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 THE MAJOR CHANGE AND RENEWAL OF A NATIONAL AUTHORISATION

Product identifier in R4BP	RATONEX LÍQUIDO 26
Product type(s):	14 (Rodenticide)
Active ingredient(s):	DIFENACOUM
Case No. in R4BP	BC-MW000085-26 (NA-RNL) BC-MC030346-56 (NA-MAC)
Asset No. in R4BP	ES-0000196-0000
Evaluating Competent Authority	Spain
Internal registration/file no	ES/APP(NA)-2018-14-00097
Date	March 2018

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1 Conclusion

The assessment presented in this report includes the major change submitted by the applicant according to Implementing Regulation 354/2013 in order to decrease the content of difenacoum active substance at a level of 0.0026% w/w due to laid down in Commission Regulation (EU) 2016/1179 of 19 July 2016 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council. In addition, this report also includes the conditions for the renewal of the active substance, according Commission Regulation (EU) 2017/1379 of 25 July 2017.

The initial evaluation of the biocidal product RATONEX LÍQUIDO containing of difenacoum active substance at a level of 0.005% w/w should be taken into account. As the name of the product refers to the content in active substance of the product, the Spanish Competent Authority requested to the applicant changed the product name in order not to mislead the user and for enforcement tasks

It is concluded after evaluation of new data submitted that the ready-to-use product, RATONEX LÍQUIDO 26, with the active substance difenacoum, at a level of 0.0026% w/w, may be authorised for use as a rodenticide (product-type 14). Some of conclusions to the initial assessment remains valid and the new information provided by the applicant to support the decrease of active substance allow granting the authorisation.

Physical, chemical and technical properties remain valid to the initial evaluation other than the long term stability test. No long-term stability test has been submitted; therefore a post-authorisation requirement should be included in the authorisation certificate.

The conclusions about physical hazards and methods for detection and identification remain valid to the initial evaluation and no new information has been submitted.

New efficacy data, semi-field and field trials, have confirmed that RATONEX LIQUIDO 26 is effective in the proposed areas of use, at the recommended dose rate.

According to Commission Regulation (EU) 2016/1179 the product RATONEX LÍQUIDO 26, with the active substance difenacoum, at a level of 0.0026% w/w is classified as SPECIFIC TARGET ORGAN TOXICITY AFTER REPEATED EXPOSURE. CATEGORY 2 (STOT RE 2); H373 May cause damage to organs (blood) through prolonged or repeated exposure.

The risk assessment for the environment has been performed for the intended indoors, outdoors around buildings and outdoor in open areas and waste dumps. Since the concentration of the active substance has been reduced, the new evaluation shows that the conclusions for the first evaluation remain valid.

Therefore, RATONEX LIQUIDO 26 can be authorised as a rodenticide product against house mice (*Mus musculus*) and brown rats (*Rattus norvegicus*). It is to be used indoors, outdoors around buildings and outdoor in open areas and waste dumps. The users can be trained professional. The product must be supplied in non-refillable bottles with a safety childproof cap.

The specific intended uses of the product are in section 2.4. of this assessment report.

2 Summary of the product assessment

2.1 Administrative information

2.1.1 Identifier in R4BP

RATONEX LÍQUIDO 26

2.1.2 Manufacturer(s) of the product

Name of manufacturer	WILL KILL, S.A.
Address of manufacturer	C/4 de Noviembre, 6
Location of manufacturing sites	07011 – Palma de Mallorca, España

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

Active substance	DIFENACOUM
Name of manufacturer	ACTIVA S.r.l. / Dr. TEZZA S.r.l.
Address of manufacturer	ACTIVA S.r.l. Via Feltre, 32 20132 – Milano - ITALY
Location of manufacturing sites	Dr. TEZZA S.r.l. Via Tre Ponti, 22 37050 – S. Maria di Zevio (VR) ITALY

2.2 Composition and formulation

2.2.1 Qualitative and quantitative information on the composition

Table 1

Common name	IUPAC name	Function	CAS number	EC number	Content (%)
Pure Difenacoum	3-(3-biphenyl-4-yl-1,2,3,4-tetrahydro-1-naphthyl)-4-hydroxycoumarin	Active Substance	56073-07-5	259-978-4	0,0026%

Common name	IUPAC name	Function	CAS number	EC number	Content (%)
Technical Difenacoum	3-(3-biphenyl-4-yl-1,2,3,4-tetrahydro-1-naphthyl)-4-hydroxycoumarin	Active Substance	56073-07-5	259-978-4	0.0027083%
-	-	Non-active substance	-	-	-

- The product contains a bittering agent and a dye.

Information on the full composition is provided in the confidential annex

- According to the information provided the product contains no nanomaterial as defined in Article 3 paragraph 1 (z) of Regulation No. 528/2012

2.2.2 Information on the substance(s) of concern

No substance of concern was identified upon initial assessment (the application for authorisation was submitted and the assessment took place before the Biocidal Products Regulation 528/2012 entered into force).

2.2.3 Candidate(s) for substitution

No candidate for substitution was identified upon initial assessment (the application for authorisation was submitted and the assessment took place before the Biocidal Products Regulation 528/2012 entered into force).

Now that the Biocidal Products Regulation 528/2012 entered into force, the following substance(s) was/were identified as candidate(s) for substitution upon this renewal:

Difenacoum does meet the exclusion criteria according to Article 5(1) BPR. Because the following exclusion criteria are met:

- toxic for reproduction category 1B
- persistent and very persistent, bioaccumulative and toxic

And therefore, difenacoum does meet the conditions laid down in Article 10 BPR, and is consequently a candidate for substitution.

2.2.4 Type of formulation

Ready-to-use bait: Liquid

2.3 Classification and Labelling according to the Regulation (EC) No 1272/2008

Table 2

Classification	
Hazard classes, Hazard categories	**Hazard statements**
Specific target organ toxicity after repeated exposure. Category 2	H373 May cause damage to organs (blood) through prolonged or repeated exposure

Table 3

Labelling		
	Code	**Pictogram / Wording**
Pictograms	GHS08	
Signal word		WARNING
Hazard statements	H373	May cause damage to organs (blood) through prolonged or repeated exposure
Supplemental hazard information	-	
Supplemental label elements	-	
Precautionary statements	P201	Obtain special instructions before use.
	P202	Do not handle until all safety precautions have been read and understood.
	P260	Do not breathe dust/fume/ gas/mist/vapours/spray
	P280	Wear protective gloves.
	P314	Get medical advice/attention if you feel unwell.
	P501	Dispose of contents and/ or container as a hazardous waste to a registered establishment or undertaking, in accordance with current regulations.
Note	-	

2.4 Use(s) appropriate for <u>further</u> authorisation

In order to make proper use of the standard sentences for SPCs for rodenticides it is considered necessary to split the uses currently evaluated in Spain further down:

Table 4

Use(s) considered appropriate for authorisation after former assessment (uses currently evaluated in SPAIN		Use(s) appropriate for further authorisation	
1	House mice and/or brown rats – trained professionals – indoor, outdoor around buildings, outdoor open areas & waste dumps	1	House mice and/or brown rats – trained professionals - indoor
		2	House mice and/or brown rats – trained professionals – outdoor around buildings
		3	Brown Rats – trained professionals – outdoor open areas & waste dumps

2.4.1 Use 1 - House mice and/or brown rats – trained professionals – indoor

Product Type(s)	14
Where relevant, an exact description of the use	Not relevant for rodenticides
Target organism(s) (including development stage)	*Mus musculus* (house mice) *Rattus norvegicus* (brown rats)
Field(s) of use	Indoor
Application method(s)	The product must be supplied in non-refillable bottles with a safety childproof cap. The bottles will be opened by removing the stopper and, without breaking the membrane; the roll-on dispenser will be placed. Once inverted this device must always be placed in a tamper-resistant bait station correctly labelled.
Application rate(s) and frequency	**Rats:** bait station with a maximum of 250ml of product placed each 5-10m depending on the level of infestation. **Mice**: bait station with a maximum of 100ml of product placed each 2-5m, depending on the level of infestation.
Category(ies) of users	Trained professionals
Pack sizes and packaging material	Millilitres/Litres of bait per packed bag: Non-reusable set of 100ml or 250ml Packaging material: Bottles with a childproof cap and sealed with a membrane, roll-on dispenser with safety cap and a base. Material: HDPE

2.4.1.1 Use-specific instructions for use

- Remove the remaining product at the end of treatment period.

- Follow any additional instructions provided by the relevant code of best practice.

2.4.1.2 Use-specific risk mitigation measures

- Where possible, prior to the treatment inform any possible bystanders (e.g. users of the treated area and their surroundings) about the rodent control campaign - Consider preventive control measures (e.g. plug holes, remove potential food and drinking as far as possible) to improve product intake and reduce the likelihood of reinvasion. - To reduce risk of secondary poisoning, search for and remove dead rodents during treatment at frequent intervals, in line with the recommendations provided by the relevant code of best practice. - Do not use the product as permanent baits for the prevention of rodent infestation or monitoring of rodent activities. - Do not use the product in pulsed baiting treatments. - This product shall only be used indoors and in places that are not accessible to children or non-target animals.

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

- When placing bait points close to water drainage systems, ensure that bait contact with water is avoided.

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

-See section 2.5.4.

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

-See section 2.5.5.

2.4.2 Use 2 – House mice and/or brown rats – trained professionals – outdoor around buildings

Product Type(s)	14
Where relevant, an exact description of the use	Not relevant for rodenticides

Target organism(s) (including development stage)	*Mus musculus* (house mice) *Rattus norvegicus* (brown rats)
Field(s) of use	Outdoor around buildings
Application method(s)	The product must be supplied in non-refillable bottles with a safety childproof cap. The bottles will be opened by removing the stopper and, without breaking the membrane; the roll-on dispenser will be placed. Once inverted this device must always be placed in a tamper-resistant bait station correctly labelled.
Application rate(s) and frequency	**Rats:** bait station with a maximum of 250ml of product placed each 5-10m depending on the level of infestation. **Mice**: bait station with a maximum of 100ml of product placed each 2-5m, depending on the level of infestation.
Category(ies) of users	Trained professionals
Pack sizes and packaging material	Millilitres/Litres of bait per packed bag: Non-reusable set of 100ml or 250ml Packaging material: Bottles with a childproof cap and sealed with a membrane, roll-on dispenser with safety cap and a base Material: HDPE

2.4.2.1 Use-specific instructions for use

-Protect bait from the atmospheric conditions. Place the baiting points in areas not liable to flooding.

- Replace any bait in baiting points in which bait has been damaged by water or contaminated by dirt.
- Remove the remaining product at the end of treatment period.
- Follow any additional instructions provided by the relevant code of best practice.

2.4.2.2 Use-specific risk mitigation measures

- Where possible, prior to the treatment inform any possible bystanders (e.g. users of the treated area and their surroundings) about the rodent control campaign.
- Consider preventive control measures (plug holes, remove potential food and drinking as far as possible) to improve product intake and reduce the likelihood of reinvasion.
- To reduce risk of secondary poisoning, search for and remove dead rodents during treatment at frequent intervals, in line with the recommendations provided by the relevant code of best practice.
- Do not use this product as permanent baits for the prevention of rodent infestation or monitoring of rodent activities.
- Do not use this product in pulsed baiting treatments.
- Do not apply this product directly in the burrows.

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

- When placing bait points close to surface waters (e.g. rivers, ponds, water channels, dykes, irrigation ditches) or water drainage systems, ensure that bait contact with water is avoided.

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

-See section 2.5.4

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

See section 2.5.5

2.4.3 Use 3 – Brown Rats – trained professionals – Outdoor open areas & waste dumps

Product Type(s)	14
Where relevant, an exact description of the use	Not relevant for rodenticides
Target organism(s) (including development stage)	*Rattus norvegicus* (brown rats)
Field(s) of use	Outdoor open areas Outdoor waste dumps
Application method(s)	The product must be supplied in non-refillable bottles with a safety childproof cap. The bottles will be opened by removing the stopper and, without breaking the membrane; the roll-on dispenser will be placed. Once inverted this device must always be placed in a tamper-resistant bait station correctly labelled.
Application rate(s) and frequency	**Rats:** bait station with a maximum of 250ml of product placed each 5-10m depending on the level of infestation.
Category(ies) of users	Trained professionals
Pack sizes and packaging material	Millilitres/Litres of bait per packed bag: Non-reusable set of 250ml Packaging material: Bottles with a childproof cap and sealed with a membrane, roll-on dispenser with safety cap and a base Material: HDPE

2.4.3.1 Use-specific instructions for use

-- Protect bait from the atmospheric conditions. Place the bait stations in areas not liable to flooding.

