Product Assessment Report

RAVIOX L

July 2013

Updated document (October 2014)

Amended sections: 1.5.2; 2.2.2; 2.6.1; 2.7.1; 2.9.1; 3; Annex 1: Summary of products characteristics

Internal registration/file no:	
Authorisation/Registration no:	ES/AA-2013-14-00100
Granting date/entry into force of authorisation/ registration:	26/07/2013
Expiry date of authorisation/ registration:	31 march 2015
Active ingredient:	Difenacoum
Product type:	14

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

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1 General information about the product application

1.1 Applicant

Company Name:	WILL KILL, S.A.
Address:	C/. 4 de noviembre, 6
City:	Palma de Mallorca
Postal Code:	07011
Country:	Spain
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1.1.1 Person authorised for communication on behalf of the applicant

Name:	Onofre Sureda Juan
Function:	Regulatory Affairs
Address:	C/. 4 de noviembre, 6
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1.2 Current authorisation holder[1]

Company Name:	WILL KILL, S.A.
Address:	C/. 4 de noviembre, 6
City:	Palma de Mallorca
Postal Code:	07011
Country:	Spain
Telephone:	971203013
Fax:	971759434
E-mail address:	laboratorio@willkill.com
Letter of appointment for the applicant to represent the authorisation holder provided (yes/no):	Yes

[1] Applies only to existing authorisations

1.3 Proposed authorisation holder

Company Name:	WILL KILL, S.A.
Address:	C/. 4 de noviembre, 6
City:	Palma de Mallorca
Postal Code:	07011
Country:	Spain
Telephone:	971203013
Fax:	971759434
E-mail address:	laboratorio@willkill.com
Letter of appointment for the applicant to represent the authorisation holder provided (yes/no):	Yes

1.4 Information about the product application

Application received:	9 april 2010
Application reported complete:	-
Type of application:	authorisation
Further information:	ES has RAVIOX L currently authorised under national legislation for use as a rodenticide (PT14). The current application is for PT14 use and that will be assessed and authorised under 98/8/EC.

1.5 Information about the biocidal product

1.5.1 General information

Trade name:	RAVIOX L
Manufacturer's development code number(s), if appropriate:	-
Product type:	14
Composition of the product (identity and content of active substance(s) and substances of concern; full composition see confidential annex):	Difenacoum
Formulation type:	Liquid
Ready to use product (yes/no):	yes
Is the product the very same (identity and content) to another product already authorised under the regime of directive 98/8/EC (yes/no); **If yes: authorisation/registration no. and product name:** **or**	No

Has the product the same identity and composition like the product evaluated in connection with the approval for listing of active substance(s) on to Annex I to directive 98/8/EC (yes/no):	No

1.5.2 Information on the intended use(s)

Overall use pattern (manner and area of use):	The product is intended for the control of rats and mice, by: • Trained professional use, indoors (inside private, public and farm buildings), in and around (private, public and farm buildings) and outdoors (waste dumps/landfill sites and open areas) • Non trained professional use, indoors and around (maximum: 0.5 m) farm buildings • Non professional use, indoors (only inside private houses and outbuildings) and around (maximum: 0.5 m) private building premises and private gardens.
Target organisms:	Brown rat (*Rattus norvegicus*) and house mouse (*Mus musculus*).
Category of users:	Trained and non trained professional users and non professional users
Directions for use including minimum and maximum application rates, application rates per time unit (e.g. number of treatments per day), typical size of application area:	Baits of 100 or 250 mL inside a bait station should be placed each 2 to 5 m.
Potential for release into the environment (yes/no):	Yes
Potential for contamination of food/feedingstuff (yes/no)	No
Proposed Label:	Please, see the authorisation
Use Restrictions:	Use within bait stations

1.5.3 Information on active substance(s)[2]

Active substance chemical name:	Difenacoum	3-(3-biphenyl-4-yl-1,2,3,4-tetrahydro-1-naphthyl)-4-hydroxycoumarin
CAS No:	56073-07-5	
EC No:	259-978-4	
Purity (minimum, g/kg or g/l):	≥ 960 g/kg	
Inclusion directive:	Directive 2008/81/EC	

[2] Please insert additional columns as necessary

Date of inclusion:	1 April 2010
Is the active substance equivalent to the active substance listed in Annex I to 98/8/EC (yes/no):	Yes
Manufacturer of active substance(s) used in the biocidal product:	Activa Srl. / Tezza
Company Name:	*Activa s.r.l./Tezza*
Address:	Via Tre Ponti
City:	Maria de Zevio
Postal Code:	37050 S
Country:	Italy
Telephone:	+39 0456069004
Fax:	+39 0456069118
E-mail address:	

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

The biocidal product does not contain any substance of concern according to the Technical Notes for Guidance on data requirements.

1.6 Documentation

1.6.1 Data submitted in relation to product application

The applicant has sent new data about the active substance. Regarding analytical methods, in order to support the product authorisation, the manufacture of the active substance (Activa S.r.l. as a member of the Activa/Pelgar Difenacoum and Brodifacoum Task Force) has sent studies on difenacoum regarding identity of impurities and additives concerning, validate analytical methods in water, in animal matrices and in sediments.

The applicant has not provided any ecotoxicological study with the biocidal product. The environmental risk assessment for RAVIOX L has been done using the Competent Authority Report on the active substance difenacoum supported by the Task Force Activa/Pelgar.

The biocidal product is a liquid ready to use and it does not contain any substances of concern according to the Technical Notes for Guidance on data requirements.

1.6.2 Access to documentation

The applicant has submitted a letter of access from Activa source (notifier and having on all the data included in the dossier for difenacoum presented by The Activa/Pelgar Brodifacoum e Difenacoum Task Force).

All substances data sheets are included in the dossier.

[3] Please insert additional columns as necessary

2 Summary of the product assessment

2.1 Identity related issues

The active substance was included in the Annex I of Directive 98/8/EC (Commission Directive 2008/81/EC of 28 July 2008). The letter of access is from Activa source.

Data on the active substance were required at the product authorization stage as stated in the AR about the active substance and were provided by Activa:

- Analytical data to prove the isomeric composition and impurity profile of the active substance

The assessment of the technical equivalence of the source of difenacoum from Activa versus the reference source of Pelgar used for annex I inclusion has been performed by France. The conclusion is that the source of Activa is technically equivalent to the source of Pelgar assessed for annex I inclusion.

Results of the assessment:

→ The method provided doesn't allow to identify and quantify separately the two diastereoisomers. Nevertheless FR CA considers that the provided data allow the determination of the isomeric composition.

→ The submitted data allow to determine the impurity profile.

The co-formulants are not substances of concern. The formulation includes bittering agent, preservative, flavouring, dye, adjuvants and solvent. Information on the full composition of the product and assessment are detailed in additional confidential annex of this document.

2.2 Classification, labelling and packaging

On basis of the submitted data and the Annex VI to Regulation No 1272/2008 on classification, labelling and packaging of dangerous substances, we suggest the following classification:

According to Directive 1999/45/EC:

Class of danger	No classification
R-phrases	Any risk phrase is considered necessary
S-phrases	S2: Keep out of the reach of children S13: Keep away from food, drink and animal feedingstuffs S37: Wear gloves S46: If swallowed, seek medical advice immediately and show this container or label

2.2.1 Harmonised classification and labelling of the biocidal product

Until 1 June 2015, mixtures shall be classified, labelled and packaged in accordance with Directive 1999/45/EC. Nevertheless, the biocidal product, according to Regulation 1272/2008, does not require classification and the Precautionary statements are:

GHS Pictograms		
Signal Word		
Classification	Hazard class and category: Hazard statement	

General precautionary statement	P102: Keep out of reach of children. P103: Read label before use.
Prevention precautionary statement	P280: Wear protective gloves/protective clothing/eye protection/face protection
Response precautionary statements	P301+P310: IF SWALLOWED: Immediately call a POISON CENTER or doctor/physician.
Storage precautionary statements	
Disposal precautionary statements	

2.2.2 Packaging of the biocidal product

For **non-professional users: 100 ml bottles.** RAVIOX L is sold as 100 mL bottle to be placed inside the bait station. In order to prevent spills and the exposure of the applicant, the bottle is sealed with a film under the top that only should be opened itself inside the roll-on dispenser (with a trough) placed inside the bait station. After use, all the pack is throw out.

For **non-trained professional users**: **100 ml bottles**. RAVIOX L is sold as 100 mL bottle to be placed inside the bait station. In order to prevent spills and the exposure of the applicant, the bottle is sealed with a film under the top that only should be opened itself inside the roll-on dispenser (with a trough) placed inside the bait station. After use, all the pack is throw out.

For **trained professional users: 250 ml bottles.** RAVIOX L is sold as 250 mL bottle to be placed inside the bait station. In order to prevent spills and the exposure of the applicant, the bottle is sealed with a film under the top that only should be opened itself inside the roll-on dispenser (with a trough) placed inside the bait station, when used outdoors. For indoor applications, the liquid will be poured directly from the bottle into a though inside the bait station.

The following picture shows the roll-on dispenser: [redacted]

2.3 Physico/chemical properties and analytical methods

No new studies have been submitted about the physical/chemical properties for the active substance (which have been copied from the assessment report on the active substance). Regarding analytical methods, in order to support the product authorisation, the manufacture of the active substance (Activa S.r.l. as a member of the Activa/Pelgar Difenacoum and Brodifacoum Task Force) has sent studies on difenacoum regarding identity of impurities and additives concerning, validate analytical methods in water, in animal matrices and in sediments.

2.3.1 Physico-chemical properties

Regarding the active substance, difenacoum, the table has not been filled in because a letter of access has been submitted. Regarding the biocidal product, these are the physico-chemical properties:

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

	Method	Purity/Specification	Results	Reference
Physical state and nature	Visual		Liquid	B3.1
Colour			Blue	B3.1
Odour				
Explosive properties	Directive 92/69/EC		Product is a liquid bait. Consideration of structure and physico-chemical properties does not suggest any explosive potential. Any component is considered explosive	B3.2
Oxidizing properties	Directive 92/69 EC		Any component is considered oxidizing	B3.3
Flash point			The flash point of a volatile material is the lowest temperature at which it can vaporize to form an ignitable mixture in air. "Flash point" refers to both flammable liquids and combustible liquids. The formulation is not considered a volatile material, flammable or combustible---	B3.4
Autoflammability			No evidence of flammability in use and consideration of chemical structure suggest no flammable properties. Given the nature and content of the formulants of the biocidal product it is not considered that the formulation itself should be classified as flammable. No data is thus requested.	B3.4
Other indications of flammability				
Acidity / Alkalinity	pH-meter CIPAC MT 75.3		5.38	B3.5
Relative density / bulk density	Density Meter		1.0161g/ml	B3.6
Storage stability -	CIPAC M.T 46.3	0.005%	Stable	B3.7
Effects of temperature				
Effects of light				
Reactivity towards container material				
Technical characteristics in dependence of the formulation type				
Compatibility with other products			Not relevant as the product is not intended for mixtures with any other products.	B3.9

	Method	Purity/Specification	Results	Reference
Surface tension			68,9 mN/m (without GLP)	B3.10
Viscosity	Viscometer		1.5 cps	B3.10
Particle size distribution				

2.3.2 Analytical methods

	Principle of method
Technical active substance as manufactured:	Difenacoum quantified in technical grade material by HPLC with u.v. detection at 254 nm using an internal standard.
Impurities in technical active substance:	Impurities in technical grade material quantified by HPLC with u.v. detection using either an internal or external standard.
Active substance in the formulation:	Difenacoum determination was made by Liquid Chromatography with Mass detector. The determination method is in the dilution of the sample with methanol at acidic pH and the subsequent injection in the liquid chromatograph. The method is described in the internal procedure AGQ PE-827.

Analytical methods for residues

Soil (principle of method and LOQ)	After extraction of the soil samples by chloroform acetone, concentrated extracts are purified with a Florisil –sodium sulphate column. Quantification is done by HPLC–DAD detector. The method has been acceptably validated for samples of soil containing difenacoum at levels of 0.016, 0.063 and 0.158 mg/Kg. LOQ is 0.0214 mg/Kg
Air (principle of method and LOQ)	Not relevant, due to the low vapour pressure of difenacoum
Water (principle of method and LOQ)	The test method for determination of difenacoum in drinking, ground and surface waters is based on extraction by dichloromethane. Quantification is done by LC-MS/MS (both SIM and SMR mode). LOQ is 0.05 µg/L for drinking water and groundwater and 0.5 µg/L for surface water.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Method of residue analysis for cucumber, wheat and lemon has been validated acceptably. The purified extracts are analysed for residues of difenacoum by LC-MS. LOQ is 0.01 mg/kg

Data on the active substance difenacoum were required at the product authorization stage as stated in the AR of the active substance and were provided by Activa:

- A validated method for the analysis of difenacoum in animal and human tissues,
- Validation data for the determination of residues of difenacoum in meat and oil-seed rape (food/feeding stuffs),
- Validation data for the determination of difenacoum in sediment.

Results of the assessment of the analytical methods provided by Activa on the active substance as required in the CAR:

- A validated method for the analysis of difenacoum in animal and human tissues

Results of the assessment: The method is validated and is acceptable.

- Validation data for the analytical method for determination of residues of difenacoum in meat and oil-seed rape (food/feeding stuffs)

Results of the assessment: The data provided were not validation data based on the analysis method already provided in the dossier, as requested. The submitted study report provided a new method with validation data. This new method is validated and is acceptable.

- Validation data for analytical method for determination of difenacoum in sediment (based on the analysis method for difenacoum in soil)

Results of the assessment: The data provided were not validation data based on the analysis method for difenacoum in soil, as requested. The submitted study report provided a new method with validation data. This new method is validated and is acceptable.

2.4 Risk assessment for Physico-chemical properties

The active substance Difenacoum is stable with the temperature. Difenacoum is not highly flammable, neither is oxidizing. The a.i. is not explosive.

The biocide RATONEX LIQUIDO, which is a liquid, is stable.

No hazardous risk is exposed for users and bystanders, with regard to the physical and chemical properties of this formulation. It is not recommended to be used with other products.

