1	500	5	up to 2.70 applications	n.a.	Reverse reference scenario
Scenario 3, hand-mouth transfer, child (6-12)	1	500	5	up to 0.97 applications	n.a.	Reverse reference scenario
Scenario 3, hand-mouth transfer, child (2-6)	1	500	5	up to 0.86 applications	n.a.	Reverse reference scenario
Scenario 3, hand-mouth transfer, toddler	1	500	5	up to 0.78 applications	n.a.	Reverse reference scenario
Scenario 3, hand-mouth transfer, infant	1	500	5	up to 0.73 applications	n.a.	Reverse reference scenario
Scenario 4, inhal+oral, adult	1	500	5	0.0613	1.2	Yes
Scenario 5, inhal, adult	1	500	5	4.81	96.2	Yes
Scenario 5, inhal, child	1	500	5	7.07	141.4	No
Scenario 5, inhal, child	1	500	5	7.65	153	No
Scenario 5, inhal, toddler	1	500	5	8.44	168.8	No
Scenario 5, inhal, infant	1	500	5	6.01	120.2	No

Combined scenarios

Scenarios combined	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+2 – ADULT 2 applications/day	Tier 1 / no PPE	500 mg/kg bw/d	5 mg/kg bw/d	12.97	259.41	No
Scenario 1+2 – CHILD (6-12) 1 application/day	Tier 1 / no PPE	500 mg/kg bw/d	5 mg/kg bw/d	9.04	180.85	No
Scenario 1+2 – CHILD (2-6) 1 application/day	Tier 1 / no PPE	500 mg/kg bw/d	5 mg/kg bw/d	10.25	205.06	No
Scenario 1+2 – TODDLER 1 application/day	Tier 1 / no PPE	500 mg/kg bw/d	5 mg/kg bw/d	11.32	226.35	No
Scenario 1+2 – INFANT 1 application/day	Tier 1 / no PPE	500 mg/kg bw/d	5 mg/kg bw/d	12.06	241.24	No
Scenario 1+2 – ADULT 1 application/day	Tier 2 / no PPE	500 mg/kg bw/d	5 mg/kg bw/d	6.49	129.70	No

Local effects

The biocidal product is classified as eye damage/irritation cat 2, H319. However, appropriate risk mitigation measures will be imposed and taken up on the label: 'Do not spray into the eyes or apply to eye area. An adult should apply the product to children below 12 years of age. Do not use on children's hands.' Consequently, there is no need to consider local effects separately.

Conclusion

The biocidal product presents a risk for human health. No safe use can be determined for this product.

(IV) Risk for the general public

Systemic effects

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)
n.a.						

Combined scenarios

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

Local effects

n.a.

Conclusion

n.a.

(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

2.2.9 Risk assessment for the environment

For the product Insect Repellent Aerosol IR3535® 30 % 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.

The composition of the representative product from the CAR is not identical to that of Insect Repellent Aerosol IR3535® 30 %. However, the intended use is identical as well as the amount of active substance in both products. Only the active substance is of relevance for the environmental exposure assessment of this product.

2.2.9.1 Effects assessment on the environment

All data used for the effect assessment of Insect Repellent Aerosol IR3535® 30% 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 Aerosol IR3535® 30% 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, but was not yet assessed in the CAR due to the lack of an endorsed scenario.

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.

2.2.9.2 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 TGD 2003
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	

(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 from $Qform_{appl}$ must coincide with the efficacy of the product and must be adapted accordingly.

The validated efficacious dose for the product 'Insect Repellent Aerosol IR3535 30%' is 0.987 mg/cm² to protect against mosquitoes for up to 10 hours and 1.34 mg/cm² to protect against ticks for up to 11 hours, in temperate areas. Instead of using the default value from the ESD in the environmental risk assessment, calculations will be done using both validated efficacious doses.

$Qform_{appl\ -\ ticks}$ = 1.34 mg product/cm² skin

$Qform_{appl\ -\ mosquitoes}$ = 0.987 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.

As stated above, the efficacy expert for this product stated that the product can be seen as efficacious for up to 11 hours when used at 1.34 mg/cm² and up to 10 hours when used at 0.987 mg/cm². Following the ESD Table 3-2, 2 applications per day will be used in the further assessment for both application rates.

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	300	g/kg	(30 %)
Consumption per application	(D2) Qformappl ticks mosquitoes	 1.34 0.987	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 ticks mosquitoes	 7.34 5.41	 /

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 both validated efficacious doses will be applied.

$Qform_{appl\ -\ ticks}$ = 1.34 mg product/cm² skin

$Qform_{appl\ -\ mosquitoes}$ = 0.987 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 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) $C_{formweight}$	300	g/kg	(30%)
Consumption per application	(D2) Qformappl ticks mosquitoes	 1.34 0.987	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**
Surface water ticks mosquitoes	 1.00 0.737	/

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.