- Replace any bait in baiting points in which bait has been damaged by water or contaminated by dirt.

- Remove the remaining product at the end of treatment period

-Follow any additional instructions provided by the relevant code of best practice.

2.4.3.2 Use-specific risk mitigation measures

- Where possible, prior to the treatment inform any possible bystanders (e.g. users of the treated area and their surroundings) about the rodent control campaign

- To reduce risk of secondary poisoning, search for and remove dead rodents during treatment at frequent intervals, in line with the recommendations provided by the relevant code of best practice.

- Do not use this product as permanent baits for the prevention of rodent infestation or monitoring of rodent activities.

- Do not use this product in pulsed baiting treatments.

- Do not apply this product directly in the burrows.

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

- When placing bait points close to surface waters (e.g. rivers, ponds, water channels, dykes, irrigation ditches) or water drainage systems, ensure that bait contact with water is avoided.

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

See section 2.5.4

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

See section 2.5.5

2.5 General directions for use

2.5.1. Instructions for use

- Read and follow the product information as well as any information accompanying the product or provided at the point of sale before using it.

- Carry out a pre-baiting survey of the infested area and an on-site assessment in order to identify the rodent species, their places of activity and determine the likely cause and the extent of the infestation.

- Remove food which is readily attainable for rodents (e.g. spilled grain or food waste). Apart from this, do not clean up the infested area just before the treatment, as this only disturbs the rodent population and makes bait acceptance more difficult to achieve.

- The product should only be used as part of an integrated pest management (IPM) system, including, amongst others, hygiene measures and, where possible, physical methods of control.

- The product should be placed in the immediate vicinity of places where rodent activity has been previously explored (e.g. travel paths, nesting sites, feedlots, holes, burrows etc.).

- Where possible, bait stations must be fixed to the ground or other structures.

- Bait stations must be clearly labelled to show they contain rodenticides and that they must not be moved or opened *(see section 2.5.3 for the information to be shown on the label)*.

-When the product is being used in public areas, the areas treated should be marked during the treatment period and a notice explaining the risk of primary or secondary poisoning by the anticoagulant as well as indicating the first measures to be taken in case of poisoning must be made available alongside the baits.

- Bait should be secured so that it cannot be dragged away from the bait station.

- Place the product out of the reach of children, birds, pets and farm animals and other non-target animals.

- Place the product away from food, drink and animal feeding stuffs, as well as from utensils or surfaces that have contact with these.

-Wear protective chemical resistant gloves during product handling phase (glove material to be specified by the authorisation holder within the product information).

- When using the product do not eat, drink or smoke. Wash hands and directly exposed skin after using the product.

- The frequency of visits to the treated area should be at the discretion of the operator, in the light of the survey conducted at the outset of the treatment. That frequency should be consistent with the recommendations provided by the relevant code of best practice.

- If bait uptake is low relative to the apparent size of the infestation, consider the replacement of bait points to further places and the possibility to change to another bait formulation.

- If after a treatment period of 35 days baits are continued to be consumed and no decline in rodent activity can be observed, the likely cause has to be determined. Where other elements have been excluded, it is likely that there are resistant rodent so consider the use of a non-anticoagulant rodenticide, where available, or a more potent anticoagulant rodenticide. Also consider the use of traps as an alternative control measure.

- Fix the bait station to the ground.

- In case of accidental spillage of the liquid, dispose of the bait station as hazardous waste.

2.5.2 Risk mitigation measures:

- Where possible, prior to the treatment inform any possible bystanders about the rodent control campaign

- The product information (i.e. label and/or leaflet) shall clearly show that the product shall only be supplied to trained professional users holding certification demonstrating compliance with the applicable training requirements (e.g. "for trained professionals only").

- Do not use in areas where resistance to the active substance can be suspected.

- Products shall not be used beyond 35 days without an evaluation of the state of the infestation and of the efficacy of the treatment

- Do not rotate the use of different anticoagulants with comparable or weaker potency for resistance management purposes. For rotational use, consider using a non-anticoagulant rodenticide, if available, or a more potent anticoagulant.

- Do not wash the bait stations non refillable bottles with water between applications

- Dispose dead rodents in accordance with local requirements *[The method of disposal shall be described specifically in the national SPC and be reflected on the product label]*.

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

- This product contains an anticoagulant substance. If ingested, symptoms, which may be delayed, may

include nosebleed and bleeding gums. In severe cases, there may be bruising and blood present in the faeces or urine.
- Antidote: Vitamin K1 administered by medical/veterinary personnel only.
- In case of:
- Dermal exposure, wash skin with water and then with water and soap.
- Eye exposure, always check for and remove contact lenses, rinse eyes with eyes-rinse liquid or water, keep eyes lids open at least 10 minutes.
- Oral exposure, rinse mouth carefully with water. Never give anything by mouth to unconscious person. Do not provoke vomiting. If swallowed, seek medical advice immediately and show the product's container or label *[insert* country specific information*]*. Contact a veterinary surgeon in case of ingestion by a pet *[insert* country specific information*]*
- Bait stations must be labelled with the following information: "do not move or open"; "contains a rodenticide"; "product name or authorisation number"; "active substance(s)" and "in case of incident, call a poison centre *[insert national phone number]*"
- Hazardous to wildlife.

2.5.4 Instructions for safe disposal of the product and its packaging

- At the end of the treatment, dispose uneaten bait and the packaging in accordance with local requirements [*The method of disposal shall be described specifically in the national SPC and be reflected on the product label*.
-Use for gloves is recommended

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

- Store in a dry, cool and well ventilated place. Keep the container closed and away from direct sunlight.
- Store in places prevented from the access of children, birds, pets and farm animals.
- Shelf life: two years

2.5.6. Other information

- Because of their delayed mode of action, anticoagulant rodenticides take from 4 to 10 days to be effective after consumption of the bait.
- Rodents can be disease carriers. Do not touch dead rodents with bare hands, use gloves or use tools such as tongs when disposing them.
- This product contains a bittering agent and a dye.

Post-authorisation requirements:

- Long-term stability test within 2 years

3 Assessment of the product

3.1 Use(s) considered appropriate for authorisation after former assessment (Uses currently under authorisation)

3.1.1 Use 1 – Brown rats and mice - Trained professional users – in and around (private, public and farm buildings), transports and outdoors (waste dumps/landfill sites and open areas)

Product Type(s)	14
Where relevant, an exact description of the use	Not relevant for rodenticides
Target organism(s) (including development stage)	*Mus musculus* (house mice) *Rattus norvegicus* (brown rats)
Field(s) of use	Indoors (inside private, public and farm buildings), in and around (private, public and farm buildings), transports and outdoors (waste dumps/landfill sites and open areas) into labelled tamper-resistant bait stations. Indoor use is considered inside industrial, commercial and residential buildings, parking lots and fixed or mobile closed installations. In and around use is considered, along the perimeter of buildings or installations, (not exceeding a maximum distance of 0.5 meters between the bait and the building/installation). Car parks that do not fall within the definition of interior or open areas, open bus or train stations, or port areas would also be included. Open areas use is considered that is carried out in areas such as parks, golf courses, open parking and the surrounding of crop fields, stations or port areas. Use in transports is considered that is carried out into the own transport (goods and/or people) and never outside of vehicles or in open vehicles.
Application method(s)	The sealed non-reusable bottles only will be opened when inserting the bottle into a roll-on dispenser within an additional small trough placed inside the bait station. This device must always be placed in a tamper-resistant bait station correctly labelled.
Application rate(s) and frequency	**Rats:** bait station with a maximum of 250ml of product placed each 5-10m depending on the level of infestation. **Mice**: bait station with a maximum of 100ml of product placed each 2-5m, depending on the level of infestation.
Category(ies) of users	Trained professionals
Pack sizes and packaging material	Millilitres/Litres of bait per packed bag: Non-reusable set of 100ml or 250ml Packaging material: Bottles with a childproof cap and sealed with a membrane, roll-on dispenser with safety cap and a base Material: HDPE

3.2 Physical, chemical and technical properties

<table>
<tr><th>Property</th><th>Guideline and Method</th><th>Purity of the test substance (% (w/w)</th><th>Results</th><th>Reference</th></tr>
<tr><td>Storage stability test – accelerated storage</td><td>CIPAC MT46.3</td><td>0.0026</td><td>Results obtained after 14 days storage at 54°C:
Difenacoum active ingredient initial content: 0.0025% w/w
Difenacoum active ingredient final content: 0.0025% w/w
Δ[C] = 0%. The result complies with the tolerance value (-10%).

<table><tr><th>Test</th><th>Initial value</th><th>Final value</th></tr><tr><td>pH</td><td>4.24</td><td>4.39</td></tr></table>
<table><tr><th>Test</th><th>Initial value</th><th>Final value</th></tr><tr><td>Relative density</td><td>1.0177 g/cc</td><td>1.0189 g/cc</td></tr></table>
<table><tr><th>Test</th><th>Initial value</th><th>Final value</th></tr><tr><td>Surface tension</td><td>31.8 mN/m</td><td>31.8 mN/m</td></tr></table>
<table><tr><th>Test</th><th>Initial value</th><th>Final value</th></tr><tr><td>Appearance</td><td>Liquid
Cobalt blue</td><td>Liquid
Cobalt blue</td></tr></table></td><td>IUCLID 3.4.1</td></tr>
</table>

Property	Guideline and Method	Purity of the test substance (% (w/w)	Results	Reference
			<table><tr><td></td><td>Slightly acidic</td><td>Slightly acidic</td></tr></table> <table><tr><td>**Test**</td><td>**Initial value**</td><td>**Final value**</td></tr><tr><td>Cinematic Viscosity</td><td>1.26 mm^2/s at 20°C 1.98 mm^2/s at 40°C</td><td>1.20 mm^2/s at 20°C 1.98 mm^2/s at 40°C</td></tr></table>	
Storage stability test – **long term storage at ambient temperature**	Guidance on Data Requirements for Active Substances and Biocidal Products	0.0026	Study ongoing Final results: May 2019 Results obtained after 4 months storage at ambient temperature: Difenacoum active ingredient initial content: 0.0026 ± 0.00003% w/w Difenacoum active ingredient final content: 0.0026 ± 0.00004% w/w Δ[C] = 0%. Up to now the result complies with the tolerance value (-10%).	IUCLID 3.4.1
Storage stability test – **low temperature**	CIPAC MT 39.3	0.0026	After being stored 7 days inside the refrigerator at 0°C±2°C, the sample remains unchanged, does not generate solid or oily material after storage.	IUCLID 3.4.1

Apart from the properties mentioned above, neither new data was not provided nor had new guidance to be taken into account for re-assessment.

Accordingly, the conclusion from the former assessment regarding those physical, chemical and technical properties not provided remains valid.

The renewal is conditioned to the presentation of the long term stability test; therefore a post-authorisation condition should be showed in the authorisation certificate.

3.3 Physical hazards and respective characteristics

Neither new data was not provided nor had new guidance to be taken into account for re-assessment. Accordingly, the conclusion from the former assessment regarding physical hazards and respective characteristics remains valid.