Its technical properties indicate that no particular problems are to be expected when it is handled, stored or applied as recommended.

2.5 Effectiveness against target organisms

2.5.1 Function

PT14: Rodenticide

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

RATONEX LIQUIDO is a liquid rodenticide ready-to-use bait containing 0.005% Difenacoum. The efficacy of the product was assessed against the proposed label claims.

Pest organisms to be controlled by RATONEX LIQUIDO are animals belonging to:

- Order: Rodents (I.1).
- Family: Murids (I.1.1).

Please find the specific species in the following table:

Codes*	Specific names*	Common English Terms*
I.1.1.1	*Rattus norvegicus*	Brown rats
I.1.1.3	*Mus musculus*	House mouse

*Application codes for encoding Rodenticides (PT14), edited the 16 January 2009 on website Ex-ECB.

2.5.3 Dose / mode of action / known limitations / resistance

2.5.3.1 Dose

Comprehensive laboratory and field data submitted for Annex I inclusion and evaluated in the CAR confirmed that difenacoum is an effective rodenticide for the control of mice and rats. In addition, the applicant submitted new data in the form of one trial report to verify the proposed label claims. The study is summarized in Table 2.5.3-1.

Table 2.5.3-1 Experimental data on the effectiveness of the biocidal product RATONEX LIQUIDO against the intended target organisms.

Test substance	Test organism (s)	Test system	Test conditions	Test results	References
RATONEX LIQUIDO containing 0.005% (w/w) difenacoum.	Brown rat *Rattus norvegicus* House mouse *Mus musculus*	Laboratory conditions Choice test/ 24 days 10 adult rodents for both species (5 males + 5 females)	TNG on Product Evaluation, Appendices to Chapter 7 Product Type 14. Efficacy Evaluation of Rodenticidal Biocidal Products.	The study shows that the percentage of ingested bait obtained for rats is 87.15% and the mortality rate for rats is 90% after 9-14 days from the first exposure. The percentage of ingested bait obtained for house mouse is 74.4 % and in the mortalitiy test the percentage of dead house mouse is 100% after 11-15 days from the first exposure.	[redacted]

In the study the effectiveness of RAVIOX L was determined following the guideline for laboratory studies outlined in the "TNG on Product Evaluation, Appendices to Chapter 7 Product Type 14, Efficacy Evaluation of Rodenticidal Biocidal Products".

The study was designed as a laboratory choice test and mortality test using 10 adult rodents (5 males and 5 females) of two different species, rats *(Rattus norvegicus)* and house mouse *(Mus musculus).*

During the study period, all animals were given daily the same amount of water and of rodenticide bait (about 40 ml for rats and 25ml for mice). Rodenticide intake was approximately 35 ml daily to mice of both sexes, and 15 ml to female rats and about 21 ml for male rats.

The averages consume (%) for rats for rodenticide bait and for alternative water were 87.15 % and 80.25% respectively, and the average consumption (%) for mice for rodenticide bait and for alternative water were 74.4% and 50.75% respectively.

This study demonstrates that the product RAVIOX L is a palatable and effective rodenticide bait to control brown rats (*Rattus norvegicus*) and house mouse *(Mus musculus)*. In the laboratory choice test, when rodenticide bait was offered as an alternative to laboratory diet, the percentage of ingested bait obtained was 87.15% for rats and 74.4% for mice, values exceeding 20% required by the guidance to demonstrate the efficacy of the product, and it was obtained a mortality rate of 90% for

rats after 9-14 days from the first exposure. Moreover, the mortality rate for house mouse was 100% after 11-15 days from the first exposure. These values are equal to or exceed 90%, so the product meets the criteria to be considered effective.

In conclusion, the study proves that RAVIOX L is palatable and effective against house mouse and brown rat according to the criteria given in TNsG on Product Evaluation.

2.5.3.2 Mode of action

RAVIOX L is an anticoagulant rodenticide that causes internal bleeding, killing slowly and avoiding rejection by other rodents.

The active substance difenacoum acts against both rats and mice, and this bait is specially formulated to attract rodents and eat it in preference to their usual food.

The mode of action is determined by the active substance difenacoum. Difenacoum is a second generantion anticoagulant which prevents blood clotting by inihibiting regeneration of the active form of vitamin K1.

The main site of its action is the liver, where several of the blood coagulation precursors undergo vitamin K dependent post translation processing before they are converted into the respective procoagulant zymogens. The specific point of action is thought to be the inhibition of K1 epoxide reductase. Difenacoum accumulates and is stored in the liver until broken down. The plasma prothrombin (pro-coagulant factor II) concentration provides a suitable guide to the severity of acute intoxication and to the effectiveness and required duration of the antidotal therapy (vitamin K1).

When an animal ingests a lethal dose, death occurs a few days after (due to time spent active clotting factors in blood before ingestion of the poison). This delay prevents the rejection of baits by the rodents population.

The effects are reversible with the administration of vitamin K1 antidote which stimulates regeneration of coagulation factors.

2.5.3.3 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.

Continued feeding anticoagulant baits may not be solely due to resistance, can also be caused by not eating enough bait or because of immigration. However, once these possibilities have been eliminated, the probability that the resistance is due to the continuous feeding activity is high.

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.

As described by the RMS in the Annex I dossier, difenacoum resistant brown rats are found in limited areas of Denmark, Germany and Great Britain. Monitoring of resistance occurs only in these countries and lack of information does not necessarily mean lack of resistance in the other countries. The incidence of resistance ranges from 2 to 84%. About 5-9-fold doses are needed to kill difenacoum resistant rats.

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 *Technical Monograph Anticoagulant Management Strategy for Pest.*

Measures to avoid the development of resistance in susceptible rodent populations are:

- Ensure that all baiting points are inspected weekly and old bait replaced where necessary.
- Undertake treatment according to the label until the infestation is completely cleared.
- On completion of the treatment remove all unused baits.
- Do not use anticoagulant rodenticides as permanent baits routinely. Use permanent baits only where there is a clear and identified risk of immigration or introduction or where protection is afforded to high-risk areas.
- Monitoring of rodent activity should be undertaken using visual survey, through the use of non-toxic placebo monitors or by other effective means.
- Record details of treatment.
- Where rodent activity persists due to problems other than resistance, use alternative baits or baiting strategy, extend the baits or baiting strategy, extend the baiting programme or apply alternative control techniques to eliminate the residual infestation.
- Ensure that complete elimination of the infestation is achieved.
- As appropriate during the rodenticide treatment apply effective pest management measures (remove alternative food sources, remove water sources, remove harbourage and proof susceptible areas against rodent access).

Treatment of rodent infestations containing resistant individuals:

- Where rodent infestations containing resistant individuals are identified, immediately use an alternative anticoagulant of higher potency. If in doubt, seek expert service on the local circumstances.
- Alternatively use an acute or sub-acute but non anticoagulant rodenticide.
- In both cases it is essentials that complete elimination of the rodent population is achieved. Where residual activity is identified apply intensive trapping to eliminate remaining rodents. Gassing or fumigation may be useful in specific situations.
- Apply thorough pest management procedures (environmental hygiene, proofing and exclusion).
- Do not use anticoagulant rodenticides as permanent baits as routine. Use permanent baits only where there is a clear and identified risk of immigration or introduction or where protection is afforded to high risk areas.
- Record details of treatment.

Application of area or block rodent control to eliminate resistance:

- Where individual infestations are found to be resistant or contain resistant individuals it is possible that the resistance extends further to neighbouring properties.
- Where there are indications that resistance may be more extensive than a single infestation, apply area or block control rodent programmes.
- The area under such management should extend at least to the boundaries of the area of known resistance and ideally beyond.
- The programmes must be effectively coordinated and should encompass the procedures identified above.

2.6 Exposure assessment

2.6.1 Description of the intended use(s)

The product is intended to be used by trained and non-trained professional users and non-professional users, for the control of rats and mice. Baits of 250 / 100 mL, respectively, inside a bait station should be placed each 2 to 5m, as follows:

- Professional:
  - Trained: Indoors (inside private, public and farm buildings), in and around (private, public and farm buildings) and outdoors (waste dumps/landfill sites and open areas).
  - Non-trained: Indoors and around (maximum: 0.5 m) farm buildings.
- Non-professional: Indoors (only inside private houses and outbuildings) and around (maximum: 0.5 m) private building premises and private gardens.

2.6.2 Assessment of exposure to humans and the environment

Regarding human exposure no studies have been submitted; therefore, the exposure assessment has been performed using the paper "HEEG opinion on a harmonised 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 agreed at TMII 2010.

For the environment, no new studies with the product have been presented. The estimated local environmental concentrations (C_{local}) have been calculated with the scenarios outlined in the 'Emission scenario document for biocides used as rodenticides' (Larsen, 2003, hereafter ESD) and TGD (Technical Guidance Document on Risk Assessment in support of Commission Directive 93/67/EEC on Risk Assessment for new notified substances, Commission Regulation (EC) No 1488/94) using default values.

For detailed calculations, please see sections 2.7.2 and 2.8, for human and environmental exposure, respectively.

2.7 Risk assessment for human health

2.7.1 Hazard potential

2.7.1.1 Toxicology of the active substance

The toxicology of the active substance was examined extensively according to standard requirements. The results of this toxicological assessment can be found in the CAR when the active substance difenacoum was included in the Annex I of the Directive 98/8/EC. The threshold limits and labelling regarding human health risks listed in Annex 4 "Toxicology and metabolism" must be taken into consideration.

2.7.1.2 Toxicology of the substance(s) of concern

The biocidal product does not contain any substances of concern according to the Technical Notes for Guidance on data requirements.

2.7.1.3 Toxicology of the biocidal product

The toxicology of the biocidal product RAVIOX L was examined appropriately according to standard requirements. The product was not a dummy product in the EU- review program for inclusion of the active substance in Annex I of Directive 98/8/EC. The basis for the health assessment of the biocidal product is laid out in Annex 5 "Toxicology – biocidal product".

Acute oral, dermal and inhalation toxicity, skin and eye irritation and skin sensitisation studies have not been provided on the biocidal product, which have been assessed by the ES CA. No studies are available to evaluate the dermal absorption.

Dermal absorption

Concerning dermal absorption, no study is submitted for RAVIOX L. Therefore, ES CA considers that due to the highly lipophilic nature of difenacoum (with a calculated log Kow of 7.62) and the relatively large size of the difenacoum molecule (with a molecular weight of 444.5), a default value of 10% should be considered for the risk assessment of RAVIOX L, according to the EU Technical Guidance Document (Table 3, Appendix IVA).

Acute toxicity

It is proposed that information about acute toxicity concerning the biocidal product may be derived from existing data on the active substance difenacoum and the co-formulants in order to minimise animal testing. This means that the assessment of the hazards of the preparation has been carried out by using the appropriate calculation method.

The active substance difenacoum was classified by the Rapporteur Member State, on the basis of review of the submitted data and read-across of data from warfarin. Specific concentration limits were established by the Technical Committee on Classification and Labelling but they have not already been accorded by the Committee for Risk Assessment of the European Chemicals Agency. However, the biocidal product contains 0.005% difenacoum and, according to those specific concentration limits, the classification would be harmful by inhalation, in contact with skin and if swallowed and assigned the symbol Xn and R-phrases R20/21/22 but, as the specific concentration limits have not already been accorded, they cannot be applied.

On the other hand, some of the co-formulants of the product are classified as dangerous substances, but they exist in such small concentration that none of them contribute to the classification of the product (according to the Directive 1999/45/EC).

The vapour pressure of the active substance difenacoum (P (45°C) < 0.05 mPa = < 5 x 10^{-5} Pa) and the formulation type justifies the no classification as harmful by inhalation.

For these reasons, the biocidal product does not require classification about acute toxicity and any phrase is considered necessary.

Skin and eye irritation

It is proposed that information about skin and eye irritation concerning the biocidal product may be derived from existing data on the active substance and the co-formulants in order to minimise animal testing. This means that the assessment of the hazards of the preparation has been carried out by using the appropriate calculation method. Four co-formulants are classified as irritating to eyes and assigned the symbol Xi and the R-phrase R36. The biocidal product contains ≤ 20 % of these irritating substances. One co-formulant are classified as irritating to skin and assigned the symbol Xi and the R-phrase 38. The biocidal product contains ≤ 20 % of this irritating substance. According to Directive 1999/45/EC, RAVIOX L does not trigger a particular classification.

Skin sensitisation

It is proposed that information about skin sensitisation concerning the biocidal product may be derived from existing data on the active substance and the co-formulants in order to minimise animal testing. This means that the assessment of the hazards of the preparation has been carried out by using the appropriate calculation method. The co-formulants are not considered sensitizer. On the other hand, according to the final CAR of difenacoum, the applicant submitted two sensitisation studies with a 2.5% liquid concentrate of difenacoum in solvents, one Magnusson & Kligman test and one Buehler test. These studies were negative; these mean that the active substance is not considered sensitizer and, for these reasons, the biocidal product does not require classification.

2.7.2 Exposure

Regarding human exposure no studies have been submitted; additionally we request special risk mitigation measures that could avoid any kind of exposure. Firstly, we always require the placing of the rodenticide bait inside a tamper-resistant bait station correctly labelled. Secondly, we ask to the applicant for additional risk mitigation measures for liquid rodenticides, consisting on sealed bottles of 100ml for non-professional and non trained professional users and of 250ml for trained professionals, which only will be opened when inserting the bottle into a roll-on dispenser within an additional small trough placed inside the bait station. Non-trained professionals and non professional users can only use the product indoors. Trained professionals can use it also outdoors.

Once agreed these risk mitigation measures with the applicant, we could have concluded that exposure is negligible, and thus that there is no risk for human health. Anyway, we have tried an estimation of human exposure, 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. No mixing task is required for this ready to-use-product, therefore, 3 ml/event could be considered as the worst case of leak form a well-designed roll-on to assess the dermal exposure to this product.

- the dermal absorption of the product is 10% by default.

- 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 could be considered similar to the one agreed for paste bait in prefilled cartridge. That is, 11 loadings during application and 3 cleaning events during post-application for trained professionals.