As a TIER 2 assessment, degradation in surface water can be taken into account. In the CAR of the A.S. a water/sediment degradation study is available. It is shown that IR3535 first forms its free acid, which then further degrades. In order to take into account this intermediate formation, the worst case DT50 of the free acid for the total system (299.64 days at 12°C) can be used to calculate a degradation rate constant to be used in the assessment.

$kdeg_{water}$ = 2.31x10^{-3} d^{-1}

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	$\underline{Elocal_{water}}$ ticks mosquitoes	1.00 0.737	kg/d	O (Intermediate calculation)
Volume of water body	$V_{waterbody}$	435 000	m³	D
First order rate constant for biodegradation in surface water	$kdeg_{water}$	2.31x10^{-3}	d^{-1}	(see above)
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

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

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

$$Clocal_{water,91d-ref} = Clocal_{water,1d} \times \frac{1 - (e^{-kdeg_{water} \times Temission,1d}) \ Nemission,91d}{1 - e^{-kdeg_{water} \times Temission,1d}}$$

Resulting local concentrations in the waterbody		
Compartment	**Local concentration ($Clocal_{compartment}$) [kg/m³]**	**Remarks**
Surface water – after 1 day ticks mosquitoes	 2.30x10^{-6} 1.69x10^{-6}	/
Surface water – after 91 days ticks mosquitoes	 2.09x10^{-4} 1.54x10^{-4}	(without considering possible degradation)
Surface water – after 91 days refined ticks mosquitoes	 1.89x10^{-4} 1.39x10^{-4}	(with 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, such as soil and groundwater, is not considered relevant. The soil could be exposed through sludge application, but following the STP-distribution detailed in the third table below, sorption to sewage sludge is unlikely since IR3535 is almost completely degraded.

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	g/mol	
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.m3/mol	
Biodegradability	Not readily 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	0	Not relevant	
Water	99	1		
Sludge	1	0		
Degraded in STP	0	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/l]	[mg/l]
Scenario 1	TIER 1		
	ticks	3.63	$3.63x10^{-1}$
	mosquitoes	2.68	$2.67x10^{-1}$
	TIER 2		
	ticks	$3.67x10^{-2}$	$3.67x10^{-3}$
	mosquitoes	$2.70x10^{-2}$	$2.70x10^{-3}$
Scenario 2	Day 1		
	ticks	n/a	$2.30x10^{-3}$
	mosquitoes	n/a	$1.69x10^{-3}$
	Day 91		
	ticks	n/a	$2.09x10^{-1}$
	mosquitoes	n/a	$1.54x10^{-1}$
	Day 91 - refined		
	ticks	n/a	$1.89x10^{-1}$
	mosquitoes	n/a	$1.39x10^{-1}$

(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.

2.2.9.3 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 ticks mosquitoes	 $3.63x10^{-2}$ $2.68x10^{-2}$
	TIER 2 ticks mosquitoes	 $3.67x10^{-4}$ $2.70x10^{-4}$
Scenario 2	Day 1 ticks mosquitoes	 n/a n/a
	Day 91 ticks mosquitoes	 n/a n/a
	Day 91 - refined ticks mosquitoes	 n/a n/a

Conclusion:

No adverse effect for the STP is expected

(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.

Summary table on calculated PEC/PNEC values		
		PEC/PNEC$_{water}$
Scenario 1	TIER 1 ticks mosquitoes	 **3.63** **2.67**
	TIER 2 ticks mosquitoes	 $3.67x10^{-2}$ $2.70x10^{-2}$
Scenario 2	Day 1 ticks mosquitoes	 $2.30x10^{-2}$ $1.69x10^{-2}$
	Day 91 ticks mosquitoes	 **2.09** **1.54**
	Day 91 - refined ticks mosquitoes	 **1.89** **1.39**

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 advese effects are calculated.

For the scenario 2, no adverse effects are expected at day 1. However, after 91 days, risks are calculated for both application rates, even when taking into account possible degradation.

However, this assessment was conducted assuming that the full body surface was treated before going swimming, even though the intended use limits application to face, arms hands and legs (i.e. $AREA_{skin}$ of 9130 cm²). When reducing the $AREA_{skin}$ in the calculations, no risks are calculated after 91 days when considering the lowest application rate. At the higher dose, however, the risks remain.

Summary table on calculated PEC/PNEC values		
		$PEC/PNEC_{water}$
Scenario 2 reducing $AREA_{skin}$ to 9130 cm²	Day 1 ticks mosquitoes	 $1.27x10^{-2}$ $9.32x10^{-3}$
	Day 91 ticks mosquitoes	 **1.15** $8.48x10^{-1}$
	Day 91 - refined ticks mosquitoes	 **1.04** $7.66x10^{-1}$

Conclusion:

When used at the lowest application rate, i.e. the validated efficacious dose against mosquitoes, no adverse effect for the aquatic compartment is expected

(IV) Terrestrial compartment

The terrestrial compartment is not considered a relevant receiving compartment (see point (III) above).