3.4 Methods for detection and identification

<table>
<tr><th>Parameters</th><th>Result</th><th>Conclusions</th><th>Reference</th><th>Guideline and Method</th></tr>
<tr><td>Analytical method</td><td>HPLC-MS</td><td>Valid</td><td rowspan="4">IUCLID 5</td><td rowspan="4">The validation was carried out following the document “Guidelines on method validation to be performed in support of analytical methods for agrochemical formulations”</td></tr>
<tr><td>Linearity</td><td>It was studied using four different concentration of Difenacoum (0.0010, 0.0020, 0.0030 and 0.0040 g/100mL)
$y = 4 \cdot 10^{8}x - 4495.5$
$R^2 = 0.9999$</td><td></td></tr>
<tr><td>Recovery</td><td><table><tr><th>Concentration of difenacoum added (g/100mL)</th><th>Recovery rate</th></tr><tr><td>0.003998</td><td>98.40</td></tr><tr><td>0.002999</td><td>98.80</td></tr><tr><td>0.001999</td><td>95.05</td></tr><tr><td>0.00100</td><td>95.89</td></tr></table>In all the cases the recovery is higher than 95% and lower than 105%</td><td rowspan="2">It was carried out an F-test using the results obtained from the recovery and repetivity tests. The result obtained shows no significant differences between the respective RSDr at a 95% of confidence level. Furthermore, it was carried out a Student test using the values of the recoveries obtained and the added difenacoum values show no significant differences among them at a 95% confidence level.</td></tr>
<tr><td>Accuracy</td><td><table><tr><th>% of analyte</th><th>Calculated RSDr</th></tr><tr><td>100</td><td>0.3086</td></tr><tr><td>50</td><td>0.3505</td></tr></table></td></tr>
</table>

Parameters	Result	Conclusions	Reference	Guideline and Method
	<table><tr><td>20</td><td>2.0542</td></tr><tr><td>10</td><td>2.3676</td></tr><tr><td>5</td><td>2.7854</td></tr></table> The study of repetivity was carried out determining the amount of difenacoum from 100% of the decimal fraction to 5%.			

Apart from the parameters presented above, neither new data was not provided nor had new guidance to be taken into account for re-assessment.
Accordingly, the conclusion from the former assessment regarding methods for detection and identification remains valid.

3.5 Efficacy against target organisms

RATONEX LÍQUIDO 26/ RATOLÍ SECURE LÍQUIDO is renewed with a decrease of the active substance concentration from 50 ppm to 26 ppm (major change) and a biocidal product name change (previously RATONEX LÍQUIDO) and is used against Brown rat (*Rattus norvegicus*) and House mouse (*Mus musculus*).

Taking into account that a complete efficacy data package with 0.005% w/w difenacoum was submitted, and that the change in the formulation is basically in the content of active substance, it is assumed that the level of palatability remains the same with the new composition being at least 20% of palatability in laboratory tests. Please, see the summary of the choice test (former assessment).

The applicant has submitted two new studies in order to support the efficacy of the new formulation in field conditions, against *Rattus norvegicus* and *Mus musculus*. Please, see the summary of field trials submitted by the applicant.

In conclusion, according to the test provided, ES CA consider that the biocidal product with 0.0026% w/w difenacoum is effective against rats and mice indoor and outdoor

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**
Rodenticide	Laboratory test (fresh bait)	**Difenacoum 0.005% w/w**	Brown rat (*Rattus norvegicus*) House mouse (*Mus musculus*) 10 adult rodents for both species (5 males and 5 females)	Choice test. TNG on Product Evaluation, Appendices to Chapter 7 Product type 14. Efficacy Evaluation of Rodenticide Biocidal Products.	During the study period, all animals were given daily the same amount of water and of the rodenticide bait (about 40 ml for rats and 25 ml for mice). The treatment period was during 4 days.	Consumption of water: For rats: 1563 g For mice: 570.5 g Mean consumption test item: For rats: **49.48%** (1531 g) For mice: **56.1%** (729 g) Mortality: **100%** (for rats and mice) Palatability: Acceptable (≥20%) Mortality: Acceptable (≥90%)	xx

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**
Rodenticide	Field test (Indoor)	**Difenacoum 0.0026% w/w**	House mouse (*Mus musculus*)	Field test. According The guidance on the BPR Volume II Efficacy, assessment and evaluation, parts B + C and Transitional Guidance for PT 14	The trial was set up in an animal feed storage. The test included the phases: pre-treatment census, pre-treatment lag, treatment census, post-treatment lag, post treatment census. Tracking was carried out in specific bait stations by dispersing flour inside them. Pretreatment period: 8 bait stations with water were positioned throughout the study area where high level of rodent activity existed. The chosen treated site had at least 30 mice drinking per day and the mean daily consumption in this phase was 92.25 ml of water. Treatment period: one distribution device (100 mL) of biocidal product was placed inside commercially available lockable bait stations and positioned in areas with high mouse activity at a distance of 2 to 5 m between stations. The mean daily consumption in this phase was 112.57 ml of biocidal product. Post-treatment period: bait stations were re-filled with the same reference way as in pre-census baiting and monitored daily. No consumption was observed during this phase.	Efficacy = 100 % Percentage of bait consumed after the control operation compared to the amount of bait consumed before the control operation is ≤10% (according TNG for PT 14)	IUCLID 6.7
Rodenticide	Field test:	**Difenacoum**	Brown rat	Field test.	The trial was set up in an animal feed	Efficacy = 100	IUCLID

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**
	(Indoor/ Outdoor)	**0.0026% w/w**	(*Rattus norvegicus*)	According The guidance on the BPR Volume II Efficacy, assessment and evaluation, parts B + C and Transitional Guidance for PT 14	factory. The test included the phases: pre-treatment census, pre-treatment lag, treatment census, post-treatment lag, post treatment census. Tracking was carried out in specific bait stations by dispersing flour inside them. Pretreatment period: 6 bait stations with water were positioned throughout the study area where high level of rodent activity existed. The chosen treated site had at least 12 rats drinking per day and the mean daily consumption in this phase was 240 ml of water. Treatment period: One distribution device (250 mL) of biocidal product was placed inside commercially available lockable bait stations and positioned in areas with high rat activity at a distance of 5 m between stations. The mean daily consumption in this phase was 169.16 ml of biocidal product. Post-treatment period: bait stations were re-filled with the same reference way as in pre-census baiting and monitored daily. No consumption was observed during this phase.	% Percentage of bait consumed after the control operation compared to the amount of bait consumed before the control operation is ≤10% (according TNG for PT 14)	6.7

3.5.1. Occurrence of resistance

The resistance is characterized by the ability of individuals within a population in the field to continue feeding on anticoagulant bait for many weeks without dying.

Resistance to anticoagulants can be observed under practical conditions, even when the anticoagulant has been applied correctly, being the loss of effectiveness due to the presence of a strain with a hereditary and proportional reduction in the sensitivity to the anticoagulant.

The development of resistance to the product is related to the mode of action of the active substance, difenacoum. In this case, the applicant does not provide new data on the occurrence of resistance to difenacoum.

Strategies are proposed to avoid the development of resistance to anticoagulants. These strategies are based on a monograph published by The Rodenticide Resistance Action Committee of Crop Life International (RRAC) and called *RRAC Guidelines on Anticoagulant Rodenticide Resistance Management* (October 2016).

3.6 Risk assessment for human health

3.6.1 Assessment of effects of the active substance on human health

Neither new data was not provided nor had new guidance to be taken into account for re-assessment. Accordingly, the conclusion from the former assessment regarding effects of the active substance on human health remains valid.

3.6.2 Assessment of effects of the product on human health

Neither new data was not provided nor had new guidance to be taken into account for re-assessment. Accordingly, the conclusion from the former assessment regarding effects of the product on human health remains valid.

Dermal absorption

Concerning dermal absorption, an in vitro study has been submitted for RATONEX LIQUIDO according to OECD TG 428. The study has been conducted as a multisite study where the analysis of biological samples generated in the absorption study phase has been delegated to an external GLP Certified Laboratory by LC-MSMS with the internally GLP validated analytical method.

The difenacoum content was quantified in the receptor fluid after 2h, 4h, 6h and 24h, in the residual quantity of product on skin surface, in the Stratum Corneum, and in the dermal homogenates and epidermal homogenates. Based on the analytical data the total mass balance was calculated. The values of difenacoum total mass balance on 3 skin explants calculated meet the reference acceptance criteria of ENV/JM/MONO (2011)36 which contains the same recommendations of OECD TG 428 with a caveat that for test substances unlabelled a range of 80-120% is acceptable.

In conclusion, the results of the study lead to an absorbed dose of 0.04%, an absorbable dose of 53.95% and a tape stripping content of 2.56%. This gives a total dermal absorption of **56.55%**

Neither new data was not provided. the decrease in concentration is not significant, it will not affect the initial value. In addition, a risk assessment has been made with the default value of 75% (EFSA, 2012) resulting in an acceptable risk., So it is expected that with 56.66% it is also.

3.6.3 Exposure assessment

Regarding human exposure no studies have been submitted. However, special risk mitigation measures that could avoid any kind of exposure have been proposed. Firstly, rodenticide bait is placed inside a tamper-resistant bait station correctly labelled. Secondly, additional risk mitigation measures for liquid rodenticides, consisting on sealed bottles of 100ml and 250ml for trained professionals and that are applied only when inserting the bottle into a roll-on dispenser within an additional small base placed inside the bait station. Trained professional users can use the product in and around (maximum:- 0.5m) buildings and also outdoors.

With these risk mitigation measures the exposure is negligible, and thus there is no risk for human health, because the roll on device is an appropriate risk mitigation measure that does prevent from any spillage and any contact of humans and animals.

However, in terms of completeness of the assessment, we have estimated the human exposure for a hypothetical situation where there would be any accidental exposure to the liquid, due to a misuse of the product, for example, considering a worst case scenario where:

- Leaks from the roll-on could give splashes. According to the Technical Notes for Guidance (TNsG) on Human Exposure to Biocidal Products (2007), the US-EPQA has estimated the exposure from splashes during mixing and application to be about 6 ml/event to the bare hand. In order to better define the number of splashes, the applicant has carried out a simulation test in the presence of a notary who has stated the veracity of the result. This test intends to simulate the application of the product, and it has been shown that after 50 manipulations (25 loadings and 25 cleanings), 44 manipulations did not show any splash, and 3 manipulations produced 6 splashes. This means 6 splashes / 50 manipulations = 0.12 splash / manipulation.

- The size of a splash is 33.5x 10^{-3} ml, as a worse case, according to an experimental determination, provided by the applicant. This gives an amount of exposure of: 0.12 splash/manipulation x 33.5x10^{-3} ml/splash = 4.02x10^{-3} ml/manipulation

- The dermal absorption of the product is 56.55%; according to the study submitted by the applicant.

- As the paper "HEEG opinion on a harmonised approach for the assessment of rodenticides (anticoagulants)" agreed at TMII 2011 and based on an operator exposure study conducted by CEFIC/EBPF Rodenticides Data Development Group (Chambers et al. (2004)) does not include information on liquid baits, the number of manipulations for this liquid rodenticide has been proposed by the applicant, according to information gathered from the market. After a survey among the applicators of this product, it was concluded that each operator applied two bottles a week at maximum. As a worse case, calculation will be done assuming 1 loading during application and 1 cleaning event during post application every day.

- The density of the product is the indicated by the applicant, 1.0161g/ml.

The most relevant routes of exposure are the following:

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**	
	Trained professional use	**Trained professional use**	**General public**
Inhalation	Not relevant	No	No
Dermal	Potentially significant	No	Potentially significant
Oral	Negligible	No	Relevant

The primary route of exposure to the active substance from formulation and use of the biocidal product will be the dermal route, confined to the hands only. Inhalation exposure to the active substance during manufacture and use in the biocidal product is unlikely due to the low vapour pressure of the active substance.

The secondary route of exposure will be potentially dermal and the oral route as the most relevant route.