- the density of the product is the indicated by the applicant, 1.01161g/ml.

The most relevant routes of exposure are the following:

Exposure path	Industrial use	Professional use	General public	Via the environment
Inhalation	Not relevant	Not relevant	Not relevant	Not relevant
Dermal	Not relevant	Potentially significant	Potentially significant	Negligible
Oral	Not relevant	Negligible	Relevant	Negligible

Concerning dermal absorption, no study is submitted for this RAVIOX L. Therefore, ES CA considers that due to the highly lipophilic nature of difenacoum (with a calculated log Kow of 7.62) and the relatively large size of the difenacoum molecule (with a molecular weight of 444.5), a default value of 10% should be considered for the risk assessment of RAVIOX L, according to the EU Technical Guidance Document (Table 3, Appendix IVA).

2.7.2.1 Exposure of professional users

Trained professionals (Pest Control Operators)

Pest Control Operators are trained in the correct use of the liquid bait, i.e. placement, number of bait stations required based on the infestation rate area, the amount of liquid bait per bait station and safe handling procedures. They handle the product on a daily basis and they will be exposed during loading of bait stations, application of the bait and clean-up. The exposure will be via the dermal route, with the inhalation exposure being negligible, due to the fact that the product is a liquid and that difenacoum is non-volatile. Gloves are worn when loading bait stations and disposing of remaining bait and carcasses.

During use, professional pest control operators will be exposed through the loading of bait stations and application of the bait. Exposure will be via the dermal route and to the hands only. During disposal, professional pest control operators will be exposed through the disposal of old bait and carcasses. Exposure will be via the dermal route and to the hands only.

The following points have been taken into consideration for the assessment of the potential exposure of professional users of RAVIOX L:

1. RAVIOX L is supplied in sealed bottles of 250 ml for use 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 3 ml/event 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 worst-case, the total daily exposure frequency is assumed to be 14 manipulations, for the placing of the equivalent to 200g bait (maximum dose for rats) on 11 sites and the cleaning of 3 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, no study is submitted for this RAVIOX L. Therefore a default value of 10% will be considered.

6. Operator body weight is assumed to be 60 kg.

Dermal exposure

Based on extrapolation from the operator exposure study, exposure to difenacoum of trained professional operators applying RAVIOX L is estimated to be 3.55×10^{-7} mg/kg bw/day. However, if as a worst case it is considered that operators do not use the personal protective equipment, the total systemic dose to difenacoum is estimated as 3.55×10^{-6} mg/kg bw/day. The calculation is summarised in the table below.

Table 2.7.2.1-1: Exposure for pest control operators during placing and cleaning of RAVIOX L

Dermal exposure	
Active substance content	0.005 %
Dermal absorption	10 %

Bodyweight		60 kg
Loading	Amount of exposure to product during loading	3 ml/manipulation
	Nº of manipulations during loading	11
	Density	1.0161 g/ml
	Systemic dose (no gloves)	2.79 x 10^{-6} mg/kg bw/day
	Systemic dose (with gloves, 10% penetration)	2.79 x 10^{-7} mg/kg bw/day
Cleaning	Amount of exposure to product during cleaning	3 ml/manipulation
	Nº of manipulations during cleaning	3
	Density	1.0161 g/ml
	Systemic dose (no gloves)	7.62 x 10^{-7} mg/kg bw/day
	Systemic dose (with gloves, 10% penetration)	7.62 x 10^{-8} mg/kg bw/day
Total	**Systemic dose (no gloves)**	**3.55 x 10^{-6} mg/kg bw/day**
	Systemic dose (with gloves, 10% penetration)	**3.55 x 10^{-7} mg/kg bw/day**

Inhalation Exposure

Due to the physical nature of the product, and due to the fact that difenacoum is non-volatile, the inhalation exposure is not considered relevant. Moreover, the product is supplied in a sealed bottle, therefore no inhalation exposure is expected.

Oral Exposure

It is not likely that bait reaches the mouth of professionals if label instructions are followed and hands are washed after handling the bait. Therefore, oral exposure can be considered negligible.

Non Trained professionals

Dermal Exposure

As a worst-case total daily exposure frequency, it is assumed that the non-trained professionals place the equivalent of 200g bait per site on five bait sites and cleans three bait sites per day.

Table 2.7.2.1-2: Exposure for non-trained professionals during the placing and cleaning of RAVIOX L

Dermal exposure		
Active substance content		0.005%
Dermal absorption		10%
Bodyweight		60 kg
Loading	Amount of exposure to product during loading	3 ml
	Nº of manipulations during loading	5
	Density	1.0161 g/ml
	Systemic dose (no gloves)	1.27 x 10^{-6} mg/kg bw/day
	Systemic dose (with gloves, 10% penetration)	1.27 x 10^{-7} mg/kg bw/day
Cleaning	Amount of exposure to product during cleaning	3 ml
	Nº of manipulations during cleaning	3
	Density	1.0161 g/ml
	Systemic dose (no gloves)	7.62 x 10^{-7} mg/kg bw/day
	Systemic dose (with gloves, 10% penetration)	7.62 x 10^{-8} mg/kg bw/day
Total	**Systemic dose (no gloves)**	**2.03 x 10^{-6} mg/kg bw/day**
	Systemic dose (with gloves, 10% penetration)	**2.03 x 10^{-7} mg/kg bw/day**

Inhalation Exposure

Due to the physical nature of the product, and due to the fact that difenacoum is non-volatile, the inhalation exposure is not considered relevant. Moreover, the product is supplied in a sealed bottle, therefore no inhalation exposure is expected.

Oral Exposure

It is not likely that paste baits reach the mouth of professionals if label instructions are followed and hands are washed after handling the bait. Therefore, oral exposure can be considered negligible.

2.7.2.2 Exposure of non-professional users and the general public

Non Professional User

The potential exposure of non-professional users to RAVIOX L is assessed below. The following points have been taken into consideration:

1. RAVIOX L is supplied in sealed bottles of 100ml for use by non 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 3 ml/event 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 worst-case, the total daily exposure frequency is assumed to be 8 manipulations, for the placing of the equivalent to 200g bait (maximum dose for rats) on 5 sites and the cleaning of 3 bait sites.

4. Two scenario are proposed, the first scenario with no exposure during the application phase and the second scenario assuming that the bait stations would have to be loaded by the user.

5. Non-professional users are assumed **not** to wear protective gloves (or other protective clothing) when handling the products.

6. It is assumed that 100% of inhalation exposure is absorbed. Therefore a default value of 10% will be considered.

7. Body weight is assumed to be 60 kg.

Dermal exposure

Total systemic exposure to difenacoum of non-professional operators applying RAVIOX L is estimated at 2.03 x 10^{-6} mg/kg bw/day when the product is used to control rats and mice, or 7.62 x 10^{-7} mg/kg bw/day when there is exposure only during cleaning the bait. The calculations are summarised in the tables below.

The calculations are summarised in the tables below.

Table 2.7.2.2-1: Exposure for non-professionals during the cleaning of RAVIOX L

Dermal exposure	
Active substance content	0.005 %
Dermal absorption	10 %

Bodyweight		60 kg
Cleaning	Amount of exposure to product during loading	3 ml
	Nº of manipulations during cleaning	3
	Density	1.0161 g/ml
	Systemic dose (no gloves)	**7.62×10^{-7} mg/kg bw/day**

Table 2.7.2.2-2: Exposure for non-professionals during the placing and cleaning of RAVIOX L

Dermal exposure		
Active substance content		0.005 %
Dermal absorption		10 %
Bodyweight		60 kg
Loading	Amount of exposure to product during loading	3 ml
	Nº of manipulations during loading	5
	Density	1.0161 g/ml
	Systemic dose (no gloves)	1.27×10^{-6} mg/kg bw/day
Cleaning	Amount of exposure to product during cleaning	3
	Nº of manipulations during cleaning	3
	Density	1.0161 g/ml
	Systemic dose (no gloves)	7.62×10^{-7} mg/kg bw/day
Total	**Systemic dose (no gloves)**	**2.03×10^{-6} mg/kg bw/day**

Indirect exposure as a result of use of the active substance in biocidal product

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 man, i.e. children. They are hard plastic and are either locked or sealed shut to prevent access to the bait. If bait stations are not used, the bait point should be covered or protected in such a way to prevent access to the bait.

However, indirect exposure, especially of children may happen. Two different scenarios of secondary exposure are available, the 'handling of dead rodents' scenario and the 'transient mouthing of poison bait' scenario. The former is excluded from the risk assessment due to unrealistic assumptions. For the latter, either 5g (User Guidance) or 10 mg (TNsG) of the product (which given a density of 1.0161 g/ml, is equivalent to 4.92 and $9.8 \cdot 10^{-3}$ ml) is assumed to be swallowed by an infant per poisoning event. The following systemic dose of difenacoum is then either 2.5×10^{-2} mg/kg bw or 5.0×10^{-5} mg/kg bw, respectively:

Table 2.7.2.2-3: Indirect exposure as a result of use of RAVIOX L

Quantity ingested (g)	**% ai**	**Systemic Exposure (mg)**	**bw (kg)**	**Systemic Exposure (mg/kg bw)**
5	0.005%	2.5×10^{-1}	10	2.5×10^{-2}
0.01	0.005%	5×10^{-4}	10	5×10^{-5}

2.7.2.3 Exposure to residues in food

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

2.7.3 Risk Characterisation

2.7.3.1 Risk for Professional Users

Acute risks were not considered for professional users in view of the moderate to low dermal exposure, and the anticipated negligible inhalation and oral exposure. Instead, the risk assessment was restricted to the more relevant repeated exposure. Exposure assessment is based on measurements in simulated use conditions and on daily exposure frequencies according to a questionnaire answered by selected pest control companies in 15 EU countries. The calculations have been made using assumptions related to rat control and the estimates are considered to represent reasonable worst case scenarios.

Trained professionals

The exposure assessment for professional pest control operators under reasonable worst case assumptions (11 loadings and 3 clean-ups/day), yielded a potential dermal exposure leading to a systemic dose of 3.55×10^{-6} mg/kg/day for an unprotected operator during bait handling operations. Comparison to the LOAEL of 0.001 mg/kg/day (based on a teratogenicity test in rabbits) shows that the use of rodenticide baits containing 0.005% difenacoum causes a potential health risk for pest control operators not wearing appropriate PPE (gloves), as indicated by the resulting margin of exposure (MOE = 96, see Table 2.7.3.1-1).

Nevertheless, since pest control operators are supposed to wear protective gloves during pest control operations, a refined assessment is conducted. The resulting margin of exposure (MOE = 956, see Table 2.7.3.1-1) indicates that the use of rodenticide baits containing 0.005% difenacoum does not cause a risk for pest control operators if gloves are worn.

Non-trained professionals

Likewise, the exposure assessment for non-trained professionals (e.g., farmers) under reasonable worst case assumptions (five loadings and five clean-ups/day), yielded a potential dermal exposure leading to a systemic dose of 2.03×10^{-6} mg/kg/day for an unprotected person. Without PPE, the resulting margin of exposure (MOE = 167, see Table 2.7.3.1-1) indicates that use of rodenticide baits containing 0.005% difenacoum is at risk at the stated exposure frequency. A refined assessment was conducted since wearing of protective gloves is recommended in the instructions for use. The resulting margin of exposure (MOE = 1673, see Table 2.7.3.1-1) indicates a high protection level for non-trained professional users when gloves are worn.

Overall

The result of the risk assessment concerning use of difenacoum in RAVIOX L indicates that the acceptable exposure level is not exceeded for trained professionals (pest control operators) with gloves and for non-trained professionals using the product with or without gloves. Even then, use of protective gloves is recommended in all cases for hygiene reasons and always expected for professional users. Exposure during manufacture of the active substance and formulation of products is beyond the scope of BPD and therefore has not been addressed.

Table 2.7.3.1-1. MOE value and comparison of AEL to exposure to RAVIOX L of professional users

User / Workplace operation	PPE	Exposure path	Total systemic dose (mg/kg/d)	Repeated dose Toxicity			
				Systemic NOAEL (mg/kg bw/day)	Systemic AEL (mg/kg bw/day)	MOE	%AEL

Trained professional Placing of bait (11 manipulations) and clean-up (3 manipulations)	None	Dermal, hands	3.55×10^{-6}	0.00034	0.0000011	96	323
	Gloves	Dermal, hands	3.55×10^{-7}	0.00034	0.0000011	956	32
Non Trained professional Placing of bait (5 manipulations) and clean-up (3 manipulations)	None	Dermal, hands	2.03×10^{-6}	0.00034	0.0000011	167	185
	Gloves	Dermal, hands	2.03×10^{-7}	0.00034	0.0000011	1673	18

2.7.3.2 Risk for non-professional users and the general public

Non-professional users

RAVIOX L is supplied as bottles for use in refillable bait stations. Two scenarios for non-professional exposure have been assessed; the first assuming that the refillable bait stations would have to be loaded by the user, and the second taking into account only potential exposure from the cleaning task. As a worst-case, non professionals were assumed to load five bait points and to clean five bait points per day, and to wear no gloves. The estimated daily systemic dose, 2.03×10^{-6} and 7.62×10^{-7} mg/kg/day, respectively, results in a MOE value of 167 and 446, respectively. This shows that that there is no risk for non-professional users.

Table 2.7.3.1-2. MOE value and comparison of AEL to exposure to RAVIOX L of non-professionals

User / Workplace operation	PPE	Exposure path	Total systemic dose (mg/kg/d)	Repeated dose Toxicity			
				Systemic NOAEL (mg/kg bw/day)	Systemic AEL (mg/kg bw/day)	MOE	%AEL
Non professionals Placing of bait (5 manipulations) and clean-up (3 manipulations)	None	Dermal, hands	2.03×10^{-6}	0.00034	0.0000011	167	185
Non professionals Clean-up (3manipulations)	None	Dermal, hands	7.62×10^{-7}	0.00034	0.0000011	446	69

General public

As a potential secondary exposure route, associated with the use of difenacoum in rodenticide products, ingestion of bait by infants has been assessed. The potential exposure due to dermal contact with poisoned rodents is not included in the risk assessment, because the available scenarios are unrealistic. Secondary exposure is anticipated to be acute in nature. The estimated exposure for the scenario, 2.5×10^{-2} mg/kg/day or 5.0×10^{-5} mg/kg/day, depending on the default assumptions, results in MOE values of 0.01 or 6.8, respectively. Therefore, the secondary exposure scenario of accidental poisoning of infants is of concern.