Exposure through sludge application is highly unlikely, since IR3535 almost completely degrades in the STP.

Conclusion

No adverse effects for the terrestrial compartment are expected

(V) Groundwater

Since no exposure of the terrestrial compartment is expected, it follows that neither exposure to the groundwater is expected.

Conclusion

No adverse effects for the groundwater are expected.

(VI) Primary and secondary poisoning

Primary poisoning is not applicable, since this product is a repellent and has no intention of killing.

Secondary poisoning is not relevant, since no bioaccumulation is expected.

(VII)Mixture toxicity

Not relevant, since the product does not contain other components other than the active substance that could give a risk to the environment.

2.2.10 Measures to protect man, animals and the environment

Please see §2.1.4 and §2.1.5 above.

2.2.11 Assessment of a combination of biocidal products

Not applicable

2.2.12 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
Meinerling, M.	2009	EUS26-16 Insect repellent aerosol – Determination of the storage stability at ambient temperatures	31242202	Merck KGaA	2009-05-27
Meinerling M., Fieseler A.	2016	Statement to IBACON project	-	-	2016-21-06
Fieseler A.	2015	MDA-A-197-01 Verum 1: Accelerated Storage Stability	98322204	Merck KGaA	2015-08-04
Meinerling, M.	2007	EUS26-16 INSECT REPELLENT AEROSOL – DETERMINATION OF THE ACCELERATED STORAGE STABILITY	31241204	Merck KGaA	2007-03-06
Fieseler, A.	2011	Determination of the Relative Density of Aerosol Solution (without propellant) containing 30 % IR 3535®	63183182	Merck KGaA	2011-06-27
Meinerling, M. and Hermman, S.	2011	Determination of the Low Temperature Stability of Aerosol Solution (without Propellant) containing 30 % IR 3535®	63184204	Merck KGaA	2011-06-27
Kirkpatrick, D.T.	2007	AN AEROSOL PARTICLE SIZE STUDY OF IR3535 AEROSOL SPRAY INSECT REPELLENT: A STUDY TO DETERMINE PROPORTIONS OF RESPIRABLE AND NON-RESPIRABLE AEROSOL	WIL-585012	Merck KGaA	2007-05-23
Dornhagen, J.	2011	FINAL REPORT (2nd Original of 3) Aerosol Solution (without Propellant) containing 30 % IR 3535® Batch No.: SM-0-1-2/090211 AUTO-IGNITION TEMPERATURE (LIQUIDS AND GASES) A.15	20110104.01	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
Damaska., J	2015	Ignition distance determination per UNECE Section 31	R150394	Wiskonsin Pharmacal	2015-07-23
Zur Lage, J.	2016	IR3535_Ref Formulations Surface Tention Viscosity_Reg.Aff	009093	Merck KGaA	2016-07-04
Carroll, S.P.	2007	"Test of Personal Insect Repellents – Volume 10; Carroll-Loye Biological Research, Davis, California, USA; Report No. EMD-003.3 Aerosol/Ticks"	336-1914	Merck KGaA	2007-01-27
Carroll, S.P.	2007	"Test of Personal Insect Repellents – Volume 11; Carroll-Loye Biological Research, Davis, California, USA; Report No. EMD-004.3 Aerosol/Mosquitoes"	336-1915	Merck KGaA	2007-01-26
Dippel, C. and Dautel, H.	2006	"Evaluation of 6 products against the European Sheep Tick, Ixodes ricinus, on human volunteers according to the EPA guidelines"	336-1921	Merck KGaA	2006-04-27
Lüpkes, K.-H.	2011	"Repellent Efficacy of Six Repellent Formulations on Human Arms against Mosquitoes"	336-1922	Merck KGaA	2011-07-04

[redacted] (a)	2006	Acute dermal irritation study of EUS26-16 Insect Repellent Aerosol in albino rabbits.	WIL-585009	Merck KGaA	2006-09-08
[redacted] (b)	2006	Acute Eye Irritation Study of EUS26-16 Insect Repellent Aerosol in albino rabbits.	WIL-585010	Merck KGaA	2006-09-08
[redacted] (c)	2006	Skin Sensitisation Study of EUS26-16 Insect Repellent Aerosol in albino guinea pigs (Modified Buehler Method).	WIL-585011	Merck KGaA	2006-09-08
[redacted] (d)	2006	Acute dermal toxicity study of EUS26-15 Insect Repellent Spray in albino rats.	WIL-585005	Merck KGaA	2006-09-15

3.2 OUTPUT TABLES FROM EXPOSURE ASSESSMENT TOOLS

3.2.1 Human exposure calculations

PT19 - calculation table IR3535 A 30%.›

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.