List of scenarios

Summary table: scenarios

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.	Loading and placing bait boxes	Primary exposure. During use, professional operators will be exposed through the loading of bait stations with the RTU bottle and application of the bait. Exposure will be via the dermal route and to the hands only.	Trained professional users
2.	Cleaning	Primary exposure. During disposal, professional pest control operators will be exposed through the disposal of used bait and carcasses. Exposure will be via dermal route and to the hands only.	Trained professional users
3.	Touching and mouthing unprotected bait	Secondary exposure: accidentally touched of unprotected bait. Indirect exposure, especially of children may happen.	Bystanders (children, infants and adults)

Trained professional exposure

The following points have been taken into consideration for the assessment of the potential exposure of trained professional users to “RATONEX LIQUIDO 26”:

1. “RATONEX LÍQUIDO 26” is supplied in sealed bottles of 100ml and 250 ml for use only by trained professional users.
2. As no human exposure studies have been submitted, the exposure assessment has been performed considering the exposure from splashes during application to be about 4.02 x 10^{-3} ml/manipulation to the hand.
3. The product is ready to use, then, there is no mixing and loading task. The number of contacts is considered critical rather than the size of the bait. Therefore, as a worse-case, the total daily exposure frequency is assumed to be 2 manipulations, for the placing of the equivalent to 200g bait (maximum dose for rats) on 1 sites and the cleaning of 1 bait sites.
4. Although it could be assumed that professional users wear protective gloves when handling the products, an exposure scenario without personal protective equipment is also included as a worst case. Gloves are assumed to reduce the exposure of hands by 90%.

5. It is assumed that 100% of inhalation exposure is absorbed. Concerning dermal absorption, a study is submitted for this RATONEX LIQUIDO, with a value of 56.55%.
6. Operator body weight is assumed to be 60 kg.

Trained professionals (Pest control operators)

Scenario [1] – Loading and placing bait boxes

Description of Scenario [1] - *Trained professional*		
During the process of loading the bait, the operator may be exposed by dermal contact to the bait. Trained professional users are bounded to use PPE during the development of the different tasks of their work. Total systemic exposure has been assessed without (Tier 1) and with PPE (Tier 2).		
	Parameters	Value
Tier 1	A.S. content of BP	0.0026%
	Dermal absorption:	56,55%
	Operator body weight:	60 kg
	Amount of exposure to product during loading:	4,02x10^{-3} ml/manipulation
	Density:	1,0161 g/ml
	Number of manipulations during loading:	1
Tier 2	PPE (gloves)	10%

Calculations for Scenario [1]

Summary table: estimated exposure from trained professional uses					
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake**	**Estimated dermal uptake**	**Estimated oral uptake**	**Estimated total uptake**
Scenario [1]	Tier 1 / No PPE	-	1 x 10^{-6}mg/kg bw/day	-	1 x 10^{-6}mg/kg bw/day
Scenario [1]	Tier 2 / PPE(gloves)	-	1 x 10^{-7}mg/kg bw/day	-	1 x 10^{-7}mg/kg bw/day

Scenario [2] – Cleaning

Description of Scenario [2] - *Trained professional*		
During the process of cleaning the bait, the operator may be exposed by dermal contact to the bait. Trained professional users are bounded to use PPE during the development of the different tasks of his work. The total systemic exposure has been assessed without (Tier 1) and with PPE (Tier 2).		
	Parameters	Value

Description of Scenario [2] - *Trained professional*		
Tier 1	A.S. content of BP	0.0026%
	Dermal absorption:	56,55%
	Operator body weight:	60 kg
	Amount of exposure to product during loading:	4,02x10^{-3} ml/manipulation
	Density:	1,0161 g/ml
	Number of manipulations during cleaning:	1
Tier 2	PPE (gloves)	10%

Calculations for Scenario [2]

Summary table: estimated exposure from trained professional uses					
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake**	**Estimated dermal uptake**	**Estimated oral uptake**	**Estimated total uptake**
Scenario [2]	Tier 1 / No PPE	-	1 x 10^{-6}mg/kg bw/day	-	1 x 10^{-6}mg/kg bw/day
Scenario [2]	Tier 2 / PPE (gloves)	-	1 x 10^{-7}mg/kg bw/day	-	1 x 10^{-7}mg/kg bw/day

Combined scenarios for professional users

Summary table: combined systemic exposure from Trained professional uses					
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake**	**Estimated dermal uptake**	**Estimated oral uptake**	**Estimated total uptake**
Scenarios [1+ 2] / Tier 1	Tier 1 / No PPE	-	2 x 10^{-6}mg/kg bw/day	-	2 x 10^{-6}mg/kg bw/day
Scenarios [1+ 2] / Tier 2	Tier 2 / PPE (gloves)	-	2 x 10^{-7}mg/kg bw/day	-	2 x 10^{-7}mg/kg bw/day

Exposure of the general public (indirect exposure)

Scenario [3]

In order to minimise the risk of ingestion of the bait by humans, the bait contains a bittering aversive agent. The bait stations have been manufactured to prevent incidental poisoning to both non-target animals and human, i.e. children. They are hard plastic and are either locked or sealed shut to prevent access to the bait.. However, indirect exposure, especially of children, may happen.

Description of Scenario [3]		
A reverse scenario calculation has been used to estimate the quantity of product that an infant should eat to reach the AEL $_{short-term}$. Based on this reverse scenario calculation, a child should be orally exposed to 4.16 x 10^{-4} ml to reach the AEL $_{short-term}$. Trained professional users should dispose unused or part-consumed products. Bait stations protect the product and should prevent access by infants (worse-case).		
	Parameters	Value
Tier 1	Infants Body weight	10 kg
	A.S. content of BP	0.0026%
	Oral absorption	100%
	AEL	1.1 x 10^{-6} mg/kg b.w./day
	Density	1.0161 g/ml

Calculations for Scenario [3]

Summary table: systemic exposure from general public					
Population	**Body weight (kg)**	**Oral absorption**	**AEL $_{short-term}$**	**uptake.s. %**	**Toxic amount of biocidal product (ml)**
Infant	10	100%	1.1E-6mg/kg bw/d	0.0026%	4.16E-4

Further information and considerations on scenario [3]

These values assume ingestion of bait, however, the presence of denatonium benzoate as an aversive agent and the location of the bait in a sealed bait station and in an inaccessible area have always been considered enough to mitigate the risk. Since the bittering agent is not 100% efficient in protecting against ingestion in all children, it is therefore important that the bait stations are kept out of reach of children (and other non-target species, including pets and livestock) during storage and use.

Monitoring data

The exposure assessment has been performed using the paper "HEEG opinion on a harmonized approach for the assessment of rodenticides (anticoagulants)" agreed at TMII 2011. This paper was based on an operator exposure study conducted by CEFIC/EBPF Rodenticides Data Development Group (Chambers *et al.* (2004)) and the number of manipulations has been proposed by the applicant.

Dietary exposure

Exposure to residues in food is not assessed because no contamination of food or feeding stuff is foreseen.

Aggregated exposure

No aggregated exposure is foreseeable since the product is not intended to be used under another biocidal product type.

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.	Trained-professional	Tier 1/ no PPE (unrealistic)	1 x 10^{-6}mg/kg bw/day
1.	Trained-professional	Tier 2 / PPE	1 x 10^{-7}mg/kg bw/day
2.	Trained-professional	Tier 1/ no PPE (unrealistic)	1 x 10^{-6}mg/kg bw/day
2.	Trained-professional	Tier 2/ PPE	1 x 10^{-7}mg/kg bw/day
1+2	Trained-professional	Tier 1/ No PPE	2 x 10^{-6}mg/kg bw/day
1+2	Trained-professional	Tier 2/ PPE	2 x 10^{-7}mg/kg bw/day
3	Infant	Reverse scenario	4.16 x 10-4 ml

3.6.4 Risk characterisation for human health

Reference values to be used in Risk Characterisation

Reference	**Study**	**NOAEL (LOAEL) (mg/kg bw/day)**	**AF[1]**	**Correction for oral absorption**	**Value (mg/kgbw/day)**
AEL_{acute}	-	0.00034	300 (+ factor 2 to extrapolation from LOAEL)	-	1.1 x 10^{-6}
$AEL_{medium-term}$	-	0.00034		-	1.1 x 10^{-6}
$AEL_{long-term}$	-	0.00034		-	1.1 x 10^{-6}
ARfD	Not applicable	-	Not applicable	-	Not applicable
ADI	Not applicable	-	Not applicable	-	Not applicable

[1]Assessment factor have been obtained from the Difenacoum's CAR.

The acceptable level of exposure for short, medium and long-term exposure (AEL) is established in the EU Endpoint List as 1.1 x 10^{-6} mg/kg bw/day, based on the endpoint from the teratogenicity test in rabbits (NOAEL: 0.00034 mg/kg bw/day) and a safety factor of 3. This is considered to be a suitable endpoint for all users applying rodenticide baits, and for indirect exposure.

Maximum residue limits or equivalent

Exposure to residues in food is not assessed because no contamination on food or feeding stuff is foreseen.

Risk for professional users

- ***Trained professional (Pest control operators)***

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)
Loading / Scenario [1]	Tier 1	0.00034	1.1×10^{-6}	1×10^{-6}	91	Yes
	Tier 2			1×10^{-7}	9.1	Yes
Cleaning / Scenario [2]	Tier 1			1×10^{-6}	91	Yes
	Tier 2			1×10^{-7}	9.1	Yes
Scenario [1+2]	Tier 1			2×10^{-6}	182	NO
	Tier 2			2×10^{-7}	18	Yes

Local effects

There is no need to consider local effects separately.

Conclusion

No risk can be expected for trained professional users either, with or without PPE. Nevertheless, use of protective gloves is recommended in all cases for hygiene reasons and always expected for trained professional users during pest control operations.

Risk for the general public

Adults or children may be present following application and may be incidentally exposed by touching unprotected bait under an hypothetical worse case as the product bottle is placed inside a bait station. For products applied in bait stations or outdoors, incidental exposure will be very limited.

Infants are potentially the group most at risk as they may play inside or around buildings where baits have been placed. They could be exposed orally by chewing bait or touching their mouth with contaminated fingers.

Local effects

There is no need to consider local effects separately.

Conclusion

In the hypothetical case that a child may enter in contact with unprotected bait, the calculated toxic amount was 4.16 x 10^{-4} ml based on a 1.1E-6 mg/kg b.w./d AEL. These values show that infants and children ingesting bait might be at risk. In this hypothetical worst case scenario, firstly, the bait is located inside a sealed bait station and secondly, the product contains a bittering agent which would prevent ingestion of the baits. Therefore, in practice the margins of safety are expected to be much higher than those calculated. It is also important that product labels and good practice advise users to prevent access to bait by children, for example:

- Place the product out of the reach of children, birds, pets and farm animals and other non-target animals.
- Where possible, bait stations must be fixed to the ground or other structures.
- Bait stations must be clearly labelled to show they contain rodenticides and that they must not be moved or opened.
- When the product is being used in public areas, the areas treated should be marked during the treatment period and a notice explaining the risk of primary or secondary poisoning by the anticoagulant as well as indicating the first measures to be taken in case of poisoning must be made available alongside the baits.

Bait should be secured so that it cannot be dragged away from the bait station.

The proposed uses therefore present an acceptable risk from indirect exposure.

Risk for consumers via residues in food

Neither new data was not provided nor had new guidance to be taken into account for re-assessment. Accordingly, the conclusion from the former assessment regarding risks for consumers via residues in food remains valid. Risk characterisation from combined exposure to several active substances or substances of concern within a biocidal product

There is no risk derived from a combined exposure because indirect exposure via the environment is considered negligible, the product is not intended to be mixed with other biocidal or non biocidal products and the product does not contain any other active substance of concern.

Summary of risk characterisation

Scenario number	Exposed group	Tier/PPE	AEL mg/kg bw/d	Estimated uptake mg/kg bw/d	Estimated uptake/ AEL (%)	Acceptable (yes/no)
1.	Trained professional user	Tier 1/ no PPE (unrealistic)	1.1×10^{-6}	1×10^{-6}	91	Yes
1.	Trained professional user	Tier 2/ PPE	1.1×10^{-6}	1×10^{-7}	9.1	Yes
2.	Trained professional user	Tier 1/ no PPE (unrealistic)	1.1×10^{-6}	1×10^{-6}	91	Yes
2.	Trained professional user	Tier 2/ PPE	1.1×10^{-6}	1×10^{-7}	9.1	Yes
Combined [1+2])	Trained professional user	Tier 1/ no PPE application and cleaning/combined scenarios [1+2]Tier 1/ no PPE	1.1×10^{-6}	2×10^{-6}	182	No
Combined [1+2])	Trained professional user	Tier 2/ PPE application and cleaning/combined scenarios [1+2]	1.1×10^{-6}	2×10^{-7}	18	Yes

3.7 Risk assessment for animal health

Neither new data was not provided nor had new guidance to be taken into account for re-assessment. Accordingly, the conclusion from the former assessment regarding animal health remains valid.