2.7.3.3 Risk for consumers via residues

Based on the intended uses, no contamination of food or feeding stuff is foreseen. Therefore the risk for consumers via residues was not assessed.

2.8 Risk assessment for the environment

The environmental risk assessment is performed for RAVIOX L, which contain 0.005 % of the active substance difenacoum which equals 50 mg difenacoum/kg. The product it is proposed to be used in and around buildings, open areas and waste dumps. The risk characterisation is based on the product information from the applicant, the Technical Guidance Document II (TGD II, 2003) and the EUBEES 2 emission scenario document (ESD) for biocides used as rodenticides (Larsen, 2003). The risk characterisation is performed by comparing the predicted no effect concentration (PNEC), with the predicted environmental concentration (PEC). Values for PNEC and PEC have been derived through calculations presented in detail in documents IIA and IIB, respectively. Considering the different ingredients in the product, only the active ingredient difenacoum will cause risk for the environment, no studies have been submitted with the product and the risk characterisation is therefore only performed for difenacoum.

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 trough 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.

2.8.1 Fate and distribution in the environment

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 RAVIOX L is not expected to have impact on the route or rate of degradation of the active substance difenacoum in the environment. No additional studies involving the formulated product have been presented.

2.8.2 Effects on environmental organisms

RAVIOX L does not contain substances of concern apart of difenacoum. Therefore, the ecotoxicological effects can be derived from the effect studies conducted with the active substance.

2.8.2.1 Aquatic compartment (including water, sediment and STP)

Toxicity values from Assessment Report are presented below for organisms of three trophic levels.

Difenacoum is very toxic to fish, aquatic invertebrates and algae. Fish is the most sensitive species. The toxicity in fish is based on the inhibition of blood clotting, whereas mode of action in the invertebrates and algae is unknown. The $PNEC_{water}$ is 0.06 µg/l based on the LC_{50} for the rainbow trout.

$PNEC_{sediment}$ was calculated using the equilibrium partitioning method.

$PNEC_{sediment}$ $= K_{susp\text{-}water}/RHO_{susp} \times PNEC_{water} \times 1000$ (TGD, eq. 70)

$= 4.51 \times 10^{4}/1150 \times 6.4 \times 10^{-5} \times 1000$

$= 2.51$ mg/kg wet weight.

Because all test concentrations on the activated sludge respiration inhibition exceeded the water solubility of difenacoum, the water solubility of 0.48 mg/l will be used as the $PNEC_{STP}$.

2.8.2.2 Atmosphere

No adverse effects of the product RAVIOX L are expected via atmospheric exposure due to low vapour pressure of the active substance and to the mode of use of the product.

2.8.2.3 Terrestrial compartment

Only one experimental test result is available (acute toxicity to earthworms, with a LC_{50} >994 mg/kg), and $PNEC_{soil}$ was calculated = 994 mg/kg /1000 = 0.994 mg/kg dry weight (0.877 mg/kg wet weight).

The $PNEC_{soil}$ is also derived with the equilibrium partitioning method from the aquatic PNEC.

$PNEC_{soil}$ = $K_{soil\text{-}water}$ /RHO_{soil} x $PNEC_{water}$ x 1000 (TGD, eq. 72)

= $5.41x10^{4}/1700 * 6.4x10^{-5}$ x 1000

= 2.04 mg/kg wet weight.

Because the $PNEC_{soil}$ derived from the earthworm test is lower, it will be used for the risk characterization ($PNEC_{soil}$ = 0.877 mg/kg wet weight).

2.8.2.4 Non compartment specific effects relevant to the food chain

Due to poor quality of the reproduction test, the results from the dietary test (LC_{50} of 1.4 mg/kg food) will be used for the derivation of $PNEC_{oral\ for\ birds}$. The appropriate assessment factor according to the TGD is 3000. In order to transform the LC_{50} to LD_{50}, LC_{50} is multiplied with average food consumption (13.5 g) and divided by average body weight 71.3 g. The resulting LD_{50} is 0.3 mg/kg bw/d.

$PNEC_{oral\ for\ birds}$ = 1.4 mg/kg food/3000 = 0.5 µg/kg food

$PNEC_{oral\ for\ birds}$ = 0.3 mg/kg bw/d/3000 = 0.1 µg/kg bw/d

$PNEC_{oral\ for\ mammals}$ is derived from the NOAEL of 0.03 mg/kg bw/d origin from the 90-day subchronic test in rat. The NOAEL is transformed to NOEC (concentration in food) by multiplying with the conversion factor of 20 (TGD, Table 22). The appropriate assessment factor according to the TGD is 90.

$PNEC_{oral\ for\ mammals}$ = 0.6 mg/kg food/90 = 7 µg/kg food

$PNEC_{oral\ for\ mammals}$ = 0.03 mg/kg bw/d/90 = 0.3 µg/kg bw/d

2.8.2.5 Determination and summary of PNECs

Table 2.8.2.6: Summary of the difenacoum PNECs

Compartment		Test value	AF	PNEC
Aquatic	$PNEC_{water}$	LC_{50} = 0.064 mg/l	1000	0.064 µg/l
	$PNEC_{sediment}$	$PNEC_{water}$ in eq. 70 (TGD)		2.51 mg/kg wet weight
	$PNEC_{STP}$	water solubility = 0.48 mg/l		0.48 mg/l
Terrestrial	$PNEC_{soil}$	LC_{50} >994 mg/kg	1000	0.994 mg/kg dry weight 0.877 mg/kg wet weight
	$PNEC_{oral\ for\ birds}$	LC_{50} = 1.4 mg/kg food LD_{50} = 0.3 mg/kg bw/d	3000	0.5 µg/kg food eq. to 0.1 µg/kg bw/d
	$PNEC_{oral\ for\ mammals}$	NOEC = 0.6 mg/kg food NOAEL = 0.03 mg/kg bw/d	90	7 µg/kg food eq. to 0.3 µg/kg bw/d

2.8.3 Environmental exposure assessment

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 trough 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.

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

In accordance with the approach taken in the CAR, the PEC values in surface water, groundwater and sediment were taken into account only for the in and around buildings scenario.

The exposure to surface water, STP or sediment following the use of the product in and around building is considered to be negligible.

The PEC in groundwater is calculated as a direct function of the PEC in soil, and therefore full calculations for both soil and groundwater are presented in Section 2.8.3.3.

2.8.3.2 PEC in air

The quantity of difenacoum used is very low, the vapour pressure is very low (6.7×10^{-9} Pa 20°C; EU Endpoint List), the Henry's law constant is very low (1.75×10^{-6} Pa m^3/mol; EU Endpoint List) and difenacoum is rapidly degraded in air (DT_{50} ~2 hours; EU Endpoint List). The PEC of difenacoum in air is therefore considered to be negligible.

2.8.3.3 PEC in soil

In accordance with the approach taken in the CAR, the PEC in soil was calculated for the in and around buildings scenario. The PEC_{soil} values were calculated with reference to the guidance documents EUBEES 2 Emission Scenario Document (ESD) for biocides used as rodenticides (Larsen, 2003), and the Technical Guidance Document on Risk Assessment part II (TGD II).

$PEC_{groundwater}$ is also considered below (rather than in Section 2.8.3.1) as it is calculated directly from the PEC in soil. $PEC_{groundwater}$ was calculated according to equation 67 in TGD II, 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.

2.8.3.3.1 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.

Calculation of PEC in soil

In and around building emissions to soil in the area influenced by each bait station by direct release and the total emission per campaign by indirect release are summarized in the table 2.8.3.3.2-1.

Direct release;

In the ESD it is estimated that the total direct release to the environment is 1%, which gives a direct release of (10*250*5*0.01)/21= 6 g product/day averaged over 21 days (worst case).

In a typical campaign (normal use): Roughly the equivalent of 1.5 x 100% replenishments corresponding to a total direct release of 10 x 250 x 1.5 x 0.01 / 21 = 1.8 g product/day, averaged over 21 days (CEFIC 2002).

According to the ESD the terrestrial environment is exposed via direct release at application and indirect release from the target animals' excrement. According to the ESD the fraction of release ($F_{release}$) is 0.3 + (0.6*metabolised fraction). Using the same value for the metabolised fraction as was used in the CAR (71%), the $F_{release}$ calculated according to the ESD is therefore 0.3 + 0.6*0.71 = 0.3 + 0.43 = 0.73. Since the toxicity of possible metabolites is unknown they will be assumed to be of similar toxicity as difenacoum.

Local direct emission to soil of the active substance is calculated by considering the total amount of the product used, the fraction of active substance in product, the number of application sites and refilling times and the fraction of the product released directly to soil. This is calculated according to eq. 3 in the ESD;

$Clocal_{soil\text{-}D} = Elocal_{soil\text{-}D\text{-}campaign} * 1000 / (Area_{exposed\text{-}D} * Depth_{soil} * RHO_{soil} * N_{sites})$

Where;

$Elocal_{soil\text{-}D\text{-}campaign}$	= Weight of bait*as*N.stations*No.renewals*direct release rate
$Area_{exposed\text{-}D} * Depth_{soil}$	= 0.009 m^3 (0.09 m^2 x 0.1 m assumed by ESD)
RHO_{soil}	= 1700 kg m^{-3} (TGD II)
N_{sites}	= 10

Local direct emission to soil is calculated for ESD worst case and proposed use scenarios;

ESD worst case

$Clocal_{soil\text{-}D}$ = $Elocal_{soil\text{-}D\text{-}campaign} * 1000 / (Area_{exposed\text{-}D} * Depth_{soil} * RHO_{soil} * N_{sites})$
= (250 * 0.00005 * 10 * 5 * 0.01) * 1000 / (0.009 * 0.1 * 1700 * 10)
= 0.041 mg/kg

Proposed use, worst case

$Clocal_{soil\text{-}D}$ = $Elocal_{soil\text{-}D\text{-}campaign} * 1000 / (Area_{exposed\text{-}D} * Depth_{soil} * RHO_{soil} * N_{sites})$
= (200 * 0.00005 * 10 * 5 * 0.01) * 1000 / (0.009 * 0.1 * 1700 * 10)
= 0.032 mg/kg

Indirect release;

The local concentration in soil due to indirect release was calculated according to eq. 4 in the ESD. A calculation of the worst-case soil concentrations with the assumptions made above would then give;

$Clocal_{soil\text{-}ID}$ = $(Q_{prod}*Fc_{prod}*N_{sites}*N_{refill}*10^3*F_{release\text{-}ID,soil}*(1-F_{release\text{-}D,soil}))/(Area_{exposed\text{-}ID}*Depth_{soil}*RHO_{soil})$

ESD worst case

$Clocal_{soil\text{-}ID}$ = (250*0.00005*10*5*1000*0.73*0.99) / (550*0.1*1700)
= 0.0048 mg/kg

Proposed use, worst case

$Clocal_{soil\text{-}ID}$ = (200*0.00005*10*5*1000*0.73*0.99) / (550*0.1*1700)
= 0.0038 mg/kg

Total release;

The total local exposure to the soil around the bait stations is obtained by adding the contributions from direct and indirect release, as calculated above.

ESD worst case

$Clocal_{soil}$ = $Clocal_{soil\text{-}D}$ + $Clocal_{soil\text{-}ID}$
= 0.041 + 0.0048 mg/kg
= 0.046 mg/kg

Proposed use, worst case

$Clocal_{soil}$ = $Clocal_{soil\text{-}D}$ + $Clocal_{soil\text{-}ID}$
= 0.032 + 0.0038 mg/kg
= 0.036 mg/kg

Emissions to soil in the area influenced by each bait station by direct release, and the total emission per campaign by indirect release, can be calculated from the values above. These values, together with the calculations for $Clocal_{soil}$, which is equivalent to PEC_{soil}, are summarized in table 2.8.3.3.2-1.

Table 2.8.3.3.2-1: Summary of difenacoum emissions and concentrations in soil after the use in and around buildings

Scenario	**$Elocal_{soil}$ Direct release per bait station* (mg as/0.09 m^2)**	**$Elocal_{soil}$ Indirect release per campaign** (mg as/550 m^2)**	**PEC_{soil} = $Clocal_{soil}$ Total released (mg as/kg)**
ESD worst case	0.625	452	0.046
ESD normal use	0.19	136	0.014
Proposed use	0.500	362	0.036

* Emission by direct release from individual bait station

** Emission by indirect release per campaign

For risk assessment purposes the worst case PEC_{soil}, represented by the ESD worst-case scenario, is selected. Therefore;

PEC_{soil} = 0.046 mg difenacoum/kg soil

Calculation of PEC in groundwater

PEC groundwater was calculated according to equation 67 in TGD II, 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.

$PEClocal_{soil, porewater}$ = $PEClocal_{soil}$* RHO_{soil} / ($k_{soil-water}$*1000)
= 0.0458 * 1700 / (54090.74*1000)
= 1.439 x 10^{-6} mg/l

An average K_{oc} value of 1803018 ml/g (EU Endpoint List) was used in the calculations for derivation of $k_{soil-water}$. 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.

2.8.3.3.2 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.

Calculation of PEC in soil

Direct release;

Number of emission days per campaign is estimated to be 6 days during which the treatment is repeated twice. However, it is assumed that only the lower half of the hole and its surrounding environment is exposed.

$Clocal_{soil-D} = Elocal_{soil-D-campaign} * 1000 / (Area_{exposed-D} * Depth_{soil} * RHO_{soil})$

Where;

$Elocal_{soil-D-campaign}$ = Weight of bait*as*N.stations*No.renewals*direct release rate
$Area_{exposed-D} * Depth_{soil}$ = 0.009 m^3 (0.09 m^2 x 0.1 m assumed by ESD)
RHO_{soil} = 1700 kg m^{-3} (TGD II)

N_{sites} = 10

ESD worst case

The exposed soil area is assumed to be the lower half of the burrow wall surrounding an 8 cm diameter tunnel, with the mixing soil depth of 10 cm and up to 30 cm from the entrance hole. Thus the total soil volume is:

$Vsoil_{exposed}$ = 0.0085 m^3 (ESD page 31)

$Clocal_{soil\text{-}D}$ = $Elocal_{soil\text{-}D\text{-}campaign}$ * 1000 / ($Vsoil_{exposed}$ * RHO_{soil})
= (200 * 0.000005 * 1 * 2 * (0.05+0.2)) * 1000 / (0.0085/1700)
= 0.283 mg/kg

In this scenario according to ESD $PEClocal_{soil}$ = $Clocal_{soil\text{-}D}$ then,

$PEClocal_{soil}$ = 0.283 mg/kg

Calculation of PEC in groundwater

PEC groundwater was calculated according to equation 67 in TGD II, 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.

$PEClocal_{soil,\ porewater}$ = $PEClocal_{soil}$* RHO_{soil} / ($k_{soil\text{-}water}$*1000)
= 0.283* 1700/ (54090.74*1000)
= 8.89 x 10^{-6} mg/l

2.8.3.3.3 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.

Calculation of PEC in soil

Direct release;

See in/around buildings calculus.

$Clocal_{soil\text{-}D}$ = $Elocal_{soil\text{-}D\text{-}campaign}$ * 10^6 / ($Area_{exposed\text{-}D}$ * $Depth_{soil}$ * RHO_{soil})

Where;

$Elocal_{soil\text{-}D\text{-}campaign}$ = Q_{prod}*Fc_{prod}*N_{app}*10^3*$F_{release\text{-}ID,soil}$
$Area_{exposed\text{-}D}$ * $Depth_{soil}$ = 1000 m^3 (10,000 m^2 x 0.1 m assumed by ESD)
RHO_{soil} = 1700 kg m^{-3} (TGD II)
$F_{release\text{-}ID,soil}$ = 0.73 (See in/around building calculus)

Local direct emission to soil is calculated for ESD worst case and proposed use scenarios;

ESD worst and proposed cases

$Clocal_{soil\text{-}D}$ = $Elocal_{soil\text{-}D\text{-}campaign}$ * 1000 / ($Area_{exposed\text{-}D}$ * $Depth_{soil}$ * RHO_{soil})
= (40 * 0.00005 * 7 * 0.73) * 10^6 / (10000 * 0.1 * 1700)

= 0.006 mg/kg soil

In this scenario according to ESD $PEClocal_{soil}$ = $Clocal_{soil-D}$ and considering the worst case,

$PEClocal_{soil}$ = 0.006 mg/kg

Calculation of PEC in groundwater

PEC groundwater was calculated according to equation 67 in TGD II, 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.

$PEClocal_{soil, porewater}$ = $PEClocal_{soil}$* RHO_{soil} / ($k_{soil-water}$*1000)
= 0.006* 1700/ (54090.74*1000)
= 1.89×10^{-7} mg/l

2.8.3.4 Summary of calculated PEC values used for risk assessment purposes

The summary of calculated PEC values used for risk assessment purposes are presented in the table below:

Table 2.8.3.4: Summary of PEC values

Scenario of proposed use (ESD worst case)	PEC_{sw} (mg/l)	PEC_{stp} (mg/l)	PEC_{sed} (mg/kg)	PEC_{soil} (mg/kg)	PEC_{grw} (mg/l)
In/around buildings	Negligible	Negligible	Negligible	0.046	1.439×10^{-6}
Open areas	Negligible	Negligible	Negligible	0.283	8.89×10^{-6}
Waste dumps	Negligible	Negligible	Negligible	0.006	1.89×10^{-7}

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

The exposure of difenacoum via direct consumption of the bait, i.e. primary poisoning, or indirectly via consumption of living or dead rodents that have been exposed to the bait, i.e. secondary poisoning to non-target birds and mammals is quantified in section 2.8.4.4.

2.8.4 Risk characterisation for the environment

The risk assessment is performed for RAVIOX L, i.e. liquid bait which contain 0.005% of the active substance difenacoum which equals 50 mg difenacoum/kg. The product is intended to be used in and around buildings, open areas and waste dumps. The risk characterisation is based on the product information from the applicant, the Technical Guidance Document II (TGD II, 2003) and the EUBEES 2 emission scenario document (ESD) for biocides used as rodenticides (Larsen, 2003). The risk characterisation is performed by comparing the predicted environmental concentration (PEC), with the predicted no effect concentration (PNEC). Considering the different ingredients in the product, only the active ingredient difenacoum will cause risk for the environment, no studies have been submitted with the product and the risk characterisation is therefore only performed for difenacoum.

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 trough placed inside the bait station which prevent spillage in case of leaking.

2.8.4.1 Aquatic compartment (including sediment)

2.8.4.1.1 In and around buildings

Regarding the use of RAVIOX L as a rodenticidal product for the use in and around buildings, risk assessment is only performed for groundwater since this is the only water compartment that can be contaminated.

2.8.4.1.1.1 Ground water

Concentration in soil pore water was calculated both for the use of RAVIOX L around buildings, open areas and waste dumps in section 2.8.3.3.2 above. This was calculated according to equation 67 and 68 in the TGD II and must be regarded as a worst case scenario since pore water concentrations are assumed to be the same as the concentrations in groundwater, i.e. dilution is not taken into account. The maximum permissible concentration according to directive 80/778/EEC is 10^{-4} mg/l, which is not exceeded as shown by the calculation.

Predicted concentration = 1.439 x 10^{-6} mg/l

Permissible concentration = 1 x 10^{-4} mg/l

The comparison above indicates there is not a significant risk of groundwater contamination. However, the in and around buildings scenario is a true worst case scenario which describes the situation in very localised spots of soil, and no consideration is given to dilution when difenacoum migrates through soil layers.

2.8.4.1.2 Open areas

Regarding the Use of RAVIOX L as a rodenticidal product for the use in open areas, risk assessment is only performed for groundwater since this is the only water compartment that can be contaminated.

2.8.4.1.2.1 Ground water

Concentration in soil pore water was calculated both for the use of RAVIOX L in section 2.8.3.3.3 above. The maximum permissible concentration according to directive 80/778/EEC is 10^{-4} mg/l, which is not exceeded as shown by the calculation.

Predicted concentration = 8.89 x 10^{-6} mg/l

Permissible concentration = 1 x 10^{-4} mg/l

The comparison above indicates there is not a significant risk of groundwater contamination.

2.8.4.1.3 Waste dumps

Regarding the use of RAVIOX L as a rodenticidal product for the use in waste dumps, risk assessment is only performed for groundwater since this is the only water compartment that can be contaminated.

2.8.4.1.3.1 Ground water

Concentration in soil pore water was calculated both for the use of RAVIOX L in section 2.8.3.3.4 above. The maximum permissible concentration according to directive 80/778/EEC is 10^{-4} mg/l, which is not exceeded as shown by the calculation.

Predicted concentration = 1.89 x 10^{-7} mg/l

Permissible concentration = 1 x 10^{-4} mg/l

The comparison above indicates there is not a significant risk of groundwater contamination.

2.8.4.2 Atmosphere

Since difenacoum will be used only locally and since it has a low vapour pressure, as a range of 6.7 x 10^{-9} – 5.4 x 10^{-14} Pa, and low Henrys law constant the concentration of difenacoum in the atmosphere will be negligible. Therefore no risk assessment is performed for the atmosphere.

2.8.4.3 Terrestrial compartment

Difenacoum can contaminate soil from use of RAVIOX L in and around buildings, open areas and waste dumps. Therefore, the risk for soil organisms is assessed.

2.8.4.3.1 In and around buildings

Difenacoum contamination of soil around buildings will occur both from direct contamination when baits are deployed outdoors and from indirect contamination via dead bodies, urine and faeces from the target organisms. The worst case PEC_{soil} which is the sum of the direct and indirect contamination was determined to 0.046 mg /kg (section 2.8.3.3).

The PNEC was determined in the Assessment Report. $PNEC_{soil}$ = 0.877 mg/kg

The risk quotient for the ESD worst case scenario is PEC/PNEC = 0.046/0.877 = 0.052

$PEC/PNEC_{soil}$ = 0.052

This indicates that the risk for soil organisms when difenacoum is used around buildings is not unacceptable.

2.8.4.3.2 Open areas

The PEC local soil in open areas has been calculated in section 2.8.3.3.3 as 0.283 mg/kg.

The PNEC was determined in the Assessment Report. PNECsoil = 0.877 mg/kg

According to the available data from this study (see Assessment Report) the $PEC/PNEC_{soil}$ value will be:

PEC/PNEC = 0.283/0.877 = 0.32

$PEC/PNEC_{soil}$ = 0.32

This indicates that the risk for soil organisms when difenacoum is used in open areas is not unacceptable.

2.8.4.3.3 Waste dumps

In some instances, applications of rodenticides to refuse dumps take place. Mostly the use is limited to occasions of population outbreaks of rats. Often the rodenticides are deployed around the perimeter of the dump, more than in the disposal area itself. The worst case PEC_{soil} to 0.006 mg /kg (section 2.8.3.3.4).

The risk quotient for the ESD worst case scenario is PEC/PNEC = 0.006/0.877 = 0.0068.

$PEC/PNEC_{soil}$ = 0.0068

This indicates that the risk for soil organisms when difenacoum is used in waste dumps is not unacceptable.

2.8.4.3.4 Summary of risk assessment for the aquatic, terrestrial compartments and the atmosphere

When RAVIOX L containing difenacoum are used in and around buildings, open areas and waste dumps, the risk assessment shows that the risks for the atmosphere, organisms in surface waters and the soil compartment are not all inacceptable.

Table 2.8.3.4: Summary of PEC/PNEC values

	$PEC/PNEC_{sw}$	$PEC/PNEC_{stp}$	$PEC/PNEC_{sed}$	$PEC/PNEC_{soil}$	PEC_{grw} (mg/l)
In/around buildings	-	-	-	0.052	1.439×10^{-6}
Open areas	-	-	-	0.32	8.89×10^{-6}
Waste dumps	-	-	-	0.0068	1.89×10^{-7}

2.8.4.4 Non compartment specific exposure relevant to food chain (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 TGD II section 3.8.3.1 page 125. According to the calculations performed with the ESD and TGD II, the evaluated product with difenacoum will cause unacceptable risks both for primary and secondary poisoning.

It has been shown in numerous scientific reports (Newton *et al*., 1997; Fournier-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. Secondary poisoning could e.g. pose a threat to snakes, and this animal group may not be regarded as protected by tests on mammals.

The risk of difenacoum to non-target birds and mammals has been assessed according to the ESD and the TGD II. 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 in section 2.8.4.1 above 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 potentially is contaminated by difenacoum around buildings and the limited number of earthworms inhabiting this area.

It seems from monitoring data published on barn 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.

2.8.4.4.1 In and around buildings

2.8.4.4.1.1 Primary poisoning

Non-target animals such as wild and domestic animals may come in contact with baits if the bait is incompletely protected or if bait stations have been damaged. Also 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 may be subject to primary poisoning.

- ***Tier 1 assessment***

In the Tier 1 assessment of primary poisoning it is assumed that the whole day's food requirement is satisfied by consumption of baits, and therefore the concentration in food will be the same as the concentration of active substance in the bait, 50 mg/kg. This is then compared to the long-term PNECs for birds and mammals. The resulting PEC/PNEC ratios in table 2.8.4.4.4.1-1 reveal a high risk for both birds and mammals of long-term primary poisoning.

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.

Table 2.8.4.4.4.1-1: PEC/PNEC ratios for primary poisoning – Tier 1 assessment

	PEC (conc. in food, mg/kg)	PNEC (conc. in food)	PEC/PNEC
Long-term			
Birds	50	0.0005 mg/kg	100000
Mammals	50	0.00019 mg/kg	7142.85

- ***Tier 2 assessment***

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 meal 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 (FIR) 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. The results are presented in tables 2.8.4.4.4.1-2 and -3 below.

$$ETE = (FIR/BW)*C*AV*PT*PD \text{ (mg /kg bw*day)} \qquad \text{Eq. 19}$$

Table 2.8.4.4.4.1-2: ETE values calculated for acute exposure (ETE)

Non-target animal	Typical bodyweight (g)	Daily mean food intake (g dw/day)	Concentration of difenacoum in bait (mg/kg)	ETE (mg/kg bw)	
				Step 1	Step 2
Dog	10 000[a]	456[b]	50	2.28	1.64
Pig	80 000 [a]	600 [a]	50	0.38	0.27

Pig, young	25 000 [a]	600 [a]	50	1.20	0.86
Tree sparrow	22 [a]	7.6 [a]	50	17.27	12.44
Chaffinch	21.4 [a]	6.42 [a]	50	15.00	10.8
Wood pigeon	490 [a]	53.1 [a]	50	5.42	3.90
Pheasant	953 [a]	102.7 [a]	50	5.39	3.88

[a] According to table 3.1 in the ESD

[b] Calculated from log FIR=0.822 log BW-0.629 according to equation on page 50 ESD

Table 2.8.4.4.4.1-3: PEC values calculated for birds and mammals

Non-target animal	PEC_{oral} = ETE, concentration of difenacoum after one meal (mg/kg)		LD_{50} (mg/kg bw/d)	PEC_{oral} higher than LD_{50} (y/n)	
	Step 1	Step 2		Step 1	Step 2
Dog	2.28	1.64	1.8	y	n
Pig	0.38	0.27	1.8	n	n
Pig, young	1.20	0.86	1.8	n	n
Tree sparrow	17.27	12.44	56	n	n
Chaffinch	15.00	10.8	56	n	n
Wood pigeon	5.42	3.90	56	n	n
Pheasant	5.39	3.88	56	n	n

The ETE values calculated for acute exposure for the worst case (step 1) and realistic worst case (step 2) are compared to the LD_{50} values in the table 2.8.4.4.4.1-3. This comparison indicates that birds are not at risk for acute primary poisoning; while the situation for mammals is more uncertain. Dogs are at risk and pigs are very close to being at risk.