3.8 Risk assessment for the environment

Neither new data was not provided nor had new guidance to be taken into account for re-assessment with the new active substance concentration.

3.8.1 Exposure assessment

General information

Assessed PT	PT 14
Assessed scenarios	Scenario [1]: in and around buildings Scenario [2]: open areas Scenario [3]: waste dumps
ESD(s) used	– EUBEES 2 Emission Scenario Document (ESD) for biocides used as rodenticides (Larsen, 2003) Calculations were performed using (ESD)
Approach	The product is a ready to use bait. Under the proposed use up to 250 ml of baits are placed in each bait station. The bait stations are regularly inspected, refilled, and dead rodents are removed. The bait points are placed 5-10 m apart and the baiting programmes are repeated 2-3 times a year.
Distribution in the environment	Guidance on the BIocidal Products Regulation, Vol IV part B
Groundwater simulation	BPR Guidance
Confidential Annexes	Yes, please see section 3.6
Life cycle steps assessed	Scenarios [1], [2] and [3] Production: No Formulation No Use: Yes Service life: No
Remarks	“RATONEX LIQUIDO 26’ is proposed for use in and around buildings, open areas or waste dumps; hence PEC calculations are required for these uses.

Emission estimation

In order to avoid any spillage of the product or intake by other animals, a specific dosing system has been required, consisting of sealed bottles which only will be opened when inserting the bottle into a roll-on dispenser. All the system is within an additional small base placed inside the bait station which prevent spillage in case of leaking. This dosing system substantially minimizes the exposure to the environment and therefore, the EUBEES scenario used in the assessment can be considered a worst

case and the calculated values showed are referred to the worst realistic case, taking in account no this dosing system

Parameter	Value	Source
Molecular weight (g/mol)	444.5	EU endpoint list
Melting point	211-215 ^{o}C	EU endpoint list
Boiling point	-	EU endpoint list
Vapour pressure 20^{o}C	6.7 x 10^{-9} Pa	EU endpoint list
Vapour pressure 25^{o}C	1.9 x 10^{-11} Pa	EU endpoint list
Henry's law constant	1.75 x 10^{-6} Pa.m^{3}.mol^{-1}	EU endpoint list
Log Kow	7.6	EU endpoint list
Water solubility 20^{o}C	0.48 mg/L	EU endpoint list
Koc	1.8 x 10^{6} L/kg 426579 (acidic conditions) 17 to 165 (basic conditions)	QSAR (value used in Difenacoum's CAR)
$RHO_{product}$	1.1100 g/ml *	Physichal-chemical properties of the product.

* In view of the next to 1 g/ml and in order to simplify the calculations, 1 g/ml is considered as product density in the following assessments.

Scenario [1] - Use in and around buildings

The product is a ready to use bait. Under the proposed use up to 250 ml of baits are placed in each bait station. The bait stations are regularly inspected, refilled, and dead rodents are removed. The bait points are placed 5-10 m apart and the baiting programmes are repeated 2-3 times a year.

In the ESD worst case scenario 10 tamper resistant bait stations is used each filled with 250 g liquid bait, inspected and replenished 5 times (day 1, 3, 7, 14, 21). It is an assumption that all of the bait has been eaten. There is a large variation of the duration of a rodenticide campaign and a 21 days period represent a realistic worst case.

In a typical campaign (normal use), bait would be applied on day 1, replenished 100% on day 3, on day 7 there would be 25-50% replenishment, on day 14, 10%, on day 21 0%. Roughly the equivalent of 1.5 x 100% replenishments. (CEFIC 2002)

In the so-called 'typical' scenario the replenishment is done only 1.5 times. The scenario represented by the proposed use differs from the ESD worst case scenario only regarding the amount of bait in each station, i.e. 200 g instead of 250 g; the other parameters are considered as equal to the worst case scenario.

A summary of in and around buildings scenario input values are provided in the following table:

Input variable/parameters for calculating the local emission				
Variable/parameter	***Symbol***	***Value***		***Unit***
Scenario: Use in and around buildings		***(Tier 1) Worse case***	***(Tier 2) Proposed use***	
Amount of product used operation for each application site	Q_{prod}	250	200	[g]
Fraction of active substance in product	$Fc_{product}$	0.0026	0.0026	[%]
Number of application sites	N_{sites}	10	10	[-]
Number of refilling times	N_{refil}	5	1.5	[-]
Number of emission days per year	$T_{emission}$	21	21	[d]
Fraction of product released to soil during use	$F_{release, soil, use}$	0.01	0.01	[-]
Area directly exposed to rodenticide	$AREA_{exposed-D}$	0.09	0.09	[m^2]
Fraction of product released indirectly to soil	$F_{released-ID,soil}$	0.9	0.9	[-]
Area indirectly exposed to rodenticide	$AREA_{exposed-ID}$	550	550	[m^2]
Depth of exposed soil	$DEPTH_{soil}$	0.1	0.1	[m]
Density of wet exposed soil	RHO_{soil}	1700	1700	[$kg.m^{-3}$]

Calculus have been performed according to EUBEES, Emission document for biocides used as rodenticides

Direct release in the realistic worst case farm scenario based on bait in bait boxes has been calculated as following (equation 2 ESD):

ESD worst case

Parameter	Definition	Units	Value
Amount of product used at each refill/application	Qprod	g	250
Fraction of active substance in product	Fc_{prod}	-	0,000026
Number of application sites	N_{sites}	-	10

Number of refills per site	N_{refil}	-	5
Fraction of active substance released directly to soil	$F_{release, soil}$	-	0,01
Local direct emission rate of active substance to soil from a campaign	**$Elocal_{soil\text{-}campaing} = (Q_{prod} \times Fc_{prod} \times N_{sites} \times F_{release, soil})$ (2)**	**g**	**0.00325**

Applicant's worst case

Parameter	Definition	Units	Value
Amount of product used at each refill/application	Qprod	g	200
Fraction of active substance in product	Fc_{prod}	-	0,000026
Number of application sites	N_{sites}	-	10
Number of refills per site	N_{refil}	-	1.5
Fraction of active substance released directly to soil	$F_{release, soil}$	-	0,01
Local direct emission rate of active substance to soil from a campaign	**$Elocal_{soil\text{-}campaing} = (Q_{prod} \times Fc_{prod} \times N_{sites} \times F_{release, soil})$ (2)**	**g**	**0,00078**

The concentration in the soil around each bait box after direct release can be estimated by the equation (3) of the ESD for PT14:

ESD worst case

Parameter	Definition	Units	Value
Local direct emission rate of active substance to soil from a campaign	$E_{soil, D\text{-}campaing}$ (2)	g	0.00325
Area directly exposed to active substance	$AREA_{exposed\text{-}D}$	m^2	0.09
Depth of exposed soil	$DEPTH_{SOIL}$	m	0.1
Number of application sites	N_{sites}	-	10
Density of exposed soiil	RHO_{soil}	kg/m^3	1700

Local concentration in soil due to direct release after a campaign [mg/kg]	**$Clocal_{soil-D}$ = (Elocal $_{soil-D-campaign}$ x10E3)/ (AREA $_{exposed-D}$ x $DEPTH_{soil}$ X RHO_{soil} x N_{sites}) (3)**	**mg/kg**	**0.0212**

Applicant's worst case

Parameter	Definition	Units	Value
Local direct emission rate of active substance to soil from a campaign	$E_{soil, D-campaing}$ (2)	g	0.000078
Area directly exposed to active substance	$AREA_{exposed-D}$	m^2	0.09
Depth of exposed soil	$DEPTH_{SOIL}$	m	0.1
Number of application sites	N_{sites}	-	10
Density of exposed soil	RHO_{soil}	kg/m^3	1700
Local concentration in soil due to direct release after a campaign [mg/kg]	**$Clocal_{soil-D}$ = (Elocal $_{soil-D-campaign}$ x10E3)/ (AREA $_{exposed-D}$ x $DEPTH_{soil}$ X RHO_{soil} x N_{sites}) (3)**	**mg/kg**	**0.0051**

The concentration in the soil around the bait box taking into account only disperses release can be estimated by the equation:

ESD worst case

Parameter	Definition	Units	Value
Amount of product used at each refill/application	Qprod	g	250
Fraction of active substance in fproduct	Fc_{prod}	-	0.000026
Number of application sites	N_{sites}	-	10
Number of refills per site	N_{refil}	-	5
Fraction released indirectly to soil	$F_{release-ID, soil}$		0.9
Fraction released directly to soil	$F_{release, soil}$		0.01
Area indirectly exposed to rodenticide	$AREA_{exposed-ID}$	m^2	550
Depth of exposed soil	$DEPTH_{SOIL}$	m	0.1
Density of exposed soiil	RHO_{soil}	kg/m^3	1700
Concentration in soil due to indirect (disperse) release after a campaign	**$Clocal_{soil-ID}$ = ((Q_{prod} X Fc_{prod} X N_{sites} X N_{refil} x 10^3 x $F_{release,ID\ soil}$ x (1-$F_{release,D\ soil}$)) / (AREA exposed-ID x DEPTHsoil X RHOsoil x Nsites) (4)**	**mg/kg**	**0.0031**

Applicant's worst case

Parameter	Definition	Units	Value
Amount of product used at each refill/application	Qprod	g	200
Fraction of active substance in product	Fc_{prod}	-	0.000026
Number of application sites	N_{sites}	-	10
Number of refills per site	N_{refil}	-	1.5
Fraction released indirectly to soil	$F_{release\text{-}ID,\ soil}$		0.9
Fraction released directly to soil	$F_{release,\ soil}$		0.01
Area indirectly exposed to rodenticide	$AREA_{exposed\text{-}ID}$	m^2	550
Depth of exposed soil	$DEPTH_{SOIL}$	m	0.1
Density of exposed soil	RHO_{soil}	kg/m^3	1700
Concentration in soil due to indirect (disperse) release after a campaign	**$Clocal_{soil\text{-}ID} = ((Q_{prod} \times Fc_{prod} \times N_{sites} \times N_{refil} \times 10^3 \times F_{release,ID\ soil} \times (1\text{-}F_{release,D\ soil}))$ / (AREA exposed-ID x DEPTHsoil X RHOsoil x Nsites) (4)**	**mg/kg**	**0.000743**

Total soil concentrations around the bait boxes are the sum of the soil concentrations caused dye direct and indirect pollution o the soil:

ESD worst case

Total concentration immediately direct to the bait	**$C_{local\ soil} = C_{local\ soil\text{-}D} + C_{local\ soil\text{-}ID}$**	**mg/kg**	**0.0243**

Applicant's worst case

Total concentration immediately direct to the bait	**$C_{local\ soil} = C_{local\ soil\text{-}D} + C_{local\ soil\text{-}ID}$**	**mg/kg**	**0.00584**

Calculations for Scenario [1] - Use in and around buildings

Calculation of PEC in soil

Using the scenarios outlined in the ESD for rodenticides and the Guidance on the BIocidal Products Regulation, Vol IV part B,and the calculations and assumptions presented for “in and adround buildings” scenario, the following local PEC values have been derived for the terrestrial compartment. Proposed real case values taken forward to the risk characterisation are shown in bold for the relevant scenarios assessed for ‘RATONEX LIQUIDO 26’ are reproduced below.

SCENARIO	(Tier 1) Realistic worse case using default values	(Tier 2) Proposed realistic case*
IN/AROUND BUILDINGS		
PECsoil	0.0243 mg/kg	0.00584mg/kg

Calculation of PEC in groundwater

$PEC_{groundwater}$ was calculated according to equation 67 in Guidance on the BIocidal Products Regulation, Vol IV part B,, where it is assumed that PEC local groundwater equals to PEC local pore water in agricultural soils. The concentration in the soil pore waters is determined by the predicted difenacoum concentration in local soil, the bulk density of the soil and the soil-water partitioning coefficient.

$PECsoil_{,porewater}$ = PECsoil *RHO / ($K_{soil-water}$ *1000)

Using the scenarios outlined in the ESD for rodenticides and the Guidance on the BIocidal Products Regulation, Vol IV part B,, and the calculations and assumptions presented for each of the scenarios considered above, the following local PEC values have been derived for aquatic compartments. Proposed real-case values taken forward to the risk characterisation are shown in bold.

SCENARIO Compartment	(Tier 1) Realistic worse case using default values	(Tier 2) Proposed realistic case
IN/AROUND BUILDINGS		
Ground (pore) water		
From soil exposure	7.65×10^{-7} mg/l	**1.84×10^{-7} mg/l**

An average K_{oc} value of 1803018 ml/g (EU Endpoint List) was used in the calculations for derivation of $k_{soil-water}$ (=54090.74). However, due to the limited use of difenacoum in campaigns that last for a limited time, usually three weeks, and that good management practice prescribes that both leftover feed and dead rodents are collected and disposed of in a secure way, the exposure to groundwater is likely to be negligible.

Scenario [2] - Use in open areas

This scenario covers control of rats and water voles in open areas such as around farmland, parks and golf courses where the aim is to prevent “nuisance” from burrows or “soil heaps” or due to public hygiene reasons.

The main release to the environment is expected when impregnated grains are applied into rat holes. By a spoon or a small shovel, the product is normally poured approximately 30 cm into the rat holes, depending on the slope and general accessibility of the hole. The treated holes are closed by a stone, a piece of board or similar immediately after the application to prevent unintended exposure of children or non-target organisms (e.g. birds, cats and dogs).

A typical initial dose for a rat hole in the Nordic countries is 100-200 g bait.hole-1; and normally application is repeated twice with an interval of 5-6 days. However, in e.g. France a typical dose for a rat hole is about 50-100 g product.

Inspection of the holes to assess the effect of the control action is usually carried out some 5-6 days after application of the poison and again with similar intervals if repeated applications are necessary.

Input		**Tier 1**	
Variable/parameter	***Symbol***	***Value***	***Unit***
Amount of product used at each refilling in the control operation	Q_{prod}	200	g
Fraction of active substance in product	Fc_{prod}	0.0026	[%]
Number of application sites	N_{sites}	1	[-]
Number of refilling times	N_{refil}	2	[-]
Fraction of product released to soil during application	$F_{release, soil, appl}$	0.05	[-]
Fraction of product released to soil during use	$F_{release, soil, use}$	0.2	[-]
Radius of exposed soil around the hole	R	0.14	m
Radius of hole	r	0.04	m
Length of exposed hole	l	0.3	m
Density of wet exposed soil	RHO_{soil}	1700	$kg.m^{-3}$

<u>Calculations for Scenario [2] - Use in open areas</u>

As in the scenario before, only local emission to soil compartment may be considered of relevance for the environment. Hence, only terrestrial compartment may be exposed for this scenario and considered of concern, so PEC for industrial soil and porewater compartments have been calculated.

Calculation of $Elocal_{soil\text{-}campaign}$ (equation 9, ESD PT14)

Parameter	**Definition**	**Units**	**Value**

Amount of product used at each refilling in the control operation	Q_{prod}	g	200
Fraction of active substance in product	Fc_{prod}	-	0.000026
Number of application sites	N_{sites}	-	1
Number of refills per site	N_{refil}	-	2
Fraction of the product released to soil during application	$F_{release, soil, appl}$	-	0.05
Fraction of product released to soil during use	$F_{release, soil, use}$		0.2
Local emission of active substance to soil during a campaign	**$Elocal_{soil\text{-}campaing} = (Q_{prod} \times Fc_{prod} \times N_{sites} \times N_{refil} \times (F_{release, soil, appli} + F_{release, soil})$ (9)**	**g**	**2.60E-03**

Calculation of $Clocal_{soil\text{-}campaign}$ (equation 10, ESD PT14)

Parameter	Definition	Units	Value
Local emission to soil from the episode	$Eloca_{lsoil\text{-}campaign}$	g	5.00E-03
Soil volume exposed to rodenticide	$Vsoil_{exposed}$ (eq. 9a ESD)	m^3	8.50E-03
Density of wet exposed soil	RHO_{soil}	kg/m^3	1700
Local concentration in soil after a campaign	**$Clocal_{soil\text{-}campaing} = (E_{localsoil\text{-}campaign} \times 10^3)/(V_{soilexposed} \times RHO_{soil})$ (10)**	**mg/kg**	**1.80E-01**

Calculation of PEC in soil

Using the scenarios outlined in the ESD for rodenticides and the Guidance on the BIocidal Products Regulation, Vol IV part B, , and the calculations, the following local PEC values have been derived for the terrestrial compartment.

SCENARIO Compartment		**Tier 1 (ESD worse case)**
Open areas		
Local PEC soil	$mg.kg^{-1}$	**0.18**

Calculation of PEC in pore water (groundwater)

PEC groundwater was calculated according to equation 67 in Guidance on the BIocidal Products Regulation, Vol IV part B,I, where it is assumed that PEC local groundwater equals to PEC local pore

water in agricultural soils. The concentration in the soil pore waters is determined by the predicted difenacoum concentration in local soil, the bulk density of the soil and the soil-water partitioning coefficient.

SCENARIO Compartment		Tier 1 (ESD worse case)
Open areas		
Local PEC soil pore water	$mg.L^{-1}$	5.657×10^{-6}

Scenario [3] - Use in waste dumps

This scenario covers control of rats and disposal of rats in waste dumps and landfills where the exposure is assumed to be higher than that described in the open area scenario.

Input		Tier 1	
Variable/parameter	***Symbol***	***Value***	***Unit***
Amount of product used in the control operation	Q_{prod}	40	kg
Fraction of active substance in product	Fc_{prod}	0.0026	[%]
Number of applications	N_{app}	7	[-]
Fraction of product released to soil	$F_{release,soil}$	0.9	[-]
Area exposed to rodenticide	$AREA_{exposed}$	10000	m^2
Depth of exposed soil	$DEPTH_{soil}$	0.1	m
Density of wet exposed soil	RHO_{soil}	1700	$kg.m^{-3}$

Calculations for Scenario [3] - Use in waste dumps

Calculation of $E_{local\ soil}$ (equation 17, ESD PT14)

Parameter	Definition	Units	Value
Amount of product used per application	Qprod	g	40
Fraction of active substance in product	Fc_{prod}	-	0.000029
Number of application sites	N_{sites}	-	7
Fraction of active substance released directly to soil	$F_{release,\ soil}$	-	0.73
Local direct emission of active substance to soil from a campaign	$\mathbf{Elocal_{soil\text{-}campaing} = Q_{prod} \times Fc_{prod} \times N_{sites} \times F_{release,\ soil}}$ **(17)**	**kg**	**6.55E-03**

Calculation of C local soil (equation 18, ESD PT14)

Parameter	Definition	Units	Value

Local direct emission of active substance to soil from a campaign	$Elocal_{soil,\ campaing}$ (2)	kg/m3	6.55-03
Area directly exposed to active substance	$AREA_{exposed-D}$	m^2	10000
Depth of exposed soil	$DEPTH_{SOIL}$	M	0.1
Density of exposed soil	RHO_{soil}	kg/m^3	1700
Local concentration in soil due to direct release after a campaign [mg/kg]	**$Clocal_{soil-D}$ = (Elocal $_{soil-D-campaign}$ x10E3)/ (AREA $_{exposed-D}$ x $DEPTH_{soil}$ X RHO_{soil} x N_{sites}) (18)**	**mg/kg**	**0.000385**

SCENARIO Compartment		**Tier 1 (ESD worse case)**
Waste dumps		
Local PEC in soil	$mg.kg^{-1}$	0.000385

Calculation of PEC in pore water (groundwater)

As in the scenario before and following the Guidance on the BIocidal Products Regulation, Vol IV part B, , and the calculations and assumptions presented for each of the scenarios considered above, the following local PEC values have been derived for groundwater compartment.

SCENARIO Compartment		**Tier 1 (ESD worse case)**
Waste dumps		
Local PEC in pore water of industrial/ application soil	$mg.L^{-1}$	$1.21x10^{-8}$

Fate and distribution in exposed environmental compartments

The environmental fate and behaviour of the active substance Difenacoum has been fully evaluated during the assessment for Annex I inclusion. A summary of the fate and distribution of Difenacoum is presented in Section 2.2.2.1 of the final Assessment Report (17 September 2009), and the relevant endpoints appear in the EU List of Endpoints.

The formulation of Difenacoum as a liquid bait in RATONEX LIQUIDO 26 is not expected to have impact on the route or rate of degradation of the active substance Difenacoum in the environment.

A summary of the fate and distribution of Difenacoum in biocidal product is presented below:

Identification of relevant receiving compartments based on the exposure pathway									
	Fresh -water	Freshwater sediment	Sea-water	Seawater sediment	STP	Air	Soil	Ground-water	Other: secondary poisoning
Scenario 1	n.r.	n.r.	n.r.	n.r.	n.r.	n.r.	Yes	Yes	Yes

Scenario 2	n.r.	n.r.	n.r.	n.r.	n.r.	n.r.	Yes	Yes	Yes
Scenario 3	n.r.	n.r.	n.r.	n.r.	n.r.	n.r.	Yes	Yes	Yes

n.r.= “not relevant”

Calculated PEC values

Summary table on calculated PEC values								
	PEC_{STP}	**PEC_{water}**	**PEC_{sed}**	**$PEC_{seawater}$**	**PEC_{seased}**	**PEC_{soil}**	**PEC_{GW}[1]**	**PEC_{air}**
	[mg/m^3]	[mg/l]	[mg/kg_{wwt}]	[mg/l]	[mg/kg_{wwt}]	[mg/kg]	[mg/l]	[mg/m^3]
Scenario 1 tier 1	Neg	Neg	Neg	Neg	Neg	0.0243	7.65×10^{-7}	
Scenario 1 tier 2	Neg	Neg	Neg	Neg	Neg	0.00584	1.84×10^{-7}	
Scenario 2	Neg	Neg	Neg	Neg	Neg	0.18	$5.657\ 10^{-6}$	
Scenario 3	Neg	Neg	Neg	Neg	Neg	0.000385	1.21×10^{-8}	

[1] If the PEC_{GW} was calculated by using a simulation tool (e.g. one of the FOCUS models), please provide the results for the different simulated scenarios in a separate table.

Primary and secondary poisoning

Difenacoum is not readily biodegradable, has a relatively high bioconcentration factor and is very toxic to both aquatic organisms and mammals, and therefore a risk assessment for secondary poisoning was performed according to Guidance on the Biocidal Products Regulation, Vol IV part B, . According to those calculations performed, the evaluated product with difenacoum will cause unacceptable risks both for primary and secondary poisoning. On the other hand, in order to avoid any test on mammals, a thorough bibliographic search has shown by numerous scientific reports (Newton et al., 1997; Foumier-Chambrillon, et al. 2004; Shore et al., 1999; Gillies and Pierce, 1999; Eason and Spurr, 1995) that non-target birds and mammals have been, and are continuously, exposed to second generation anticoagulant rodenticides in the environment. This exposure occurs most likely by consumption of living or dead rodents that have been poisoned by baits containing rodenticides (secondary poisoning). Moreover, year after year there are reports (Barnett et al., 2006) of accidents where non-target mammals have been poisoned by consumption of rodenticides (primary poisoning). Species included in the latter reports are e.g. dogs, badgers and squirrels. The reports include many bird species and also honeybees but there seems to be a lack of reports, and possibly lack of research, on rodenticide effects on snakes and amphibians. The risk of difenacoum to non-target birds and mammals has been assessed according to the ESD and the Guidance on the Biocidal Products Regulation, Vol IV part B,. However, although difenacoum has a potential to bioaccumulate, assessment of secondary poisoning through the aquatic food chain is not performed for the following reasons: the risk assessment for the aquatic compartment indicates that there will be very low concentrations of difenacoum in the aquatic compartment, and there was no risk identified of

difenacoum for surface water or sediment dwelling organisms. The justification for not performing an assessment of secondary poisoning via the terrestrial food chain is that secondary poisoning will be limited due to the small area that is potentially contaminated by difenacoum around buildings and the limited number of earthworms inhabiting this area. It seems from monitoring data published on bam owls that 1% of the owls had died from secondary poisoning by rodenticides (Newton et al., 1997). The question is whether this 1-% lethality will have any effect on population level. Looking at the barn owl population in England it seems as it has stabilised during the two last decades after a 60-70% decline between 1930 and 1980. Figures for mammals are more uncertain, especially since many mammals may hide before they die. The probability of poisoning will depend on the duration of the treatment campaign, since the longer the campaign the higher is the probability for long-term toxic effects. Moreover, the frequency of campaigns in a specific area has to be considered, which means that campaigns have to be coordinated locally or regionally, taking into consideration the size of the hunting grounds of the species to protect. Otherwise predatory birds may catch rats with abnormal behaviour on one farm for a week and then on the next farm the next week and so forth. If the hunting grounds for a barn owl cover something like five farms the length of the exposure period to owls for poisoned rats could theoretically increase from 3 to 15 weeks. The frequency and length of the campaigns should be recorded by the professional users and could also be connected to monitoring programmes, e.g. monitoring of dead birds regarding cause of death and liver concentrations of rodenticides where the pattern of rodenticide use could be related to the variation over time of the recorded liver concentrations.