- ***Tier 2 assessment long term***

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 above in table 2.8.4.4.4.1-2. 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.

Calculations are performed according to equation 20 in the ESD;

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

The long-term PNEC values used for mammals and birds are those from rabbit and Japanese quail according to the calculations performed in section 2.8.2.4, and they are presented in table 2.8.4.4.4.1-4.

Table 2.8.4.4.4.1-4: PEC/PNEC ratios for primary poisoning - Tier 2 assessment long term

Non-target animal	PEC = EC, concentration of difenacoum after one day of elimination (mg/kg)	PNEC dose (mg/kg bw/day)	PEC/PNEC
Dog	1.15	0.0001	11500
Pig	0.19	0.0001	1900
Pig, young	0.60	0.0001	6000

Tree sparrow	8.71	0.0003	29033
Chaffinch	7.56	0.0003	25200
Wood pigeon	2.73	0.0003	9100
Pheasant	2.72	0.0003	9066

The result of the PEC/PNEC 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 animals 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.

2.8.4.4.1.2 Secondary poisoning

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 that there is less prey available in the winter season. It should also be 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, acute***

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 PEC_{oral} is then compared to the LC_{50} values presented in section 2.8.2.4 for a qualitative risk assessment in accordance with the decision from TM III-06. 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 worst 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 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;

$$ETE = (FIR/BW)*C*AV*PT*PD \text{ (mg /kg bw*day)} \qquad \text{Eq. 19}$$

This equation gives the concentration of difenacoum in the rat (PEC_{oral}) after a meal the first day. Considering the elimination rate and that the mean time to death is seven days the concentration in the rodents each day can be calculated by;

$$EC_n = \sum_{n=1}^{n-1} ETE * (1-El)_n \qquad \text{Eq } 21$$

Table 2.8.4.4.4.2-1: Residues in target animals at specific point in times and varying bait consumptions.

	Residues in target animal (mg/kg bw), with bait consumption in % of daily consumption (PD)		
	20%	**50%**	**100%**
Day 1 after the first meal	1.0	2.5	5.0
Day 2 before new meal	0.7	1.8	3.5
Day 5 after the last meal	2.8	6.9	13.9
Day 7 mean time to death	1.4	3.4	6.8

The concentrations of difenacoum in rats are at peak after consuming bait for 5 days; thereafter the concentrations in rodents are decreasing until day 7 due to excretion and metabolism of the rodenticide. The values from day 5 are used as PEC_{oral}. The effect data used for birds is the LD_{50} for Japanese quail of 56 mg/kg bw recalculated, using equation 77 in the TGD II and the conversion factor bw/dfi of 8 (domestic hen) from table 22 in the TGD II, which seems in good agreement with the actual food consumption noted in the study. The result is LC_{50} = 448 mg/kg food, which seems rather high. The effect data used for mammals is the LD_{50} for the rat of 1.8 mg/kg bw recalculated, using the conversion factor bw/dfi of 20 from table 22 in the TGD II, resulting in an LC_{50} = 36 mg/kg food.

Table 2.8.4.4.4.2-2: Calculated PECs and recalculated LC_{50} values for mammals and birds.

	PEC Expected concentration in rodent (mg/kg) caught on day 5 after meal			LC_{50} (mg/kg food)
	PD = 0.2	PD = 0.5	PD = 1	
Mammals	2.8	6.9	13.9	36
Birds	2.8	6.9	13.9	448

This qualitative assessment indicates that birds and mammals are likely to survive if they eat poisoned rats.

- ***Tier 1 assessment, long term***

To assess the risk of long-term secondary poisoning to birds and mammals, the PEC in rodents after 5 days is used and compared to the long-term $PNEC_{oral}$ for birds and mammals (table 2.8.4.4.4.2-3). For birds, the PNEC value from the reproduction test is used, and for mammals the PNEC value calculated from the 90 day test with rabbits (see section 2.8.2.4).

Table 2.8.4.4.4.2-3: PEC/PNEC ratios for secondary poisoning - Tier 1 assessment long term

	$PNEC_{oral}$ (conc. in food)	PEC_{oral} Difenacoum conc. in target rodent (mg/kg bw), ESD default values	PEC/PNEC
Birds	0.0005 mg/l	13.9	27800
Mammals	0.0003 mg/kg	13.9	46333

The PEC/PNEC ratios indicate very high risks for long-term secondary poisoning of birds and mammals by consumption of rodenticide poisoned rodents.

- ***Tier 2 assessment, long term***

For the Tier 2 assessment the average food intake for each species and the average weight of the species have been considered, and the values are taken from table 3.5 in the ESD. The amount of

active substance consumed by the non-target animal is 13.9 mg/kg bw for rodents caught on day 5 and 16.6 mg/kg bw for resistant rodents caught on day 14, also assuming that the non-target animals feed to 50% on the rodents, all in accordance with the ESD. By knowing the amount of active substance consumed by the non-target animal and the weight of the animal the PEC (concentration in non-target animal) after one day consumption of rodents can be calculated. The results are presented below in table 2.8.4.4.4.2-4.

Table 2.8.4.4.4.2-4: Concentrations in non-target animals (PEC) after one day consumption of rodents

Species	Body weight (g)	Daily mean food intake (g/day)	Normal susceptible rodents caught on day 5		Resistant rodents caught on day 14	
			amount a.i. consumed by non-target animal (mg)	Conc. in non-target animal (mg/kg)	amount a.i. consumed by non-target animal (mg)	Conc. in non-target animal (mg/kg)
Barn owl *(Tyto alba)*	294	72.9	0.51	1.7	0.61	2.1
Kestrel *(Falco tinnunculus)*	209	78.7	0.55	2.6	0.65	3.1
Little owl *(Athene noctua)*	164	46.4	0.32	2.0	0.39	2.3
Tawny owl *(Strix aluco)*	426	97.1	0.67	1.6	0.81	1.9
Fox *(Vulpes vulpes)*	5700	520.2	3.60	0.6	4.32	0.8
Polecat *(Mustela putorius)*	689	130.9	0.9	1.3	1.09	1.6
Stoat *(Mustela erminea)*	205	55.7	0.40	1.9	0.46	2.3
Weasel *(Mustela nivalis)*	63	24.7	0.17	2.7	0.21	3.3

The results of the PEC/PNEC calculations are presented in table 2.8.4.4.4.2-5, below. For birds the PNEC (dose) from the reproduction test is used, and for mammals the PNEC (dose) calculated from the 90 day rabbit test, as presented in section 2.8.2.4.

Table 2.8.4.4.4.2-5: Expected concentrations (PEC) in non-target animals after a single day of exposure and resulting PEC/PNEC ratios. PNEC values expressed as dose (mg/kg bw/day) are used in the calculations

Species	PEC day 5 (conc. in food, mg/kg bw)	PNEC (dose, mg/kg bw/day)	PEC/ PNEC (day 5)	PEC day 14 (conc. in food, mg/kg bw)	PNEC (dose, mg/kg bw/day)	PEC/ PNEC (day 14)
Barn owl *(Tyto alba)*	1.7	0.0001	17000	2.1	0.0001	1600
Kestrel *(Falco tinnunculus)*	2.6	0.0001	26000	3.1	0.0001	2400
Little owl *(Athene noctua)*	2.0	0.0001	20000	2.3	0.0001	1800
Tawny owl *(Strix aluco)*	1.6	0.0001	16000	1.9	0.0001	1500
Fox *(Vulpes vulpes)*	0.6	0.007	857	0.8	0.007	114
Polecat *(Mustela putorius)*	1.3	0.007	185	1.6	0.007	228
Stoat *(Mustela erminea)*	1.9	0.007	271	2.3	0.007	328
Weasel *(Mustela nivalis)*	2.7	0.007	385	3.3	0.007	471

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 3-6 orders of magnitude in order to bring down the risk for non-target animals to acceptable levels.

Conclusions based on monitoring data

It seems from monitoring data published on barn 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.

Monitoring data for Barn owls (Newton *et al*., 1997) provides a basis for calculations to determine what relevance the worst case calculations above, 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 ca 1% of the collected birds had died of rodenticide poisoning (table 2.8.4.4.4.2-6).

Table 2.8.4.4.4.2-6: Rodenticide residues in livers of Barn owls killed by rodenticides (from Newton *et al*., 1997)

Owl no.	Rodenticide	Rodenticide concentration (mg/kg liver)
1	Bromadiolone	0.13
2	Bromadiolone Brodifacoum Flocoumafen	0.05 0.002 0.003
3	Difenacoum	0.17
4	Bromadiolone	1.07
5	Brodifacoum	0.87
6	Bromadiolone Brodifacoum	1.72 0.07
7	Bromadiolone	0.33
8	Brodifacoum	0.42

For difenacoum, the 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.

2.8.4.4.2 Open areas

2.8.4.4.2.1 Primary poisoning

The bait may also attract other vertebrates. The situation in the open area and waste dumps scenarios is basically similar to what is mentioned for commensal rodents above regarding the risk of primary poisoning. See point 2.8.4.4.1.

2.8.4.4.2.2 Secondary poisoning

Secondary poisoning hazard may occur in the open area and waste dumps scenarios. Predators among mammals and birds may occur in the immediate vicinity of buildings or landfills. When moving around the rats may be caught by raptors and scavengers may find dead rats. See point 2.8.4.4.1.

2.8.4.4.3 Waste dumps

2.8.4.4.3.1 Primary poisoning

Concerning the risk of primary poisoning the situation is regarded similar to that described above for vole control in the open areas. See point 2.8.4.4.1.

2.8.4.4.3.2 Secondary poisoning

The secondary poisoning hazard applies to predators among mammals and birds and scavengers and thus the situation is comparable to that described for commensal rodents; however, there might be more predators around a landfill than in the open areas e.g. sea gulls, craws, etc. See point 2.8.4.4.1.

2.8.4.5 Discussion on risks of primary and secondary poisoning in comparison to monitoring data and proposal of risk mitigation measures

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 trough placed inside the bait station which prevent spillage in case of leaking. This dosing system avoids the primary poisoning for birds and non-target species that can be found in buildings and therefore, the EUBEES scenario used in the assessment can be considered a worst case.

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 rodenticidal 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 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. 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 difenacoum 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 µg/kg 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 barn 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.

2.8.4.6 PBT assessment

According to the PBT assessment in the TGD, criteria for substance to be persistent is fulfilled when halflife is >60 days in marine water or >40 days in freshwater or halflife is 180 days in marine sediment or 120 days in freshwater sediment. For being very persistent (vP) a halflife 60 days in marine or freshwater or 180 days in marine or freshwater sediment is required.

According to the TGD a substance is considered to fulfil the B criterion when measured BCF exceeds the value of 2000 and if BCF exceeds 5000 a substance is considered very bioacummulative (vB). If measured BCF values are not available, a substance is considered to potentially fulfil the B criterion if log Kow exceeds a value of 4.5.

A substance is considered to fulfil the T criterion if long-term NOEC for marine or freshwater organisms is less than 0.01 mg/l or long-term avian NOEC less than 30 mg/kg food (TGD). If no long-term data is available a substance is considered potentially toxic when the $L(E)C_{50}$ to aquatic organisms is less than 0.1 mg/l.

Difenacoum is not readily or inherently biodegradable and half-life in marine or freshwater sediment is expected to be more than 180 days or 120 days, respectively. Difenacoum is also hydrolytically stable. Difenacoum has a high potential for bioaccumulation based on the calculated log Kow = 6.2 and BCF = 35645. Based on both the ecotoxicological and toxicological data, difenacoum fulfils the T criterion.

Difenacoum is considered a potential PBT and vPvB substance. Nevertheless, difenacoum is not a candidate for a persistent organic pollutant (POP), as it does not have a potential for long-range atmospheric transport.

2.9 Measures to protect man, animals and the environment

2.9.1 Recommended method and precautions concerning handling, use, storage, transport or fire

Handling and use:

- Always read the label before use and follow the instructions provided.
- Avoid contact with eyes, skin and mouth. Avoid ingestion.
- Wear gloves for the handling and disposal of the product.
- Do not smoke eat or drink while handling this product.
- Wash hands after application and use of the product, and before eating, drinking or smoking
- Keep away from food, drink and animal feeding stuffs.
- Keep out of reach of pets.
- Use secured tamper-resistant bait stations and place them in inaccessible areas to prevent the access of children, non-target species and pets.
- Bait stations must always be correctly labelled.
- The liquid bait will be contained in sealed bottles of 100 ml for non-professional and non-trained professional users and of 250 ml for trained professionals, which only will be opened when inserting the bottle into a roll-on dispenser within an additional small trough placed inside the bait station.

- Dispose of residues in a suitable labelled container for subsequent management and disposal of as hazardous waste.

Storage:

- Store in the original container in dry, well-ventilated place
- Store original container tightly closed
- Keep away from sun radiation and all other heat sources
- Protect against frost
- Keep away from strong smelling stuff
- Keep/store out of reach of children and companion animals
- Keep/store away from food, drink and animal feedstuffs

Transport:

- The transport of the product will meet the legal requirements

Fire:

Suitable Extinguishing Media: Keep fire exposed containers cool by spraying with water if exposed to fire. Carbon dioxide (CO2), alcohol-resistant foam, dry powder, water spray, mist or foam.
Extinguishing media which must not be used for safety reasons: Avoid the use of water jets to prevent dispersion.
Special protective equipment for fire-fighters: In the event of fire, wear self-contained breathing apparatus, suitable gloves and boots
Residues: Dispose of residues to certified waste disposal operator for incineration and licensed waste disposal site.

2.9.2 Specific precautions and treatment in case of an accident

In general, for the product RAVIOX L, we propose the following conditions

Human health precautions

Poisoning may cause:

Bleeding diathesis, derivated from antiprothrombin efect – prolonged prothrombin time – that may became evident at minimum 24 – maximum 72 hours (A normal prothrombine time when the patient is admitted in the hospital, does not exclude the diagnosis)

First aid:

Move the person away from the contaminated zone
Remove contaminated or spattered clothing
Rinse the eyes with plenty of water for 15 minutes. Do not forget to remove the contact lenses
Wash off the skin with soap and plenty of water, without rubbing
If swallowed, do not make him/her vomit
Keep the patient warm and at rest
Check the breath. If necessary, give artificial respiration
If the person is unconscious, make him/her lay on his/her side, with the head at lower level than the rest of the body, bending the legs.
Take person to a hospital and show the label or packaging when possible

DO NOT LEAVE POISONED PERSON ALONE UNDER ANY CIRCUMSTANCE

Medical advice for doctors and sanitary staff

If less than 2 hours has passed from the intake, gastric emptying must be performed, and activated carbon dispensed (25 g)
Antidote: Vitamin K
Check the prothrombine time
Treat symptomatically

IN CASE OF ACCIDENT CONTACT THE POISON CENTER

Environmental precautions

Avoid uncontrolled disposal into the environment. The product must not penetrate the sewers, surface water, ground water and neighbouring areas. Any spillage should be collect with mechanical means, store it in tight containers and dispose of as hazardous waste according to local legislation.

2.9.3 Procedures, if any, for cleaning application equipment

No application equipment is needed.

2.9.4 Identity of relevant combustion products in case of fire.

2.9.5 Procedures for waste management of the biocidal product and its packaging for industry, professional users and the general public.

Dispose of empty packaging, remains of unused product and dead rodents as hazardous waste according to local legislation.

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

a) Difenacoum has a very low vapour pressure, and decomposes at around 220°C and therefore does not boil. Hence, the risk of release of the active ingredient to atmosphere is negligible. The formulated product is a solid paste bait, hence release of the product to air is extremely unlikely, and therefore not of concern.

b) The octanol-water partition coefficient of difenacoum is high, and hence it will remain in the product. The product is known not to inhibit activate sludge respiration, and the rapid partitioning to the solid phase and very low water solubility, would suggest that product exposure by use in sewer systems, would not result in contamination of water, but would contaminate the sludge.

   Directions for use of the product, requires users not to place bait points where water could become contaminated, so there will be no direct exposure to surface or drinking water.

   Indirect exposure by leaching is very unlikely, as the very low water solubility of the active ingredient, and its affinity for soil means that any release into an environmental aquatic compartment will result in rapid partitioning to the solid phase, usually soil.

c) In the event of spillage of product, this material should be collected for incineration.

2.9.7 Observations on undesirable or unintended side-effects, for example, on beneficial and other non-target organisms.

Toxic to mammalian and avian species, including domesticated animals, wildlife and humans.

2.9.8 Specify any repellents or poison control measures included in the preparations that are present to prevent action against non-target organisms.

The liquid baits are dyed blue to make them unattractive to wildlife.

Risk mitigation measures.

The labels shall include:

- Baits must be securely deposited in a way so as to minimise the risk of consumption by other animals or children. Where possible, baits should be secured so that they cannot be dragged away.
- Unless under the supervision of a pest control operator or other competent person, do not use anticoagulant rodenticides as permanent baits.
- Search for and remove dead rodents at frequent intervals during treatment, at least as often as when baits are checked and/or replenished.

For professional users:

- Packaging, uneaten baits, bait stations and dead rodents must be managed in accordance with current regulations through registered establishment or undertaking carrying out waste management operations.

For non professional users:

- Packaging, uneaten baits, bait stations and dead rodents must be deposited at collection points or points established by the local authority in accordance with their respective ordinances.

3 Proposal for decision

The assessment presented in this report has shown that the ready-to-use product, RAVIOX L, with the active substance difenacoum, at a level of 0.005% w/w, may be authorised for use as a rodenticide (product-type 14) for the control rats and mice by:

- Professional users:
  - Trained: Indoors (inside private, public and farm buildings), in and around (private, public and farm buildings) and outdoors (waste dumps and open areas)
  - Non trained: Indoors and around (maximum: 0.5 m) farm buildings

- Non professional users: Indoors (only inside private houses and outbuildings) and around (maximum: 0.5 m) private building premises and private gardens.

The product has been shown not to present a physical-chemical hazard to end users and does not classify as flammable, oxidising or explosive.

The product was shown to be efficacious against the intended target organisms (*Mus musculus, Rattus norvegicus* and *Rattus rattus*), in the proposed areas for use at the proposed dose rate.

Concerning the human health, an exposure and effects assessment for RAVIOX L has been carried out for professionals and non-professionals, based on the larger baiting quantities for rats. Both the MOE and AEL approaches for risk assessment indicate that there is a satisfactory margin between the predicted exposure and the NOAEL (LOAEL) as well as exposures below the threshold value for the AEL for all intended uses by trained professionals, non-trained professionals and non-professionals (with and without PPE). The product is deemed suitable for authorisation and appropriate personal protective equipment is advised.

However, secondary exposure from transient mouthing of the product exceeds the AEL reference value (1.13×10^{-6} mg/kg bw/day), both with the assumption of 0.01 g and 5 g of product ingested by

infants. This is of concern. There is no margin of safety using the existing data and models. There is no safe scenario for indirect exposure if estimated according to TNsG and User Guidance. Mitigation and protection measures such as the inclusion of bittering agents and the enclosure of product secured in sealed packs and tamper resistant bait stations are essential to reducing the risk of secondary exposure. Baits should not be placed where food, feeding stuffs or drinking water could be contaminated. Additionally, baits should be placed in areas inaccessible to children.

The risk for the environment for the use of RAVIOX L in and around buildings, in open areas and in waste dumps/landfill sites has been evaluated. The overall conclusion is that the uses applied for of RAVIOX L do not pose an unacceptable risk to the sewage treatment plant, soil, air, surface water, sediment, and groundwater compartments. However, an unacceptable risk is identified for the primary and secondary poisoning of non-target vertebrates, and specific risk mitigation measures on the use of the product are required to reduce the risk for the environment.

The measures include use of a specific dosing system consisting of sealed bottles with a roll-on dispenser, troughs to avoid any spillage in case of leaking, tamper resistant bait stations, collection of unconsumed baits after termination of the control campaign and collection of dead rodents during and after the control campaign at frequent intervals, proper disposal of dead rodents and unused baits, restriction of the use in open areas and waste dumps to trained professional users only.

Conditions of authorisation

It is concluded that the evaluation has shown that sufficient data have been provided to verify the outcome and conclusions, and permit authorisation of the product RAVIOX L according to the following restrictions:

- This authorisation of RAVIOX L is valid until 31 March 2015.
- The concentration of the active substance, difenacoum, in RAVIOX L shall not exceed 0.05 g/kg (0.005% w/w).
- Only ready-to-use RAVIOX L product is authorised.
- The product is authorised to be applied in tamper-resistant bait stations in and around buildings by non-professional, non-trained professional and trained professional users.
- The product is authorised to be used in tamper-resistant bait stations in open areas and waste dumps/landfill sites only by trained professional users.
- As a poison control measure, the authorisation requires that the product shall contain an aversive or bittering agent.
- The authorisation requires that the product be dyed with a colour to make them unattractive to wildlife, and birds in particular.
- The product is authorised only for use against rats (*Rattus norvegicus* or *Rattus rattus*) and mice (*Mus musculus*). Authorisation of this product does not allow use against non-target organisms.
- The size of the package placed on the market should be proportionate to the duration of the treatment. For non- professional use products placed on the market packaging restrictions are to be limited to a maximum size of 100 ml.
- The product must be used in tamper resistant bait stations and they must be placed in areas inaccessible to prevent the access of children, non-target species and pets.
- Bait stations should be correctly labelled to show that they contain rodenticides.
- Additionally, the liquid bait will be contained in sealed bottles of 100 ml for non-professional and non trained professional users and of 250 ml for trained professional users, which only will be opened when inserting the bottle into a roll-on dispenser within an additional small trough placed inside the bait station

- Difenacoum baits must not be placed where food, feeding stuffs or drinking water can become contaminated.
- Apply hygiene measures: do not eat, drink or smoke during the handling of the product and wash hands after use
- The product and the bottle labels have to mention “Do not open the bottle”.
- Baits must be securely deposited in a way so as to minimize the risk of consumption by other animals or children. Where possible, baits should be secured so that they cannot be dragged away.
- Search for and remove dead rodents at frequent intervals during treatment, at least as often as when baits are checked and/or replenished, to minimise the risk of consumption and poisoning to children, companion animals and other non-target animals.
- Dispose of dead rodents in compliance with local requirements.
- Remove all baits and bait stations after treatment and dispose of them in accordance with local requirements.
- In order to prevent resistance for non-target animals, do not use the product as permanent bait.
- Do not clean the bait stations with water between two applications.
- Do not throw the product on the ground, into a water course, into the sink or down the drain.

To avoid resistance and because of cross-resistances occurrence to rodenticides:

- Do not use the product as permanent bait.
- The treatment has to be alternated with other kinds of active substances.
- The use of anticoagulant rodenticides as permanent baits is not permitted.
- Integrated pest management (combination of chemical control, physical and hygienic measures) has to be taken into account.
- The level of efficacy have to be monitored (periodic check), and the case of reduced efficacy has to be investigated for possible evidence of resistance.

Further information is required:

The authorization holder has to report any observed suspected incidents of rodenticide poisoning of vertebrate wildlife, pets or some livestock to the Spanish Competent Authorities previously to the renovation of the authorisation. Data should be collected from veterinary clinics, NGOs of animal protection or citizen complaints.

Annex:

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

Annex 1: Summary of product characteristics

[redacted]

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(c) Manufacturer(s) of the active substance(s) (name(s) and address(es) including location of plant(s))[4]

Name of the active substance: Difenacoum

Manufacturer

Company Name:	Activa S.r.l				
Address:	Via Tree Ponti, 22				
City:	Maria de Zevio	Postal Code:	37050 S	Country:	Italy
Telephone:	+39 0456069004	Fax:	+39 0456069118	E-Mail:	

Intra-Community VAT number or, for non EU companies, company registration number:

Manufacturing site(s) (if different)

Company Name:	.				
Address:					
City:		Postal Code:		Country:	
Telephone:		Fax:		E-Mail:	

Intra-Community VAT number or, for non EU companies, company registration number:

(d) Formulator(s) of the biocidal product (name(s) and address(es) including location of plant(s))[4]

Formulator

Company Name:	Will Kill, S.A.				
Address:	C/. 4 de noviembre, 6				
City:	Palma de Mallorca	Postal Code:	07011	Country:	Spain
Telephone:	971 203013	Fax:	971 759434	E-Mail:	laboratorio@willkill.com

Intra-Community VAT number or, for non EU companies, company registration number:

Formulation site(s) (if different)

Company Name:					
Address:					
City:		Postal Code:		Country:	
Telephone:		Fax:		E-Mail:	

Intra-Community VAT number or, for non EU companies, company registration number:

4 All sites involved in the manufacturing process of each active substance and of the product must be listed.

Physical state and nature of the biocidal product:

(e) Type of formulation: Liquid

(f) Ready-to-use product: ☐no ☒ yes

Classification and labelling statements of the biocidal product:

(g) Product classification: No classification

(h) Risk and Safety Phrases:

a. Risk phrases: Any risk phrase is considered necessary

b. Safety phrases:

S2: Keep out of the reach of children
S13: Keep away from food, drink and animal feedingstuffs
S37: Wear gloves
S46: If swallowed, seek medical advice immediately and show this container or label

(i) Product classification according to GHS: The biocidal product does not require classification and precautionary statements are:

P102: Keep out of reach of children.
P103: Read label before use.
P280: Wear protective gloves
P301+P310: IF SWALLOWED: Immediately call a POISON CENTER or doctor/physician.

(j) Hazard statement according to GHS: any hazard statement is considered necessary

Intended uses and efficacy:

(k) PT: 14 (rodenticide)

(l) Target harmful organisms:

I.1. R*odentia*
I. 1.1 *Muridae Murids*
I.1.1.1. *Rattus norvegicus*
I.1.1.3. *Mus musculus*

(m) Development stage of target organisms:

II.1. Juveniles
II.2. Adults

(n) Function/mode of action:

III.2 long-term action
III.2.1 anticoagulant
III.2.1.1 ingestion toxin
III.2.1.1.1 ingestion by eating

(o) Field of use:

IV.1 indoor use
IV.2 outdoor use

(p) Application aim:

VII.1 Stored product protection
VII.2 Health protection
VII.3 Material protection

(q) User category:

V.1 non-professional / general public
V.2 non-trained professional

V.3 trained professional
(r) Application method[5]:
VI.2.1 in bait stations

(Repeat box as necessary)

Directions for use[6]:

(s) Manner and area of use[7]:

The product is an anticoagulant rodenticide / Vitamin K antagonists intended to control rats and mice by trained professionals (in and around buildings, open areas and waste dumps) and and non-trained professionals non-professional users (in and around buildings)

(t) Conditions of use[8]:

Baits of 100 or 250ml should be placed each 2 to 5 m.

The bait has to be placed in tamper resistant bait stations, correctly labelled.

(u) Instructions for safe use of the product:[9]

For non-professional and non-trained professionl users RAVIOX L is sold as 100 mL bottle to be placed inside the bait station. In order to prevent spills and the exposure of the applicant, the bottle is sealed with a film under the top that only should be opened itself inside the roll-on dispenser (with a trough) placed inside the bait station. After use, all the pack is throw out.

For trained professional users, RAVIOX L is sold as 250 mL bottle

Bait points have to be checked every 2-3 days during the first 14 days of treatment. Bait points should be removed, in a typical campaign, 6 weeks after initial placement

Do not use anticoagulant rodenticides as permanent baits. Alternate the use of difenacoum baits with other active substance baits, in order to avoid resistance.

Use tamper-resistant bait stations and place them in inaccessible areas to prevent the access non-target species, children and companion animals.

Collect dead rodent during all control operations to minimise the risk of consumption and poisoning to children, companion animals and other non-target animals.

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5 Indicate how the product will be applied (e.g. brush, spray, dipping, bait, etc). Where the product is to be used by more than one user category, indicate the application method(s) intended for each user category.