Primary poisoning

Non-target animals such as wild and domestic animals may come in contact with baits if the bait is unprotected (bad use of the product) or if bait stations have been damaged. As it was mentioned before, a tamper resistant bait station of category 1 is recommended to use for RATONEX LIQUIDO 26 in order to avoid both scenarios above. Even so, well-protected bait may be encountered by animals which are small enough to be able to reach the bait, e.g. weasels, stoats and young cats (kittens), and therefore they may be subject to primary poisoning.

- ***Tier 1 assessment***

Acute exposure:

For the acute situation of primary poisoning only a qualitative risk assessment will be carried out in accordance with the decision from TM III-06. This will be done in the Tier 2 assessment below.

Long-term exposure:

In the Tier 1 assessment of primary poisoning from long-term exposure it is assumed that the whole day's food requirement is satisfied by consumption of bait, and therefore the concentration in food will be the same as the concentration of Difenacoum in the bait i.e. 26 mg/kg. This is then compared to the long-term PNEC values for birds and mammals, as calculated in the table below:

	PEC (conc. in bait)	PNEC (conc. in food)	PEC/PNEC
Birds	26mg/kg	0.0005 mg/kg	52000
Mammals	26mg/kg	7 X 10^{-3} mg/kg	3714.3

The resulting PEC/PNEC ratios reveal a high risk for both birds and mammals from long-term primary poisoning.

- ***Tier 2 assessment***

Acute exposure:

In the Tier 2 acute qualitative risk assessment the daily uptake (ETE) of difenacoum is compared with the effect data for birds and mammals: It is important to stress that this qualitative assessment is not intended to be used in the risk characterisation of primary and secondary poisoning of rodenticides and shall not be used in a comparative assessment. To refine the risk assessment the actual dose of difenacoum consumed by the bird after one day/one me al ETE is calculated using the equation below (equation 19 in the ESD). When calculating the dose both the typical body weight of the animal (BW) and daily mean food intake (Fill.) are considered. The calculations are performed in two steps where the avoidance factor (AV), the fraction of the diet obtained from the rodenticide treated are (PT) and the fraction of food type in the animals diet (PD) are all considered in accordance with the ESD. In the worst case calculations performed in the first step avoidance factors, fraction of the diet from treated areas and fraction of food type in diet are all set to the default value of 1. In the realistic worst case calculations, step 2, performed according to the ESD the AV = 0.9, PT = 0.8 and PD = 1.

ETE = (FIR/BW)*C* AV*PT*PD (mg /kg bw*day)

Eq 19

ETE values calculated for acute exposure (ETE)

Non-target animal	Typical bodyweight (g)	Daily rnean food intake (g dw/day)	Concentration of difenacoum in bait (mg/kg)	ETE (rng/kg bw)	
				Step 1	Step 2
Dog	10 OOOa	456[b]	26	1.1856	0.85
Pig	80000 a	600 a	26	0.195	0.14
Pig, young	25000 a	600 a	26	0.624	0.449
Tree sparrow	22 a	7.6 a	26	8.98	6.47
Chaffinch	21.4 a	6.42 a	26	7.80	5.62
Wood pigeon	490 a	53.1 a	26	2.82	2.03
Pheasant	953 a	102.7 a	26	2.80	2.02

- According to table 3.1 in the ESD

- Calculated form log FIR=0.822 log BW-0.629 according to equation on page 50 ESD

The ETE values calculated for acute exposure for the worst case (step 1) and the realistic worst case (step 2) are compared to the LD50 values in the table below. Risk is foreseeable if the PECoral is higher than LD50.

PEC values calculated for birds and mammals

Non-target animal	PEC_{oral} = ETE, of difenacoum after one (mg/kg)		LDso (mg/kg bw/d)	PEC_{oral} higher than LDso	
	Step 1	Step 2		Step 1	Step 2
Dog	1.1856	0.85	1.8	n	n
Pig	0.195	0.14	1.8	n	n
Pig, young	0.624	0.449	1.8	n	n
Tree sparrow	8.98	6.47	56	n	n
Chaffinch	7.80	5.62	56	n	n
Wood pigeon	2.82	2.03	56	n	n
Pheasant	2.80	2.02	56	n	n

The ETE values calculated for acute exposure for the worst case (step 1) and realistic worst case (step2) are compared to the LD 50 values. This comparison indicates that birds are not at risk for acute primary poisoning while the situation for mammals is more uncertain.

• long term EXPOSURE

The long-term risks of difenacoum are determined by the expected concentrations (EC) in the animal after metabolism and elimination, which is regarded as PEC. The EC is calculated by using the actual dose of the substance consumed by a non-target animal each day (ETE) using the realistic worst case scenario (step 2), calculated in table above. When calculating the long-term risks, elimination and metabolism of the substance (El) have to be considered . According to the ESD, a default value of 0.3 for El can be used if no studies are submitted that show different.

The PNEC values used for birds (0.1 µg/kg bw/day) and mammals (0.3 µg/kg bw/day) are those calculated in the final Assessment Report for difenacoum (September 2009).

Calculations are performed according to equation 20 in the ESD;

$$EC = ETE*(1 - El) \qquad \text{Eq.20}$$

. The following table shows the maximum and minimum values of PEC calculated for each group of organism for a long-term exposure:

PEC/PNEC ratios for primary poisoning - Tier 2 assessment long term

Non-target animal	PEC* = EC_i Concentration of difenacoum after one day of elimination (mg/kg)	PNEC dose (mg/kg bw/day)	PEC/PNEC
Dog	0.784	0.0001	7840
Pig	0.098	0.0001	980
Pig, young	0.3143	0.0001	3143
Tree sparrow	4.529	0.0003	15097
Chaffinch	3.934	0.0003	13113
Wood pigeon	1.421	0.0003	4737
Pheasant	1.414	0.0003	4713

*considering 5.28% as the daily uptake eliminated of difenacoum

The result of the PECIPNEC calculations shows that there are very high risks for long-term primary poisoning of both mammals and birds. The calculations are based on that bait is consumed only during one day and then eliminated from the animal, but it should also be considered that an animal might consume bait again before the first dose is eliminated. On the other hand it should been taken into consideration that the actual doses are strictly worst case and that consumption of these quantities of difenacoum bait by the non-target animal exemplified above are generally not realistic. These results are discussed and compared to monitoring data after the assessment of secondary poisoning in the next section.

Secondary poisoning

- **Secondary poisoning via the terrestrial food chain**

Secondary poisoning of difenacoum occurs when poisoned rodents are caught by predators and eaten by scavengers that hunt and forage around difenacoum treated areas. It has been reported by Shore et al. (1999) that there is an increased hazard of exposure for predators during the winter months which might be caused by the fact that there are less preys available in the winter season. It should be also considered that behaviour of poisoned rodents might change as presented in two reports referred to in the ESD. According to these reports more than half of the rats that died by rodenticide poisoning died away from cover. Moreover, it seemed as the rats changed their behaviour when still alive and were more active during the days than rats normally are and also spent more time unprotected above ground. Such behaviour can make them a more easy prey to predators and they are also more easily found by scavengers. It was found, when water voles were studied during a campaign that 38% of them died above ground (Saucy et al., 2001, in ESD).

Tier 1 assessment (Short term) and Tier 2 assessment (long term)

Calculations of the risk for secondary poisoning of scavengers and predators are done by determining the concentration of difenacoum in their food, i.e. the poisoned rodents. This PECoral is then compared to the LC50 values presented in section 2.2.8 for a qualitative risk assessment.

According to the ESD section 3.3.1 the consumption of rodenticides makes up at least 20% of total consumptions in a choice test and could in a worse case be up to 100%, whilst 50% would be considered the normal situation. Therefore, in the calculations PD values are set to 0.2, 0.5 and 1.0. The fraction of daily uptake eliminated is 0.3 (EI). The FIR/BW quotient is a default value set to 0.1, i.e. it is assumed that the rats eat 10% of their bodyweight each day. The avoidance factor (AV) is 1, which means no avoidance, since rats is their natural prey, and the fraction of diet (PD) obtained in the area is set to 1. The calculation is done according to equation 19 in the ESD (ETE = (FIR/BW)*C* AV*PT*PD (mg /kg bw*day)).

	Residues in target animal (mg/kg bw) with bait consumption in % of daily consumption (PD)		
	20%	**50%**	**100%**
Day 1 after the first meal	0.5	1.25	2.5
Day 2 after the first meal	0.35	0.875	4.25
Day 5 after the first meal	0.887	2.22	6.93
Day 7 after the first meal	1.03	2.57	7.65
Day 14 after the first meal	1.16	2.89	8.28

The difenacoum concentration in rats goes on increasing after consuming bait for 7 days. On the other hand, regarding that LD50 in rat for acute toxicity is established at 1.8 mg/kg (male rat), it seems reasonable to think that when the target animal consumes 50% of bait it will die after the 5th day because the expected concentration of active substance in the rat is above the LD50. Therefore, this concentration will be considered in the subsequent calculations for non-target organisms.

Toxicity derived by the active substance concentration in the non-target animal is calculated according ESD excel-datasheet for short-term (tier 1) and long-term (tier 2) for all expected predators (non-target animals).

The rodents are assumed to eat the bait over five or fourteen successive days, whereas the predator or the scavenger is assumed to eat the poisoned rodents during one day.

The predator is assumed to have caught the rodent after the last meal on day 5 or day 14. Only resistant rodents are assumed to eat bait over 14 days. In the following table, values used to estimate the concentration in predators are shown:

Non-target animal Predator	Body weight (Bw) [g]	Food intake rate (FIR) [g.d^{-1}]	Concentrations in the non-target animals (short term)	Concentrations in the non-target animals (long term)
			$ETE_{non\text{-}target}$ (mg.kg^{-1}bw.d^{-1}))	$ETE_{non\text{-}target}$ (mg.kg^{-1}bw.d^{-1}))
Barn owl	294	72.9	0.894	0.447
Kestrel	209	78.7	1.36	0.679
Little owl	164	46.4	1.02	0.51
Tawny owl	426	97.1	0.822	0.411
Fox	5700	520.2	0.316	0.165
Polecat	689	130.9	0.685	0.342
Stoat	205	55.7	0.98	0.49
Weasel	63	24.7	1.41	0.707

As in the case of primary poisoning, risk is for secondary poisoning is calculated as the quotient of PEC/PNEC for each animal. For birds the PNEC (dose) from the reproduction test is used, whereas for mammals the PNEC (dose) calculated from the 90 day rabbit test is chosen. Risk quotients can be seen in the table below:

Non-target animal	Tier 1			Tier 2		
	PEC short term (mg/kg bw)	PNEC dose (mg/kg/day)	PEC/ PNEC	PEC long term (mg/kg bw)	PNEC dose (mg/kg/day)	PEC/ PNEC
Barn owl	0.86	0.0001	8940	0.43	0.0001	4470
Kestrel	1.31	0.0001	13600	0.653	0.0001	6790
Little owl	0.98	0.0001	10200	0.49	0.0001	5100
Tawny owl	0.79	0.0001	8220	0.395	0.0001	4110
Fox	0.316	0.007	45.1	0.158	0.007	23.6
Polecat	0.659	0.007	97.9	0.329	0.007	48.9
Stoat	0.942	0.007	140	0.471	0.007	70
Weasel	1.36	0.007	201	0.68	0.007	101

The worst case calculations according to the ESD show very high risks for secondary poisoning of difenacoum to both birds and mammals. The concentrations in the rodents in principle need to be reduced with 2-4 orders of magnitude in order to bring down the risk for non-target animals to acceptable levels. The PNECoral is based on the highest concentration causing no effects in the test with long- term exposure.