6 Provide in the following sections the information as it is proposed to appear on the product label or appropriate product literature.

7 Indicate information on the target organisms, the mode of action, the field of use, the application aim, the user category and the application method. All efficacy claims should be reflected.

8 Include the details of the directions for use. This should be expressed in terms of amount of product per unit area or a length of application (e.g. dip for 3 minutes). For aerosols and sprays a discharge rate should be included. If the product is a concentrate, indicate the dilution rate(s) here (e.g. *dilute 1 part of product with x parts of water*).

9 Where appropriate, indicate here the period of time needed for the biocidal effect, the interval to be observed between applications of the biocidal product or between application and the next use of the product treated, or the next access by man or animals to the area where the biocidal product has been used, including particulars concerning decontamination means and measures and duration of necessary ventilation of treated areas; particulars for adequate cleaning of equipment; particulars concerning precautionary measures during use, storage and transport (e.g. personal protective clothing and equipment, measures for protection against fire, covering of furniture, removal of food and feedingstuff and directions to prevent animals from being exposed).

For professional users: Remove all dead rodents after treatment and dispose of them in accordance with current regulations through registered establishment or undertaking carrying out waste management operations.

For non-professional users: Dead rodents must be deposited at collection points or points established by the local authority in accordance with their respective ordinances.

(v) Particulars of likely direct or indirect adverse effects and first aid instructions

Poisoning may cause:

- Bleeding diathesis, derivated from antiprothrombin efect – prolonged prothrombin time – that may became evident at minimum 24 – maximum 72 hours (A normal prothrombine time when the patient is admitted in the hospital, does not exclude the diagnosis)

First aid:

- Move the person away from the contaminated zone
- Remove contaminated or spattered clothing
- Rinse the eyes with plenty of water for 15 minutes. Do not forget remove the contact lenses
- Wash off the skin with soap and plenty of water, without rubbing
- If swallowed, do not make him/her vomit
- Keep the patient warm and at rest
- Check the breath. If necessary, give artificial respiration
- If the person is unconscious, make him/her lie on his/her side, with the head at lower level than the rest of the body, bending the legs.
- Take person to a hospital and show the label or packaging where possible

DO NOT LEAVE POISONED PERSON ALONE UNDER ANY CIRCUMSTANCE

Medical advice for doctors and sanitary staff

- If less than 2 hours has passed from the intake, gastric emptying must be performed, and activated carbon dispensed (25 g)
- Antidote: Vitamin K.
- Check the prothrombine time
- Treat symptomatically

IN CASE OF ACCIDENT CONTACT THE POISON CENTER

(w) Instructions for safe disposal of the product and its packaging

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

For professional users: Remove all packaging, uneaten baits and bait stations after treatment and dispose of them in accordance with current regulations through registered establishment or undertaking carrying out waste management operations.

For non professional users: Packaging, uneaten baits and bait stations must be deposited at collection points or points established by the local authority in accordance with their respective ordinances

(x) Conditions of storage and shelf-life of the product under normal conditions of storage

Store in the original container in dry, well-ventilated place

Store original container tightly closed

Keep away from sun radiation and all other heat sources

Protect against frost

Keep away from strong smelling stuff

Keep/store out of reach of children and companion animals

Keep/store away from food, drink and animal feedstuffs

The product is stable.

(y) Additional information:

Regarding the packaging of the product, the following types are proposed:

For non-professional users: 100 ml bottles. RAVIOX L is sold as 100 mL bottle to be placed inside the bait station. In order to prevent spills and the exposure of the applicant, the bottle is sealed with a film under the top that only should be opened itself inside the roll-on dispenser (with a trough) placed inside the bait station. After use, all the pack is throw out.

For non-trained professional users: 100 ml bottles . RAVIOX L is sold as 100 mL bottle to be placed inside the bait station. In order to prevent spills and the exposure of the applicant, the bottle is sealed with a film under the top that only should be opened itself inside the roll-on dispenser (with a trough) placed inside the bait station. After use, all the pack is throw out.

For trained professional users: 250 ml bottles. RAVIOX L is sold as 250 mL bottle to be placed inside the bait station. In order to prevent spills and the exposure of the applicant, the bottle is sealed with a film under the top that only should be opened itself inside the roll-on dispenser (with a trough) placed inside the bait station, when used outdoors. For indoor applications, the liquid will be poured directly from the bottle into a though inside the bait station.

Annex 2: List of studies reviewed

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

[redacted]

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

[redacted]

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

Annex 3: Analytical methods residues – active substance

Difenacoum

Data on the active substance difenacoum were required at the product authorization stage as stated in the AR of the active substance and were provided by Activa.

- Analytical data to prove the isomeric composition and impurity profile of the active substance,
- A validated method for the analysis of difenacoum in animal and human tissues,
- Validation data for the determination of residues of difenacoum in meat and oil-seed rape (food/feeding stuffs),
- Validation data for the determination of difenacoum in sediment.

France has evaluated them and concluded that they are acceptable.

Matrix, action levels, relevant residue and reference

matrix	limit	relevant residue	reference or comment
plant products	LOQ= 0.01mg/kg	Difenacoum	
food of animal origin	LOQ= 0.01mg/kg	Difenacoum	
soil	LOQ= 0.0214 µg/g	Difenacoum	
drinking water	LOQ 0.05µg/l	Difenacoum	
surface water	LOQ 0.5µg/l	Difenacoum	
air			Not relevant due to the low vapour pressure
body fluids / tissues	LOQ= 0.01mg/kg	Difenacoum	

Methods suitable for the determination of residues (monitoring methods)

Methods for products of plant origin

reference	matrix	LOQ (mg/kg)	principle	comment	owner
[redacted]	Oil-seed rape	LOQ is 0.01 mg/kg	LC-MS/MS	Method of residue analysis for cucumber, wheat and lemon has been validated acceptably. The purified extracts are analysed for residues of difenacoum by LC-MS	

Methods for foodstuffs of animal origin

reference	matrix	LOQ (mg/kg)	principle	comment	owner
[redacted]	Meat	LOQ is 0.01 mg/kg	LC-MS/MS		Activa / PelGar Brodifacoum and Difenacoum Task Force

Methods for soil

reference	LOQ (mg/kg)	principle	comment	owner
[redacted]	LOQ is 0.0214 mg/kg	HPLC – UV-VIS	After extraction of the soil samples by chloroform: acetone, concentrated extracts are purified with a Florisil-sodium sulphate column. Quantification is done by HPLC-DAD detector. The method has been acceptably validated for samples of soil containing difenacoum at levels of 0.016, 0.063 and 0.158 mg/kg.	Activa /Pelgar

Methods for drinking water and surface water

reference	matrix	LOQ (µg/l)	principle	comment	owner
[redacted]	water	LOQ is 0.05 µg/l for drinking water and groundwater and 0.5 µg/l for surface water.	HPLC – MS/MS	The test method for determination of difenacoum in drinking, ground and surface waters is based on extraction by dichloromethane. Quantification is done by LC-MS/MS (both SIM and SMR mode).	Activa / PelGar Brodifacoum and Difenacoum Task Force

Methods for air

reference	LOQ (µg/m3)	principle	comment	owner
			Not relevant, due to the low vapour pressure of difenacoum	

Methods for body fluids/tissue

reference	matrix	LOQ (mg/kg)	principle	comment	owner
[redacted]	Liver	LOQ is 0.01 mg/kg	LC-MS/MS		Activa / PelGar Brodifacoum and Difenacoum Task Force

* Some studies on the active substance difenacoum were required for the product authorization stage from the Task Force Activa/Pelgar. The French CA (FR) had to evaluate these studies as agreed during a PAMRFG: method for the analysis of difenacoum in animal and human tissues, analytical methods for determination of residues of difenacoum in meat and oil-seed rape (food/feeding stuffs) and in sediment (based on the analysis method for difenacoum in soil). These methods were validated and were acceptable

Annex 4: Toxicology and metabolism –active substance

Difenacoum

This information can be consulted in the Assessment Reports of the active substance Difenacoum

Annex 5: Toxicology – biocidal product

RATONEX LIQUIDO

General information

Formulation Type	Liquid
Active substance(s) (incl. content)	Difenacoum 0.005%
Category	

Acute toxicity, irritancy and skin sensitisation of the preparation (Annex IIIB, point 6.1, 6.2, 6.3)	
Rat LD50 oral (OECD 420)	It has not been provided*
Rat LD50 dermal (OECD 402)	It has not been provided*
Rat LC50 inhalation (OECD 403)	It has not been provided*
Skin irritation (OECD 404)	It has not been provided*
Eye irritation (OECD 405)	It has not been provided*
Skin sensitisation (OECD 429; LLNA)	It has not been provided*

***This means that the assessment of the hazards of the biocidal product has been carried out by using the appropriate calculation method (Directive 1999/45/EC)**
The vapour pressure of the active substance difenacoum (P (45°C) < 0.05 mPa = < 5 x 10–5 Pa) and the formulation type justifies the no classification as harmful by inhalation

Additional toxicological information (e.g. Annex IIIB, point 6.5, 6.7)	
Short-term toxicity studies	*
Toxicological data on active substance(s) (not tested with the preparation)	*
	*
Toxicological data on non-active substance(s) (not tested with the preparation)	*
	*
Further toxicological information	*

*** We do not have any additional toxicological information about biocidal product**

Classification and labelling proposed for the preparation with regard to toxicological properties (Annex IIIB, point 9)	
Directive 1999/45/EC	No classification Any risk phrase is considered necessary S2: Keep out of the reach of children S13: Keep away from food, drink and animal feedingstuffs S37: Wear gloves S46: If swallowed, seek medical advice immediately and show this container or label
Regulation 1272/2008/EC	P102: Keep out of reach of children. P103: Read label before use. P280: Wear protective gloves P301+P310: IF SWALLOWED: Immediately call a POISON CENTER or doctor/physician.

RATONEX LIQUIDO

Exposure assessment

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

Primary exposure of professionals

Component	CAS	Scenario	Actual Dermal Total [mg/day]	Actual Dermal Total [mg/kg/d]	Inhalation Exposure [mg/m³]	Model
Difenacoum	56073-07-5	Trained professional (without gloves)	2.13×10^{-4}	3.55×10^{-6}	Negligible	CEFIC study
Difenacoum	56073-07-5	Trained professional (gloves penetration factor: 10%)	2.13×10^{-5}	3.55×10^{-7}	Negligible	CEFIC study
Difenacoum	56073-07-5	Non-trained professional (without gloves)	1.22×10^{-4}	2.03×10^{-6}	Negligible	CEFIC study
Difenacoum	56073-07-5	Non-trained professional (gloves penetration factor: 10%)	1.22×10^{-5}	2.03×10^{-7}	Negligible	CEFIC study

Risk assessment

Component	CAS	Scenario	AEL [mg/kg/d]	%AEL	MOE
Difenacoum	56073-07-5	Trained professional loading and cleanig the bait (without gloves)	0.0000011	96	323
Difenacoum	56073-07-5	Trained professional loading and cleanig the bait (gloves penetration factor: 10%)	0.0000011	956	32
Difenacoum	56073-07-5	Non-trained professional loading and cleanig the bait (without gloves)	0.0000011	167	185
Difenacoum	56073-07-5	Non-trained professional loading and cleanig the bait (gloves penetration factor: 10%)	0.0000011	1673	18

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

RATONEX LIQUIDO

General information	
Formulation Type	Liquid
Active substance(s) (incl. content)	Difenacoum 0.005%
Category	
Authorisation number	

Difenacoum

Data base for exposure estimation	
according to	Appendix: Toxicology and metabolism – active substance/CAR

Exposure scenarios for intended uses (Annex IIIB, point 6.6)	
Primary exposure	Non-professional users
Secondary exposure, acute	Mouthing of poison bait - an exceptional scenario
Secondary exposure, chronic	None

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

Details for the exposure estimates:

Component	**CAS**	**Scenario**	**Actual Dermal Total [mg/day]**	**Actual Dermal Total [mg/kg/d]**	**Inhalation Exposure [mg/m³]**	**Model**
Difenacoum	56073-07-5	Non-professional loading and cleanig the bait (without gloves)	1.22×10^{-4}	2.03×10^{-6}	Negligible	CEFIC study
Difenacoum	56073-07-5	Non-trained professional cleaning the bait (without gloves)	4.57×10^{-5}	7.62×10^{-7}	Negligible	CEFIC study

Component	**CAS**	**Scenario**	**Oral Exposure (mg/kg bw)**	**Model**
Difenacoum	56073-07-5	Mouthing of poison bait - an exceptional scenario (5 g)	2.5×10^{-2}	User Guidance
Difenacoum	56073-07-5	Mouthing of poison bait - an exceptional scenario (10 mg)	5×10^{-5}	TNsG

Risk assessment

Component	**CAS**	**Scenario**	**AEL [mg/kg/d]**	**%AEL**	**MOE**
Difenacoum	56073-07-5	Non-professional loading and cleanig the bait (without gloves)	0.0000011	167	185

Difenacoum	56073-07-5	Non-trained professional cleaning the bait (without gloves)	0.0000011	446	69

Component	**CAS**	**Scenario**	**MOE**
Difenacoum	56073-07-5	Mouthing of poison bait - an exceptional scenario (5 g)	0.01
Difenacoum	56073-07-5	Mouthing of poison bait - an exceptional scenario (10 mg)	6.8

Difenacoum

Intended Use (critical application): Control of rodents (rats and mice).
Active substance(s): Difenacoum
Formulation of biocidal product: Liquid Bait
Place of treatment:

- Trained professional use, indoors (inside private, public and farm buildings), in and around (private, public and farm buildings) and outdoors (waste dumps and open areas)
- Non trained professional use, indoors and around (maximum: 0.5 m) farm buildings
- Non professional use, indoors (only inside private houses and outbuildings) and around (maximum: 0.5 m) private building premises and private gardens

No contamination is expected for food or feeding stuffs.

The intended use descriptions of the difenacoum-containing biocidal products for which authorisation is sought indicate that these uses are not relevant in terms of residues in food and feed. The product is to be used for for the control rodents (rats and mice). No further data are required concerning the residue behaviour.