Primary and secondary poisoning is deemed similar for the three scenarios.

- **Secondary poisoning via the aquatic food chain**

The risk of secondary poisoning via the aquatic food chain is considered insignificant due to the low water solubility and high adsorption of difenacoum. It is also assumed that mechanical screening of sewage water will reduce the concentration in the recipient water, although this reduction cannot be quantified.

The proposed uses of RATONEX LIQUIDO 26 were also be considered to be acceptable, with the use of appropriate risk mitigation via label warnings.

Conclusions based on monitoring data

Two experimental studies on the secondary poisoning in Barn Owls have been submitted. Tier 1 and Tier 2 risk characterization are recalculated for the Barn Owl on the basis of the measured concentrations in rats and mice with the experimental data provided in the Difenacoum Task Force Annex I inclusion dossier. The risks are significantly lower than with the ESD calculations however they are still considerably higher than 1 indicating an unacceptable risk for secondary poisoning of the Barn Owls.

On the other hand, Newton *et al.* (1997) after monitoring data for Barn owls, provides a basis for calculations to determine what relevance the worst case calculations which indicate large implications on non-target bird and mammal populations, may have in the environment The data based on 1100 collected birds shows that 30% of the birds collected the recent decades have residues of second generation rodenticides. It also shows that 1% of the collected birds had died of rodenticide poisoning. Difenacoum residues in the liver were not measured in either test, and hence the comparison to the monitoring data is difficult. The residue levels measured from dead barn owls ranged from 0.05-0.2 mg/kg in liver.

3.8.2 Risk characterisation

According to the risk calculation the proposed normal use of difenacoum causes unacceptable risk for primary and secondary poisoning of non target vertebrates. However, the risk for primary poisoning is assumed to be negligible in the ESD if the rodenticide baits are used according to the label instructions. In the aquatic food chain (fish-eating birds and mammals) risk for secondary poisoning is considered insignificant. In the terrestrial food chain secondary poisoning is possible via contaminated soil invertebrates and rodents, and the latter animals are the most likely source or difenacoum residues in raptorial birds and mammalian predators. Not only the risk characterisation shows risk for secondary poisoning, but also the published laboratory studies confirm bioaccumulation of difenacoum in the owls. Bioaccumulation of difenacoum in predators has been shown in the measurements of difenacoum residues in the animal carcasses found from the field in United Kingdom. The target organ for difenacoum is liver and difenacoum residues in the carcasses have been measured from the liver. In one laboratory study highest residues were measured in the liver, and residues in other tissues including the wax tissue were low. Owls exposed to difenacoum showed variable effects from no foreseeable effects to death.

Other observed effects were increased coagulation times and haemorrhages. The effects disappeared gradually after the end of exposure. Population level effects of difenacom have not been studied.

In the laboratory studies, the owls fed entirely or mostly on poisoned rodents which may not be probable in the field conditions. The carcasses found from the field were diagnosed to have died to other reason than difenacoum and difenacoum residues were assumed to be sublethal. It is, however, possible that

sublethal difenacoum residues have contributed to the death of predators. Reproductive effects of difenacoum in avian or mammalian predators or scavengers have not been studied in the laboratory or in field experiments. Dose-related effects on the reproduction were observed in Japanese quail in the reproduction study. The NOEC of 0.31 mg/l drinking water and NOEL of 58 ¡,tglkg bw were determined in this study. The residues in the liver were not measured in the reproduction test, and hence the comparison to the monitoring data is difficult. The residue levels measured from dead bam owls ranged from 0.05-0.2 mg/kg in liver.

In conclusion difenacoum does not fulfil the environmental acceptance criteria due to bioaccumulation and unacceptable effects in the non-target vertebrates.

Atmosphere

Conclusion: Due to the physical-chemical properties of difenacoum, the release to air is considered to be negligible. Therefore no risk assessment is performed for the atmosphere.

Sewage treatment plant (STP)

Conclusion: This scenario is not considered of concern, because the product is not intended to be used in sewers or places next to water courses nor areasliable to flooding. In addition, the recommended bait station is a tamper resistant of category 1, which is resistant to tampering by children and dogs and weather-resistant. Hence the emission to the environment is really unlikely.

Aquatic compartment

Conclusion: Following ESD report for PT14 and taken in account that 'RATONEX LIQUIDO 26' is proposed for use in and around buildings, open areas or waste dumps; risk assessment is not required for the aquatic compartments because no product's release is foreseeable and any unfortunately release can be deemed not relevant.

Terrestrial compartment

Realistic worse case predicted soil concentrations (PECs) for difenacoum have been calculated for the use scenarios in and around buildings, open areas and waste dumps anticipating normal use. The resulting PEC/PNEC ratios for the soil are summarised in the Table below.

The calculated PEC/PNEC values indicate that there is no concern for the terrestrial compartment for these specific emission scenarios (Tier 1).

Calculated PEC/PNEC values					
Scenario /Tier		**PEC_{soil} (mg/kg)**	**$PNEC_{soil}$ (mg/kg)**	**$PEC/PNEC_{soil}$**	**Risk**
Scenario [1] - 'In and around buildings'		0.0243	0.877	0.03	No

Scenario [2] - 'Open areas'		0.18		0.2	No
Scenario [3] - 'Waste dumps'		0.000385		$4.4x10^{-4}$	No

Conclusion: For the authorised uses the exposure to soil estimated for the ESD worst case resulted in a PEC/PNEC ratio ≤1, indicating an acceptable risk to soil organisms.

As exposures estimated for the proposed use of 'RATONEX LIQUIDO 26" are below those calculated for the ESD worse case, the risk to soil organisms from the proposed use with 0.0026% formulation is acceptable.

Groundwater

Concentrations in soil pore water were calculated for the use of 'RATONEX LIQUIDO 26' in all proposed scenarios: in and around buildings, open areas and waste dumps. According to ESD and TGN the potential exposure to STP and surface water (and hence sediment) from the proposed use is considered to be negligible.

Exposure to groundwater for the proposed uses (realistic worst case, normal use) was derived from PECsoils and the new threshold value in groundwater for difenacoum of 0.01 µg/L was used for the risk assessment:

Calculated PEC/PNEC values for groundwater				
Scenario /Tier	**PEC_{gw} (mg/L)**	**Thresould value (mg/L)**	**$PEC_{gw}/PNEC_{gw}$**	**Risk**
Scenario [1] - 'In and around buildings' / Tier 1	$1.439X10^{-6}$	1 E-5	<1	No
Scenario [2] - 'Open areas' / Tier 1	$1.08x\ 10^{-5}$		>1	Yes
Scenario [3] - 'Waste dumps' / Tier 1	$1.89X10^{-8}$		<1	No

Conclusion: As can see in the table above, the risk is unacceptable for the "open are" scenario for the rest of scenarios evaluated, PECgw are well-below the maximum permissible according to the new threshold. Hence, as a tier 2, a FOCUS modelling was realized to refine the PEC groundwater for the "open areas" scenario.

Parameters use in FOCUS:

Model used	FOCUS PEARL
Years of simulation	1
Application rate	0.0009 kg/ha (open areas)

Standard crop for arable land	Maize (for agricultural soil) Grass (alfalfa)
Application depth	Incorporation 0 cm
Date of application	12 application per year
Molar mass	444.5 g.mol-1
Vapour pressure	$< 10^{-6}$ Pa at 20°C
Water solubility	1.7 mg.L-1 at 20°C
Kom	1048266.3 L.kg-1 at 20°C
Freundlich exponent	1
DT50soil	833 d at 12°C
Coefficient for uptake for plant	0

The same results obtained were obtained for all scenarios, see the following table:

LOCATION	MAIZE	ALFALFA
CHATEAUDUN	0.00000	0.00000
HAMBURG	0.00000	0.00000
JOKIOINEN	0.00000	0.00000
KREMSMUENSTE	0.00000	0.00000
OKEHAMPTON	0.00000	0.00000
PIACENZA	0.00000	0.00000
PORTO	0.00000	0.00000
SEVILLA	0.00000	0.00000
THIVA	0.00000	0.00000

According to the FOCUS modelling, the risk is acceptable in groundwater for the use of RATONEX LÍQUIDO 26 in all scenarios.

Primary and secondary poisoning

According to the risk calculations the proposed normal use of difenacoum causes unacceptable risk for primary and secondary poisoning of non-target vertebrates. However, the risk for primary poisoning is assumed to be negligible in the ESD if the rodenticide baits are used according to the label instructions and if security baits boxes are used (Category 1).

In the aquatic food chain (fish-eating birds and mammals), risk for secondary poisoning is considered insignificant.

In the terrestrial food chain, secondary poisoning is possible via contaminated soil invertebrates and

rodents, and the latter animals are the most likely source for difenacoum residues in raptorial birds and mammalian predators.

Not only the risk characterisation shows risk for secondary poisoning, but also the published laboratory studies confirm bioaccumulation of difenacoum in the owls. Bioaccumulation of difenacoum in predators has been shown in the measurements of difenacoum residues in the animal carcasses found from the field in United Kingdom. Owls exposed to difenacoum showed variable effects from no foreseeable effects to death. The effects disappeared gradually after the end of exposure. Population level effects of difenacoum have not been studied.

Theoretical calculations may overestimate the residues accumulating in predators. In the laboratory studies, the owls fed entirely or mostly on poisoned rodents which may not be probable in the field conditions. The carcasses found from the field were diagnosed to have died to other reason than difenacoum and difenacoum residues were assumed to be sublethal. It is, however, possible that sublethal difenacoum residues have contributed to the death of predators. Reproductive effects of difenacoum in avian or mammalian predators or scavengers have not been studied in the laboratory or in field experiments.

Mixture toxicity

No mixture toxicity is foreseeable, as the only substance of concern is Difenacoum.

Overall conclusion on the risk assessment for the environment of the product
Since the proposed use of ‘RATONEX LIQUIDO 26’ falls within the ‘risk envelope’ of the uses already evaluated and authorised. The proposed use of ‘RATONEX LIQUIDO 26’ is acceptable and may also be authorised for its use in and around buildings, in open areas and waste dumps.

3.9 Assessment of a combination of biocidal products

A use with other biocidal products is not intended.

3.10 Comparative assessment

As difenacoum is a Candidate for Substitution, a comparative assessment must be carried out as part of the evaluation process.

The Biocidal Products Committee of the European Chemicals Agency published its Opinion on Questions regarding the comparative assessment of anticoagulant rodenticides on 02 March 2017 (Document no. ECHA/BPC/145/2017).

The opinion states that:

- In the absence of anticoagulant rodenticides, the use of rodenticide biocidal products containing other active substances would lead to an inadequate chemical diversity to minimize the occurrence of resistance in the target harmful organisms. These products also show some significant practical or economical disadvantages for the relevant uses.
- There is insufficient scientific evidence to prove that non-chemical alternative methods of rodent control are sufficiently effective according to the criteria established in agreed Union guidance with a view to prohibit or restrict the authorised uses of anticoagulant rodenticides.

The Opinion forms the basis of the COMMISSION IMPLEMENTING DECISION (EU) 2017/1532 of 7 September 2017 addressing questions regarding the comparative assessment of anticoagulant rodenticides in accordance with Article 23(5) of Regulation (EU) No 528/2012 of the European Parliament and of the Council.

On the basis of this comparative assessment, the authorisation of rodenticide products containing difenacoum is justified.